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IN THIS ISSUE:

EDITORIAL

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Contents

Editorial

Articles

Review article

Viewpoint

Clinical correspondence

Letter

100 years ago in the *NZMJ*

Erratum

Summaries

The Firearms Review threatens to walk back gains in public safety

Jonty Morreau, Christopher Wakeman

Gun control is a pressing issue in Aotearoa New Zealand that has garnered the attention of policymakers and the general public. Given the physical and social harms that guns potentiate, healthcare workers in Aotearoa New Zealand have a critical role in analysing and advocating for evidence-based legislation to ensure low levels of gun-related harm. The current Coalition Government is undertaking a review of the *Arms Act*, which could lead to weakening of current gun legislation. We, as healthcare providers, advocate for an evidence-based approach in relation to gun laws in Aotearoa New Zealand.

Disparities in patient mortality following intensive care admission due to adult community-acquired sepsis in Aotearoa New Zealand, 2009–2019

Sharla McTavish, Alice Hyun Min Kim, Amanda Kvalsvig, June Atkinson, Colin McArthur, Michael G Baker

In Aotearoa, many people are still dying after being admitted for critical care due to community-acquired sepsis, both in hospital (16.3%) and following discharge (12.9%). The link between the risk of dying following intensive care unit admission due to community-acquired sepsis and a person's social and economic circumstances becomes pronounced in the first year after hospital discharge. These findings suggest we need to focus on preventing community-acquired sepsis, treating it quickly and ensuring all patients have a fair chance at a good recovery—not just while they're in the hospital, but in the longer term as well.

Clinical alert: arrival of terbinafine resistant Trichophyton indotineae in New Zealand

Wendy P McKinney, Matthew R Blakiston, Sally A Roberts, Arthur J Morris

Skin fungal infections (ring worm) are usually easy to treat. In recent years there has been a global spread of a dermatophyte that is often resistant to the most commonly used treatment (terbinafine). This organism, *Trichophton indotineae*, is now present in New Zealand. We alert those seeing patients with suspicious infections to get cultures and order full identification so patients can be managed appropriately.

The historical and projected prevalence of dysphagia in Aotearoa New Zealand

Philip Gunby, Josh McSkimming, Maggie-Lee Huckabee

Dysphagia is a swallowing disorder that is a potentially life-threatening condition, as it can result in pneumonia, malnutrition and dehydration. Dysphagia is associated with a wide range of neurological disorders, cancer, reflux disease and intellectual disabilities. We estimate that dysphagia affects 1.78% of the general population using information we know about how widespread these conditions are and how often they result in dysphagia. We can use this knowledge combined with official projections of New Zealand's future population to estimate how prevalent dysphagia will be in the future. We estimate that the prevalence of dysphagia in the general population and the large costs that will accrue from it will increase significantly in the future, because many of the risk factors that cause dysphagia are associated with increasing age, and New Zealand's population is ageing.

Hepatitis C virus seroprevalence in defined populations in New Zealand: data from a general practice–based screening programme

Ho Tuan Tiong, Arlo Upton, Angelle Lockie, Kirsty Moore, Catherine A M Stedman

This study looked at how common hepatitis C virus (HCV) is in New Zealand using real-world data from over 1,000 adults who visited general practitioner (GP) clinics across different regions. Only 1% of the participants had antibodies to HCV, which shows they were exposed to the virus, and just 0.2% had an active infection (indicated by a positive antigen test). These numbers are lower than what earlier international studies had estimated. The study also found that groups such as Māori, Pacific peoples and those living in poorer areas participated less often, suggesting that special approaches might be needed to ensure these groups are better screened for HCV in the future. Understanding these findings can help in planning resources and strategies to find undiagnosed cases in the country.

A descriptive observational study of B12 testing during pregnancy and infancy in New Zealand and suggested guidance for testing and treatment

Asher Henry, Natasha Heather, Campbell Kyle, Teresa Gudex, Dianne Webster, Callum Wilson

Severe B12 deficiency is harmful to infants and is usually caused by B12 deficiency in the mother during pregnancy. It is usually preventable with adequate B12 in the mother and infant's diet, and easy to treat if it is caught early. We found that B12 levels are frequently tested during pregnancy in Auckland/Northland, but much less often in infancy. Furthermore, when a pregnant woman was found to have very low B12 levels the prescribed treatment was often inadequate, and their at-risk infants were almost never tested themselves for B12 deficiency. Likewise, when an infant was found to be B12 deficient, they were often inadequately treated. The authors recommend a risk-based screening and treatment approach for B12 deficiency in pregnancy and infancy.

Consequences of COVID-19 protection measures on children's respiratory health in Aotearoa New Zealand

Claire O'Loughlin, Tali Uia, Cameron Grant, Kirsten Smiler, Marianna Churchward, Catherine Tu'akalau, Rochelle Ellison-Lupena, Mona Jeffreys

The aim of the paper was to explore the impact of COVID-19 protection measures on children's respiratory health. We examined trends in hospitalisation rates for respiratory infections among children in Aotearoa New Zealand from 2017/2018 to 2022/2023. Results showed that hospitalisation rates for respiratory illnesses were lower for all children in the years when COVID-19 protection measures were strictly enforced, followed by an increase in rates in subsequent years. There was an excess of hospitalisations for tamariki Māori and for Pacific children compared to non-Māori, non-Pacific children. Inequities in respiratory health that were present before the pandemic re-emerged rapidly following the removal of COVID-19 protection measures.

Attempt CPR—language matters inside our hospitals

Tammy Pegg, Alex Psirides, Niamh Berry-Kilgour, Jane Goodwin, Joshua Lakin, Kate Grundy

The science around cardiac arrest and CPR originated almost 70 years ago for a condition that does not commonly arise in our modern, safe hospitals. Our language is non-specific, and protocols merged with out-of-hospital, where this technique is an essential first aid measure bridging the victim to the arrival of specialist care. However, in hospitals, with staff and equipment at the bedside, this decades-old technique is largely redundant, and our approach needs a rethink.

“Front-load” your co-design—evidence in mental health supports it

Clive Bensemann, Karen O’Keeffe, Arana Pearson, Jacqueline Ryan, Karl Wairama, Wi Keelan

Often, involving patients, families and whānau in the design of healthcare solutions and projects, known as co-design, makes the mistake of bringing in people after key decisions about the project are made. These key decisions can include understanding of what the problem really is that the project is trying to address. We argue for “true” co-design where patients, families and whānau are involved right from the beginning, and show evidence from mental health, where true co-design has reduced rates of seclusion in mental health facilities. (Seclusion is where a person in need of care is placed in a room alone.)

Lead pencil: a case of intractable abdominal pain secondary to lead poisoning

Amy Van der Sluis, Kirsty Sutherland

Lead poisoning presentations are rising in New Zealand within populations using traditional Ayurvedic medicine to treat commonplace medical issues. It can cause a variety of symptoms that effect numerous body symptoms, making it difficult to diagnose. The blood film can analyse the shape and make-up of red blood cells as a tool to diagnose in acute cases, as lead levels in bloods take weeks to process at the lab. Treatment is achieved by helping to remove the lead from bodily systems by binding to medications or flushing it out where possible. Lead without treatment clears at a slow rate, so requires medical intervention to increase clearance to improve symptoms.

The Firearms Review threatens to walk back gains in public safety

Jonty Morreau, Christopher Wakeman

ABSTRACT

Gun control is a pressing issue in Aotearoa New Zealand that has garnered the attention of policymakers and the general public. Given the physical and social harms that guns potentiate, healthcare workers in Aotearoa New Zealand have a critical role in analysing and advocating for evidence-based legislation to ensure low levels of gun-related harm.

We reviewed the historical and contemporary circumstances that have created the societal and legislative landscape of gun culture in Aotearoa New Zealand. The current Coalition Government is undertaking a review of the *Arms Act*, which could lead to weakening of current gun legislation.

We, as healthcare providers, advocate for an evidence-based approach in relation to gun laws in Aotearoa New Zealand. Ongoing monitoring, evaluation and adaptation of gun control regulation is essential to ensure effectiveness and responsiveness to evolving challenges.

Gun control is a pressing issue in New Zealand that has garnered the attention of policymakers and the general public. The tragic mass shooting in Christchurch in March 2019, resulting in the loss of 51 lives and numerous injuries, underscored the devastating impact of gun violence in the country.[1] Given the physical and social harms that guns potentiate, healthcare workers in Aotearoa New Zealand have a critical role in analysing and advocating for evidence-based legislation to ensure low levels of gun-related harm.

Aotearoa New Zealand's approach to gun control has historically been comparatively relaxed. Although there have been regulations requiring gun owners to obtain licences and register their firearms, these have been somewhat less stringent than in other comparable countries like Australia and the United Kingdom (UK).[1] These regulatory settings have fostered a culture of gun ownership in Aotearoa New Zealand, with more than 1.2 million firearms in circulation among a population of just over 5 million people.[2] Gun ownership in Aotearoa New Zealand is 50% higher per capita than Australia (Aotearoa New Zealand 22.6/100 vs Australia 15/100 residents). There have been a number of attempts over the last 30 years to produce more stringent gun control legislation; ultimately, these all failed.[3]

Following the 1996 Port Arthur massacre, the Australian Government rapidly changed legislation on gun control that reduced the annual harm from firearms from 2.9/100,000 in 1996 to 0.88/100,000 in 2018. Following 1996, there were no further mass shootings for the next 22 years. This legislation change was also associated with accelerated declines in firearm deaths, particularly suicides. Total homicide rates followed the same pattern. Removing large numbers of rapid-firing firearms from civilians may be an effective way of reducing mass shootings, firearm homicides and firearm suicides.[4]

Likewise, following the Christchurch shooting, then Prime Minister Jacinda Ardern took decisive action to tighten gun laws swiftly, essentially introducing the broadly bipartisan recommendations of a select committee in 2017, recommendations that were predominately rejected by the then minister of police.[1,5] Legislation was enacted for a near-total ban on military-style semi-automatics (MSSA) weapons and high-capacity magazines, a buyback scheme was introduced to encourage gun owners to surrender their firearms for compensation and Te Tari Pūreke (Firearms Safety Authority), along with a Firearms Registry, was established. These measures garnered widespread public support as essential steps to prevent future tragedies.[1]

However, the issue of gun-related harm in Aotearoa New Zealand is complex and multifaceted, presenting several challenges that need addressing to ensure public safety. With a well-publicised *Arms Act* review being undertaken, it is important to note the nuances and complexities that must be taken into consideration when designing regulatory settings to reduce gun-related harm

in Aotearoa New Zealand. The evidence shows that countries that prioritise collective safety over individual gun rights have reduced rates of gun-related harm.[6,7] To strengthen gun control measures and prevent future tragedies, a comprehensive and evidence-based approach is necessary.

A key concern is the prevalence of illegal firearms, which constitute a significant portion of guns in circulation and are impossible to regulate effectively. A significant proportion of gun-related crime is committed by unlicenced gun owners.[8] The understanding of the scale of illegal firearms in Aotearoa New Zealand is poor, with broad estimates of their numbers and a lack of clarity in their origin.[4] This creates a challenging cohort of lethal weapons beyond the reach of the law that may potentially cause harm. Investigations have suggested that the majority of illegal guns are obtained through retail diversion, whereby guns are bought legally and on-sold on the unregulated market, as well as burglary of licenced gun-owners, and on grey weapons, where licence holders let licences lapse without disposing of their guns.[5,9] Further evidence is required to establish this information further. The introduction of a Firearms Registry allows the prospective registration of guns to improve visibility of legal and unlicenced guns in Aotearoa New Zealand, and this will result in targeted interventions to reduce access to unlicenced guns.

Enhancing gun licensing and registration requirements, closing loopholes facilitating illicit gun transactions and imposing stricter penalties for non-compliance could reduce the circulation of illegal firearms. Additionally, refining screening protocols for gun licence applicants and fostering collaboration among government agencies, healthcare providers and law enforcement are vital steps to prevent at-risk individuals from accessing firearms.

While enacting and enforcing evidence-based and efficient gun legislation is a critical component, it is only one element in reducing gun-related harm. Addressing underlying factors contributing to violence, such as poverty, inequality and social alienation, is also crucial. Gun-related harm disproportionately affects Māori, those of lower socio-economic demographics, those with mental health diagnoses and the young.[3,10] By tackling these root causes of violent crime and supporting vulnerable individuals, Aotearoa New Zealand can mitigate the despair and hopelessness that may result in harm.

While progress has been made in tightening gun control laws following the Christchurch shooting, concerns persist, and debates continue on the effectiveness. The *Arms Act* review, led by former gun advocate, now Associate Minister of Justice Nicole McKee, threatens to walk back a number of gun control mechanisms implemented to reduce gun-related harm. The claimed focus of ensuring safety of firearm users is critical but should not come at the cost of ensuring collective public safety. The suggested relaxation of legalisation of MSSA weapons only serves to increase the rates of gun crime and death, as evidenced by the United States of America's (USA) experience following the lapse of the Federal Assault Weapon Ban in 2004.[11]

The minister's challenge of the Firearms Registry may have more weight. Firearms registries are designed to improve visibility of legal and illegal firearms. However, there is little evidence showing a reduction in gun-related harm following the introduction of gun registries worldwide, and they may come at significant expense.

Hon Nicole McKee notes the failure of the Canadian gun registry at the turn of the century as evidence that a similar registry is destined to fail in Aotearoa New Zealand. However, the minister omits to express the reasons the Canadian system failed. Canada's vast rurality, coupled with the inadequacies of the registry's computing system at the time, led to inefficiencies and spiraling costs. Furthermore, the geographic position of Canada bordering the USA allowed a significant flow of illegal weapons, which formed a majority of guns in firearm-related homicides.[12] A much more aligned comparison to Aotearoa New Zealand's circumstance is Australia, where the government have recently announced their intention to introduce a federal gun registry, similar to Aotearoa New Zealand's current registry, to broad political and public support.

Hon Nicole McKee notes concerns with the potential privacy risks associated with stored information. Given the personal nature of the information, the Firearms Safety Authority must ensure its security. The Authority documents their robust principles to ensure the safety of this respected information, with privacy assured by state and independent contractors. In fact, since its induction, public trust in the Firearms Safety Authority has significantly increased.[13]

Additional concerns relate to cost of the registry. The documented cost released by the Firearms Safety Authority has a running cost of NZ$8.4 million annually.[13] This number is vastly

lower than the number purported by the current government, though it is still a significant sum. As registries worldwide remain relatively untested, it is critical that the introduction of a full registry is regularly assessed to demonstrate reduction in gun-related harm.

Gun control remains a critical issue in Aotearoa New Zealand that demands sustained attention and collaborative efforts to safeguard public safety. Vigilance, collaboration and evidence-based policymaking are crucial to navigate the complexities of gun control and prevent future tragedies from occurring. Any consideration of reintroduction of MSSA weapons cannot be supported by the medical community. By addressing illegal firearms, supporting measures enhancing mental health support and tackling underlying social issues, the country can progress towards a safer society for all citizens. Continued monitoring, evaluation and adaptation of gun control regulation is essential to ensure their effectiveness and responsiveness to evolving challenges.

COMPETING INTERESTS
Nil.

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Disparities in patient mortality following intensive care admission due to adult community-acquired sepsis in Aotearoa New Zealand, 2009–2019

Sharla McTavish, Alice Hyun Min Kim, Amanda Kvalsvig, June Atkinson, Colin McArthur, Michael G Baker

ABSTRACT

AIM: To characterise patient mortality risk following intensive care unit (ICU) admitted community-acquired sepsis (CAS) in Aotearoa New Zealand (Aotearoa), comparing in-hospital and post-discharge mortality and associated risk factors.

METHODS: We examined de-identified, linked ICU-admitted adult patient data from ICU sites in Aotearoa retrieved from the Australian and New Zealand Intensive Care Society's CORE adult patient database (ANZICS-CORE-APD) between 2009 and 2019. Patients were followed from ICU admission to death or 365 days post-hospital discharge alive, using descriptive, survival and regression analyses. The outcomes of interest were in-hospital mortality and post-discharge mortality during the first 365 days.

RESULTS: In-hospital mortality was 16.3%. Post-discharge mortality was 3.6% by 30 days after discharge, 9.1% by 180 days and 12.9% by 365 days. There was no significant difference in in-hospital mortality risk by ethnicity or New Zealand Index of Deprivation quintile of usual residence. By contrast, significant differences in post-discharge survival were observed by ethnicity, area deprivation quintile and presence of severe comorbidities, particularly for Māori usually resident in high-deprivation areas.

CONCLUSIONS: There was no evidence of associations between in-hospital mortality and ethnicity or socio-economic deprivation; however, these associations become marked post-discharge. Interventions should be implemented to support early identification and management of CAS and address health inequities following hospital discharge.

Sepsis, organ failure resulting from a dysfunctional response to infection,[1] is a common cause of ICU admission and in-hospital mortality in high-income countries. Due to improved sepsis screening, identification and treatment, in-hospital mortality due to sepsis is decreasing, although this is experienced differentially between patient populations.[2] Sepsis survival is associated with ongoing immune dysfunction, organ system impairment, hospital readmission and an increased risk of post-discharge mortality.[3–6] Disproportionately affecting older, immunocompromised, socio-economically and ethnically marginalised patient populations, sepsis-associated mortality is a substantial public health concern.

Aotearoa New Zealand has an ageing and multimorbid population, with significant health disparities existing between Māori, Pacific peoples and non-Māori, non-Pacific populations, and those living in areas with high socio-economic deprivation scores.[7,8] Exacerbated by the ongoing effects of colonisation, marginalisation and systemic violence, the life expectancy of Māori is substantially lower than that of non-Māori.[9,10] Patient populations of Māori ethnicity and those resident in areas with high socio-economic deprivation scores frequently have disparate rates of chronic disease, multimorbidity and hospitalisations compared to non-Māori populations and those resident in areas with the lowest socio-economic deprivation scores.[7,8] Increasing age, chronic comorbidities and multimorbidity are significant risk factors for sepsis-associated intensive care unit (ICU) admission and in-hospital mortality.[11]

Emerging research suggests ethnic and socio-economic deprivation disparities observed in chronic disease incidence may similarly translate into patient outcomes following sepsis-associated ICU admission in Aotearoa. A cohort study conducted over 5 years in the Waikato Region identified significant ethnic and age disparities in sepsis incidence and sepsis-associated mortality.[12] Similarly, a large, retrospectively designed, prospective cohort study characterising ethnic disparities in overall ICU admissions in

Aotearoa identified Māori as having an increased likelihood of ICU admission due to sepsis compared to non-Māori.[13]

There is a scarcity of research characterising adult ICU admission due to community-acquired sepsis (CAS) and the associated mortality risk, both in-hospital and following hospital discharge in Aotearoa. Therefore, we characterised patient outcomes following a CAS-associated ICU admission in Aotearoa between 2009 and 2019 by describing mortality and mortality risk associated with variables identifiable at hospital admission by admission status.

Materials and methods

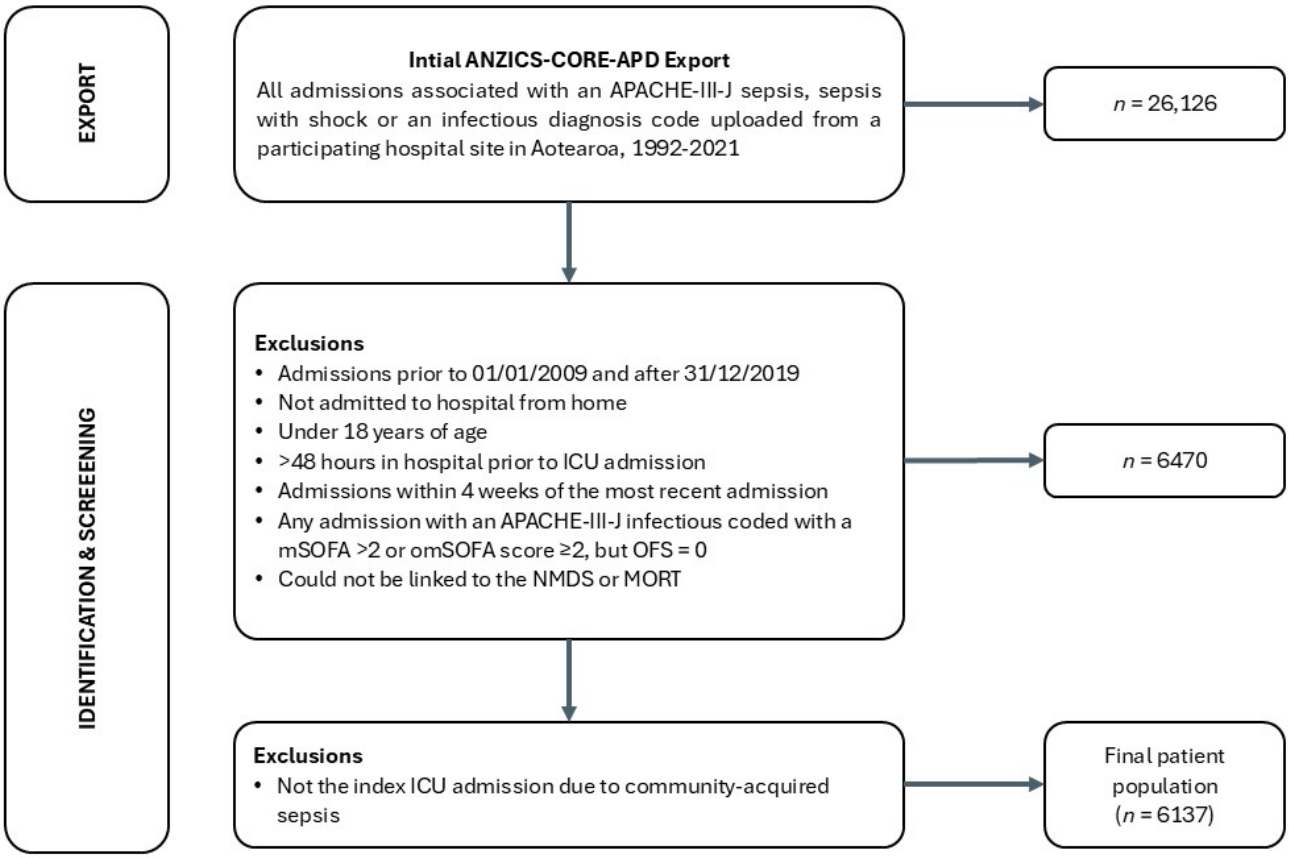
Study design and setting

We undertook a retrospective observational study using de-identified ICU admission data from hospital sites in Aotearoa between 2009 and 2019, retrieved from the Australian and New Zealand Intensive Care Society Centre for Outcome and Resource Evaluation Adult Patient Database (ANZICS-CORE-APD), deterministically linked to the National Minimum Dataset (NMDS) and the Mortality Collection (MORT) (Figure 1). Ethical approval for this study was obtained through the University of Otago Human Ethics Committee, reference ID HD20/075. Patient consent was not required as no patients were directly involved in the current study, and we used de-identified data. The ANZICS-CORE-APD is a binational, multicentre database with over 2 million ICU admissions, which has been previously described and contains admission data for most ICU sites in Aotearoa. The NMDS and MORT databases are collated and curated by Manatū Hauora (the New Zealand Ministry of Health) and contain hospital discharge codes and death data.

CAS definition and cohort identification

Sepsis was defined as explicit or implicit as per Sepsis-3.[1] Explicit sepsis was characterised by the presence of an APACHE-III-J sepsis or

Figure 1: Study population selection.



septic shock code (501, 502, 503 and 504). Implicit sepsis was characterised by the presence of an infectious APACHE-III-J code (Appendix Table 1), a modified sequential organ failure assessment (mSOFA) score >2 or an obstetrically modified SOFA[14] (omSOFA) score =2, and an organ failure score (OFS) ≥1. mSOFA and omSOFA scores were calculated based on clinical patient data (Appendix Table 2A and 2B), and OSF scores were attributed based on individual mSOFA or omSOFA organ system values. Cases with an mSOFA score of ≤2 or an omSOFA score of <2 were categorised as non-severe infections and excluded from the current study. Other exclusions included severe infection-associated admissions where an mSOFA or omSOFA score could not be calculated, admissions aged <18 years, hospital admission not from home, patients having spent >48 hours in-hospital before critical care admission and patients' subsequent events. Patients were followed from ICU admission until death or 365 days post-discharge alive. Hospital discharge was characterised as discharge from the hospital site in which the sepsis-associated ICU admission occurred.

Ethnicity and socio-economic deprivation classification

Ethnicity was defined using NMDS data and was grouped into prioritised ethnic groups: Māori, Pacific peoples, Asian and non-MPA (non-Māori, non-Pacific, non-Asian ethnicity). In 2018, this method of ethnic grouping divided the population of Aotearoa into Māori (16.5%), Pacific peoples (8.1%), Asian (15.1%) and non-MPA (European and Other; 72.9%).[15] Socio-economic status was categorised by the use of the New Zealand Index of Deprivation (NZDep),[16] a census-based small-area measure of socio-economic deprivation in Aotearoa. The NZDep is a previously validated measure of small-area socio-economic deprivation composed of eight variables (communication, income, employment, qualifications, home ownership, state support, living space and living conditions), and it is updated with each 5-year national census dataset.[16] Patients were categorised by the NZDep2018 quintile of their usual residence, NZDep Q1 (least deprived areas) to NZDep Q5 (most deprived areas).

Outcomes

The two outcomes of interest were CAS-associated in-hospital mortality and post-discharge mortality following a CAS-associated ICU-admission, censored at 365 days following discharge.

Outcome confounders

Variables evaluated in the current study included baseline population descriptors: age, sex, prioritised ethnicity, NZDep quintile, pre-existing severe comorbidities, severe multimorbidity defined using APACHE-III ("severe comorbidities") and prognostic factors identified through hospital discharge codes associated with the current sepsis-associated admission or previous hospitalisations, including substance use as identified by counselling for tobacco, hazardous alcohol use, obesity identified by counselling for obesity, hypertension, type-2 diabetes and blood or immune system deficiencies.

Statistical analyses

All statistical analyses were performed using STATA/SE 17.0 (StataCorp) and R 4.0 (R Statistical Foundation, Vienna, Austria). We calculated frequencies (*n*), percentages (%) and means (SD) as appropriate to characterise the cohort descriptively. Risk ratios (RR) and 95% confidence interval (CI) estimates for in-hospital mortality risk were computed using the quasi-Poisson distribution specification and robust variance estimation. Hazard ratios (HR) and CI estimates for post-discharge mortality were estimated using Cox proportional-hazard regression and the "survival" package 3.5.5 in R. Follow-up observations were censored if no death occurred within the pre-specified 365-day follow-up period from hospital discharge and the Efron approximation was applied to tied follow-up times. RR, HR and CI estimates were computed for univariable and multivariable models adjusted for 1) age and sex, and 2) age, sex, ethnicity, socio-economic deprivation and severe multimorbidity. A RR or HR >1.0 indicated an increased mortality risk for patients with that variable compared to patients without the variable. Kaplan–Meier curves were used to describe the survival probabilities over the follow-up period for the entire cohort, stratified by ethnicity. Cox proportional-hazard models fit post-discharge survival probabilities for the sepsis survivors identified as Māori and non-MPA, 60–79 years, usually resident in NZDep Q1 or NZDep Q5 areas, with no severe comorbidity, 1 severe comorbidity or ≥2 severe comorbidities. Two-sided tests were conducted with type I error set at 5%.

Results

From 1 January 2009–31 December 2019, 6,137 community-associated sepsis admissions were identified from 17 ICU sites across Aotearoa. The majority of the cohort was non-MPA (3,723/6,137, 60.7%), male (3,458/6,137, 56.3%), aged between 40 and 79 years (4,576/6,137, 74.6%) and usually resident in NZDep Q4 or NZDep Q5 areas (3,141/6,137, 51.2%). Most had no severe comorbidities (4,783/6,137, 77.9%). Table 1 shows prevalence differences in baseline demographics, pre-existing conditions, sepsis risk factors and clinical characteristics stratified by ethnicity.

A total of 1,663 deaths were observed after ICU admission, of which 60.2% occurred in-hospital (1,002/1,663) and 39.7% in the 365-day post-discharge follow-up (661/1,663). Table 2 reports patient mortality by admission status. Most patients surviving to hospital discharge were discharged home (4,216 /5,135, 82.1%) or to other healthcare facilities (600/5,135, 11.2%). Overall, mortality risk following CAS-associated ICU admission was 27.1%; in-hospital it was 16.3% (1,002/6,137), and in the 5,135 hospital survivors post-discharge it was (cumulatively) 3.6% by 30 days after discharge, 9.1% by 180 days and 12.9% by 1 year. Substantial differences in case fatality risk per 100 CAS ICU admissions were observed between patient populations, both in the hospital and during the follow-up period (Table 2). Post-discharge survival analyses showed marked differences in sepsis survival by ethnicity (Figure 2): survival was particularly low for Māori usually resident in NZDep Q5 areas with severe multimorbidity (Figure 3).

We identified mortality risk associated with variables observable at or within the first 48 hours of ICU admission, RRs for in-hospital mortality risk and HRs for post-discharge mortality risk (Table 2). Variables significantly associated with an increased mortality risk while in-hospital included older age, severe multimorbidity, previously identified hypertension and hazardous alcohol use, and the presence of septic shock or acute renal failure. Male sex was independently associated with a decrease of in-hospital mortality risk (Figure 4). There was no evidence that ethnicity and usual residence in NZDep Q5 areas were associated with an increased risk of in-hospital mortality (Figure 4). Comparatively, in the follow-up period, discharged patients of Māori ethnicity and those usually resident in NZDep Q5 areas had an increased mortality risk compared with non-MPA and those usually resident in NZDep Q1 areas (Figure 4). Pacific and Asian ethnicity was associated with a decreased mortality risk in the post-discharge period. Other variables independently associated with an increased mortality risk included older age, severe multimorbidity, residing in NZDep Q5 areas, previously identified hypertension and blood/immune deficiencies and acute renal failure. There was no evidence type 2 diabetes and tobacco use, although highly prevalent in the study population, were associated with in-hospital or post-discharge mortality.

Discussion

This current study is one of the few to compare mortality risk in a well-characterised population of ICU-admitted CAS and septic shock patients during their inpatient and post-discharge periods. In this study of more than 6,000 adult CAS-associated ICU admissions, we observed an in-hospital mortality rate of 16.0%. Among in-hospital survivors followed for up to 365 days, there was an additional post-discharge mortality rate of 12.9%, with a disproportionate mortality distribution over age, ethnic groups and NZDep score quintiles by admission status. Additionally, we identified a significantly inequitable spread of mortality risk among patient sub-populations, particularly after hospital discharge. The marked disparities identified in our analysis suggest the need to identify and implement interventions to reduce health inequities for patients after hospital discharge as a key part of improving outcomes for ICU-admitted CAS patients.

The in-hospital mortality found in our study is similar to the findings from previous studies in high-income countries.[2,12,17] Our results were also broadly in line with the findings of a recent meta-analysis. Fleischmann et al. (2016) estimated in-hospital severe sepsis mortality rate between 2003 and 2015 to be 18–33%, dependent on the sepsis definition followed.[2] Globally, few studies characterising post-discharge sepsis-associated mortality specifically differentiate between hospital-acquired sepsis and CAS. Consequently, post-discharge mortality at 365 days for all sepsis admissions varies markedly, up to 45% in recent studies, depending on the country and patient population.[18–23] In Aotearoa, only one study characterised sepsis-related deaths in the post-discharge period, identifying a mortality risk of 37.7% at 365 days; however, the results of the current study could not be directly compared as it measured death

Table 1: Demographic characteristics, pre-existing conditions, sepsis risk factors and clinical severity by ethnicity.

Variables	Total cohort[a] (n=6,137)	Ethnicity[a]				p-value[b]
		Māori (n=1,467)	Pacific (n=656)	Asian (n=291)	Non-MPA (n=3,723)	
Sex						
Male	3,458 (56.3)	782 (53.3)	344 (52.4)	146 (50.2)	2,186 (58.7)	<0.001
Female	2,679 (43.7)	685 (46.7)	312 (47.6)	145 (49.8)	1,537 (41.3)	
Age						
Age, years	60.5 (±17.0)	54.8 (±16.0)	53.3 (±16.5)	54.1 (±17.6)	64.5 (±16.3)	<0.001
Age group						
<40 years	868 (14.1)	284 (19.4)	160 (24.4)	74 (25.4)	350 (9.4)	<0.001
40–59 years	1,803 (29.4)	567 (38.7)	240 (36.6)	90 (30.9)	906 (24.3)	
60–79 years	2,773 (45.2)	565 (38.5)	234 (35.7)	112 (38.5)	1,862 (50.0)	
≥80 years	693 (11.3)	51 (3.5)	22 (3.4)	15 (5.2)	605 (16.3)	
Socio-economic deprivation						
NZDep Q1 (lowest)	792 (12.9)	78 (5.3)	26 (4.0)	49 (16.8)	639 (17.2)	<0.001
NZDep Q2	1,012 (16.5)	136 (9.3)	48 (7.3)	59 (20.3)	769 (20.7)	
NZDep Q3	1,146 (18.7)	200 (13.6)	69 (10.5)	61 (21.0)	816 (21.9)	
NZDep Q4	1,576 (25.7)	383 (26.1)	153 (23.3)	74 (25.4)	966 (25.9)	
NZDep Q5 (highest)	1,565 (25.5)	670 (45.7)	358 (54.6)	43 (14.8)	494 (13.3)	

Table 1 (continued): Demographic characteristics, pre-existing conditions, sepsis risk factors and clinical severity by ethnicity.

Variables	Total cohort[a] (n=6,137)	Ethnicity[a]				p-value[b]
		Māori (n=1,467)	Pacific (n=656)	Asian (n=291)	Non-MPA (n=3,723)	
Severe comorbidities						
Cardiovascular	349 (5.7)	136 (9.3)	38 (5.8)	7 (2.4)	168 (4.5)	<0.001
Hepatic	96 (1.6)	25 (1.7)	12 (1.8)	4 (1.4)	55 (1.5)	0.865
Immune[c]	474 (7.7)	96 (6.5)	36 (5.5)	17 (5.8)	325 (8.7)	0.010
Renal	329 (5.4)	138 (9.4)	63 (9.6)	14 (4.8)	138 (3.7)	<0.001
Respiratory	360 (5.9)	143 (9.7)	44 (6.7)	4 (1.4)	169 (4.5)	<0.001
Severe multimorbidity						
None	4,783 (77.9)	1,038 (70.8)	500 (76.2)	248 (85.2)	2,997 (80.5)	<0.001
1 severe comorbidity	1,140 (18.6)	343 (23.4)	121 (18.4)	40 (13.7)	636 (17.1)	
≥2 severe comorbidities	214 (3.5)	86 (5.9)	35 (5.3)	3 (1.0)	90 (2.4)	
Sepsis prognostic factors[d]						
Diabetes, type 2[e]	1,541 (25.1)	496 (33.8)	282 (43.0)	81 (27.8)	682 (18.3)	<0.001
Hypertension	1,215 (19.8)	303 (20.7)	142 (21.6)	40 (13.7)	730 (19.6)	0.009
Obesity[e]	398 (6.5)	172 (11.7)	84 (12.8)	4 (1.4)	138 (3.7)	<0.001
Hazardous alcohol use	295 (4.8)	118 (8.0)	26 (4.0)	5 (1.7)	146 (3.9)	<0.001
Tobacco use	3,199 (52.1)	987 (67.3)	290 (44.2)	71 (24.4)	1,851 (49.7)	<0.001

Table 1 (continued): Demographic characteristics, pre-existing conditions, sepsis risk factors and clinical severity by ethnicity.

Variables	Total cohort[a] (n=6,137)	Ethnicity[a]				p-value[b]
		Māori (n=1,467)	Pacific (n=656)	Asian (n=291)	Non-MPA (n=3,723)	
Blood/immune deficiencies	1,067 (17.4)	289 (19.7)	111 (16.9)	38 (13.1)	629 (16.9)	0.019
Clinical severity						
Septic shock	2,164 (35.3)	536 (36.5)	249 (38.0)	109 (37.5)	1,270 (34.1)	0.116
Invasive ventilation	1,597 (26.0)	340 (23.2)	172 (26.2)	85 (29.2)	1,000 (26.9)	0.024
Acute renal failure	955 (15.6)	233 (15.9)	119 (18.1)	36 (12.4)	567 (15.2)	0.107
ANZROD score	0.06 [0.02,0.19]	0.05 [0.02,0.16]	0.05 [0.02,0.16]	0.04 [0.02,0.16]	0.07 [0.03,0.21]	0.489
ICU LOS, days	2.0 [1.0,3.9]	2.0 [1.0,3.8]	1.8 [0.9,3.3]	1.8 [1.0,3.5]	2.1 [1.1,4.1]	0.512
Hospital LOS, days	7.2 [4.1,13.5]	7.0 [4.1,13.0]	7.4 [4.0,13.7]	7.3 [4.5,13.1]	7.2 [4.1,13.8]	0.319

[a]n (%), mean (±SD) or median [interquartile range].
[b]Pearson's Chi-squared test with Yates' continuity correction or Kruskal–Wallis >2 sample test.
[c]Includes cancer and human immunodeficiency virus (HIV).
[d]Unless otherwise identified, sepsis development risk factors were identified through previous hospital admission ICD-10-AM codes.
[e]Current hospital admission.
Non-MPA = non-Māori, non-Pacific, non-Asian; ANZROD = Australian and New Zealand Risk of Death; ICU = intensive care unit; LOS = length of stay.

Table 2: In-hospital and post-discharge mortality by admission status.

Variable	Mortality outcomes by admission status							
	In-hospital				Post-discharge			
	Deaths[a] (n=1,002)	CFR[b]	Unadjusted RR[c] (95% CI)	Adjusted RR[c] (95% CI)	Deaths[a] (n=661)	CFR[b]	Unadjusted HR[d] (95% CI)	Adjusted HR[d] (95% CI)
Sex								
Female	447 (44.6)	16.7	ref	ref	247 (37.4)	11.1	ref	ref
Male	555 (55.4)	16.0	1.0 (0.9–1.1)	-	414 (62.6)	14.3	1.3 (1.12–1.53)	-
Ethnicity								
Non-MPA	672 (67.1)	18.0	ref	ref	412 (62.3)	13.5	ref	ref
Māori	199 (19.9)	13.6	0.8 (0.6–0.9)	0.9 (0.8–1.1)	189 (28.6)	14.9	1.1 (0.93–1.31)	1.5 (1.25–1.79)
Pacific	89 (8.9)	13.6	0.8 (0.6–0.9)	1.0 (0.8–1.2)	47 (7.1)	8.3	0.6 (0.44–0.80)	0.8 (0.61–1.13)
Asian	42 (4.2)	14.4	0.8 (0.6–1.1)	1.0 (0.8–1.4)	13 (2.0)	5.2	0.4 (0.21–0.64)	0.5 (0.29–0.87)
Age								
≤39 years	41 (4.1)	4.7	ref	ref	28 (4.2)	3.4	ref	-
40–59 years	208 (20.8)	11.5	2.4 (1.8–3.4)	-	159 (24.1)	10.0	3.0 (2.04–4.56)	-
60–79 years	553 (55.2)	19.9	4.2 (3.1–5.7)	-	347 (52.5)	15.6	4.9 (3.36–7.25)	-
≥80 years	200 (20.0)	28.9	6.1 (4.4–8.4)	-	127 (19.2)	25.8	8.6 (5.73–12.99)	-
Socio-economic deprivation								
NZDep Q1 (least)	131 (13.1)	16.5	ref	ref	76 (11.5)	11.5	ref	ref
NZDep Q2	172 (17.2)	17.0	1.0 (0.8–1.3)	1.1 (0.9–1.3)	96 (14.5)	11.4	1.0 (0.7–1.3)	1.0 (0.8–1.4)

Table 2 (continued): In-hospital and post-discharge mortality by admission status.

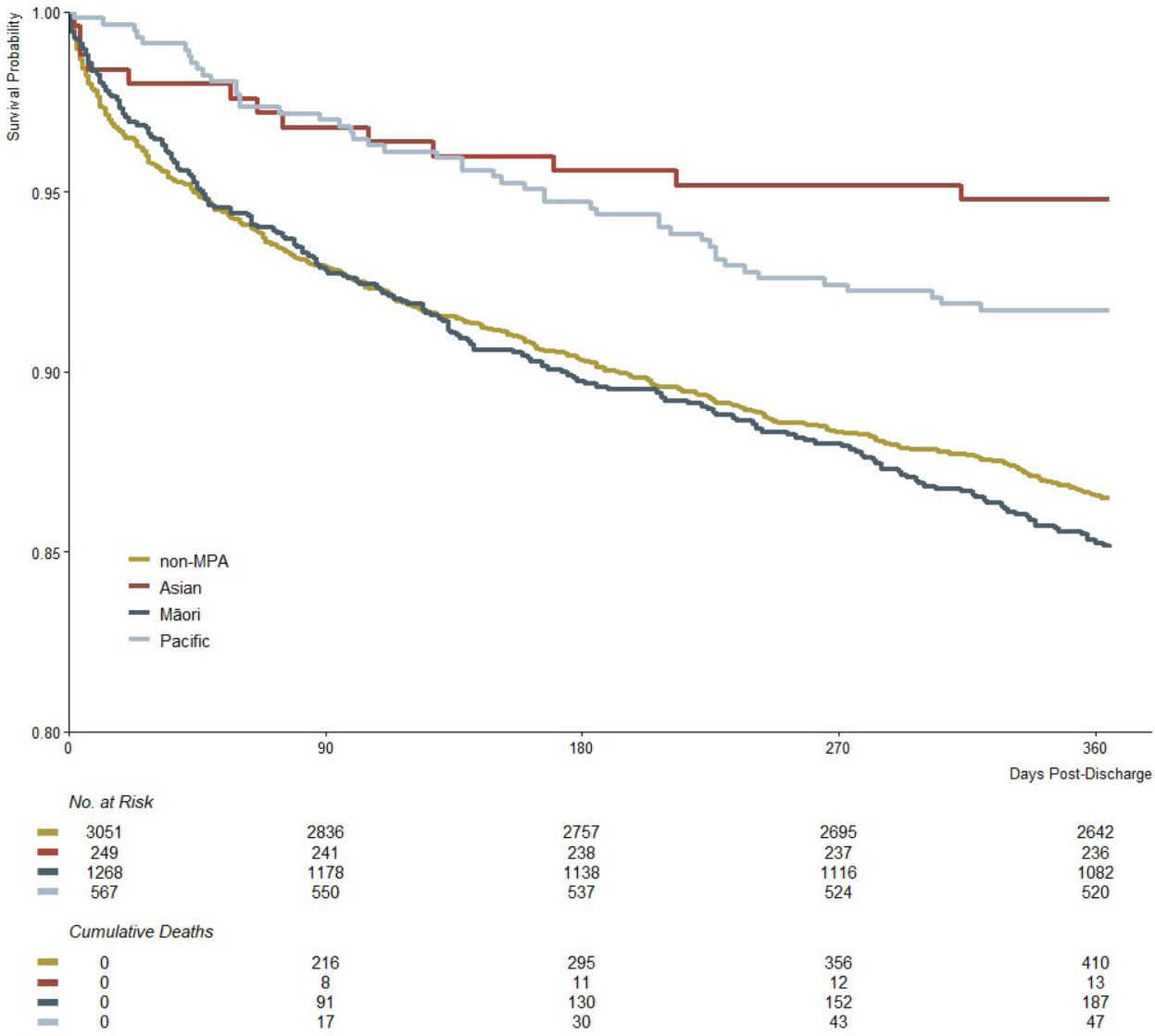
Variable	Mortality outcomes by admission status							
	In-hospital				Post-discharge			
	Deaths[a] (n=1,002)	CFR[b]	Unadjusted RR[c] (95% CI)	Adjusted RR[c] (95% CI)	Deaths[a] (n=661)	CFR[b]	Unadjusted HR[d] (95% CI)	Adjusted HR[d] (95% CI)
NZDep Q3	177 (17.7)	15.4	0.9 (0.8–1.1)	1.0 (0.8–1.2)	122 (18.5)	12.6	1.1 (0.8–1.5)	1.1 (0.9–1.5)
NZDep Q4	276 (27.5)	17.5	1.1 (0.9–1.3)	1.1 (0.9–1.4)	180 (27.2)	13.8	1.2 (0.9–1.6)	1.3 (1.0–1.7)
NZDep Q5 (most)	235 (23.5)	15.0	0.9 (0.7–1.1)	1.1 (0.9–1.3)	185 (28.0)	13.9	1.2 (0.9–1.6)	1.5 (1.2–2.0)
Severe comorbidities								
Respiratory	111 (11.1)	30.8	2.0 (1.7–2.4)	1.9 (1.6–2.2)	54 (8.2)	21.7	1.8 (1.4–2.4)	1.7 (1.3–2.2)
Cardiovascular	108 (10.8)	30.9	2.0 (1.7–2.4)	1.7 (1.4–2.0)	63 (9.5)	26.1	2.3 (1.8–3.0)	1.9 (1.4–2.4)
Hepatic	33 (3.3)	34.4	2.1 (1.6–2.8)	2.2 (1.7–2.9)	18 (2.7)	28.6	2.5 (1.6–4.0)	2.6 (1.6–4.1)
Renal	59 (5.9)	17.9	1.1 (0.9–1.4)	1.2 (0.9–1.5)	78 (11.8)	28.9	2.6 (2.1–3.3)	2.7 (2.2–3.5)
Immune	107 (10.7)	22.6	1.4 (1.2–1.7)	1.4 (1.2–1.6)	128 (19.4)	34.9	3.5 (2.9–4.3)	3.3 (2.7–4.0)
Number of severe comorbidities								
None	665 (66.4)	13.9	ref	ref	380 (57.5)	9.2	ref	ref
1	268 (26.7)	23.5	1.7 (1.5–1.9)	1.6 (1.4–1.9)	230 (34.8)	26.4	3.1 (2.7–3.7)	2.9 (2.5–3.5)
≥2	69 (6.9)	32.2	2.3 (1.9–2.9)	2.1 (1.7–2.6)	51 (7.7)	35.2	4.4 (3.3–5.8)	3.9 (2.9–5.2)
Sepsis prognostic factors								
Diabetes, type 2	278 (27.7)	18.0	1.1 (1.0–1.3)	1.0 (0.9–1.2)	197 (29.8)	27.2	1.3 (1.1–1.6)	1.2 (1.1–1.5)
Hypertension	260 (25.9)	21.4	1.4 (1.3–1.6)	1.2 (1.1–1.4)	183 (27.7)	24.7	1.8 (1.5–2.1)	1.4 (1.2–1.7)

Table 2 (continued): In-hospital and post-discharge mortality by admission status.

Variable	Mortality outcomes by admission status							
	In-hospital				Post-discharge			
	Deaths[a] (n=1,002)	CFR[b]	Unadjusted RR[c] (95% CI)	Adjusted RR[c] (95% CI)	Deaths[a] (n=661)	CFR[b]	Unadjusted HR[d] (95% CI)	Adjusted HR[d] (95% CI)
Immune suppressed	83 (8.3)	20.6	1.3 (1.1–1.6)	1.2 (1.0–1.5)	68 (10.3)	21.3	1.8 (1.4–2.3)	1.7 (1.3–2.2)
Obesity	64 (6.4)	16.1	1.0 (0.8–1.2)	1.0 (0.9–1.5)	43 (6.5)	12.9	1.0 (0.7–1.4)	1.2 (0.9–1.7)
Tobacco use	490 (48.9)	15.3	0.9 (0.8–1.0)	0.9 (0.8–1.0)	371 (56.1)	13.7	1.2 (1.0–1.4)	1.1 (1.0–1.3)
Hazardous alcohol use	62 (6.2)	21.0	1.3 (1.0–1.6)	1.5 (1.2–1.9)	26 (3.9)	11.2	0.9 (0.6–1.3)	1.0 (0.7–1.5)
Blood/immune deficiencies	209 (20.9)	19.6	1.3 (1.1–1.4)	1.1 (1.0–1.3)	158 (23.9)	18.4	1.6 (1.4–1.9)	1.5 (1.2–1.8)
Clinical severity								
Septic shock	425 (42.4)	19.6	1.4 (1.2–1.5)	1.3 (1.2–1.5)	217 (32.8)	12.5	1.0 (0.8–1.1)	0.9 (0.8–1.1)
Mechanical ventilation	464 (46.3)	29.1	2.4 (2.2–2.7)	2.7 (2.4–3.0)	98 (14.8)	8.6	0.6 (0.5–0.8)	0.7 (0.6–0.9)
Acute renal failure	361 (36.0)	37.8	3.1 (2.8–3.4)	2.8 (2.5–3.1)	106 (16.0)	17.8	1.5 (1.2–1.9)	1.4 (1.2–1.7)

Patient outcomes are presented by admission status, in-hospital and post-discharge as [a]number of deaths (%), [b]case fatality risk per 100 community-acquired sepsis intensive care unit admissions, and mortality risk ([c]RR = risk ratio; [d]HR = hazard ratio, unadjusted and adjusted for sex and age).
CFR = case fatality rate; CI = confidence interval.

Figure 2: Kaplan–Meier survival plot indicating the probability of patient survival by ethnicity from hospital discharge to 365 days post-discharge.

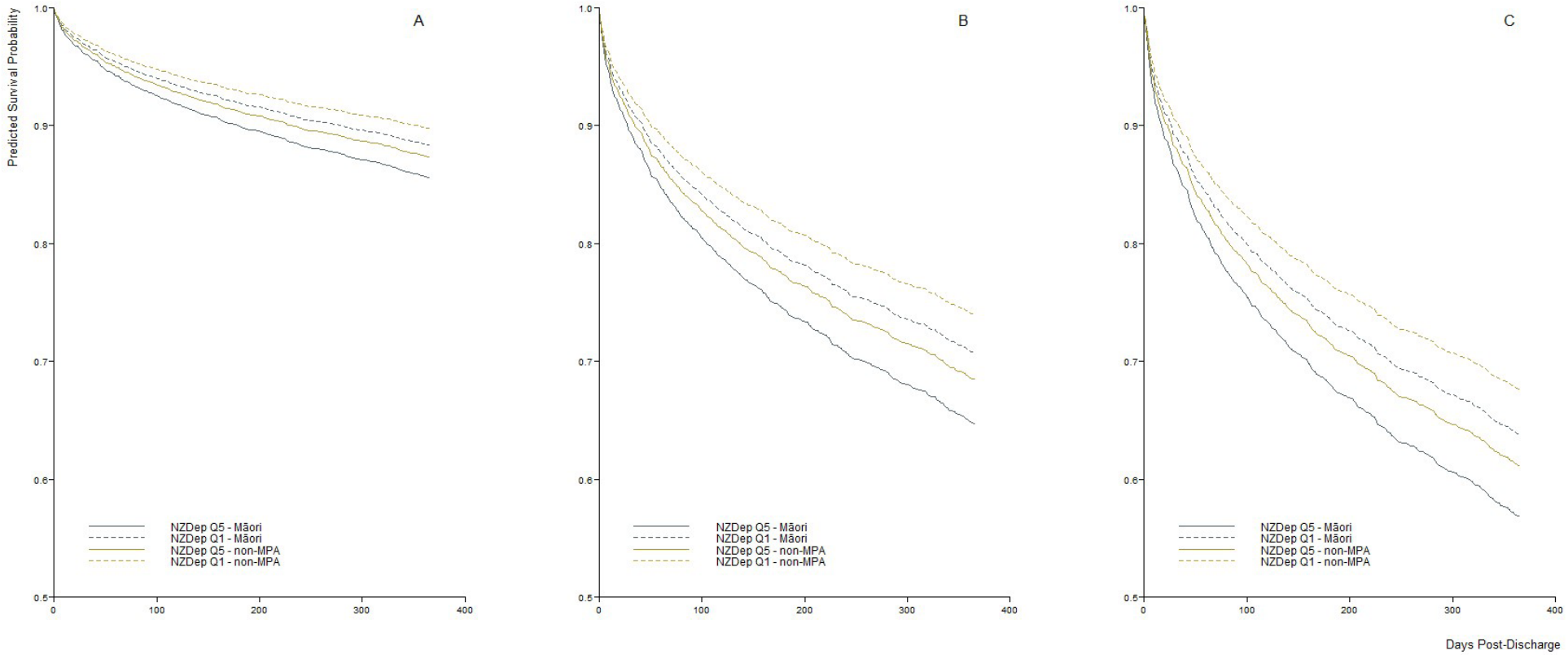


Kaplan–Meier curve for short-term survival following an index community-acquired sepsis intensive care unit admission by ethnicity. Survival analysis was censored at 365 days.

in the year from admission instead of specifically following discharge.[12] Our 365-day post-discharge mortality risk of 12.9% is lower than previous estimations from France and the United States,[21,24] potentially due to excluding hospital-acquired sepsis admissions.

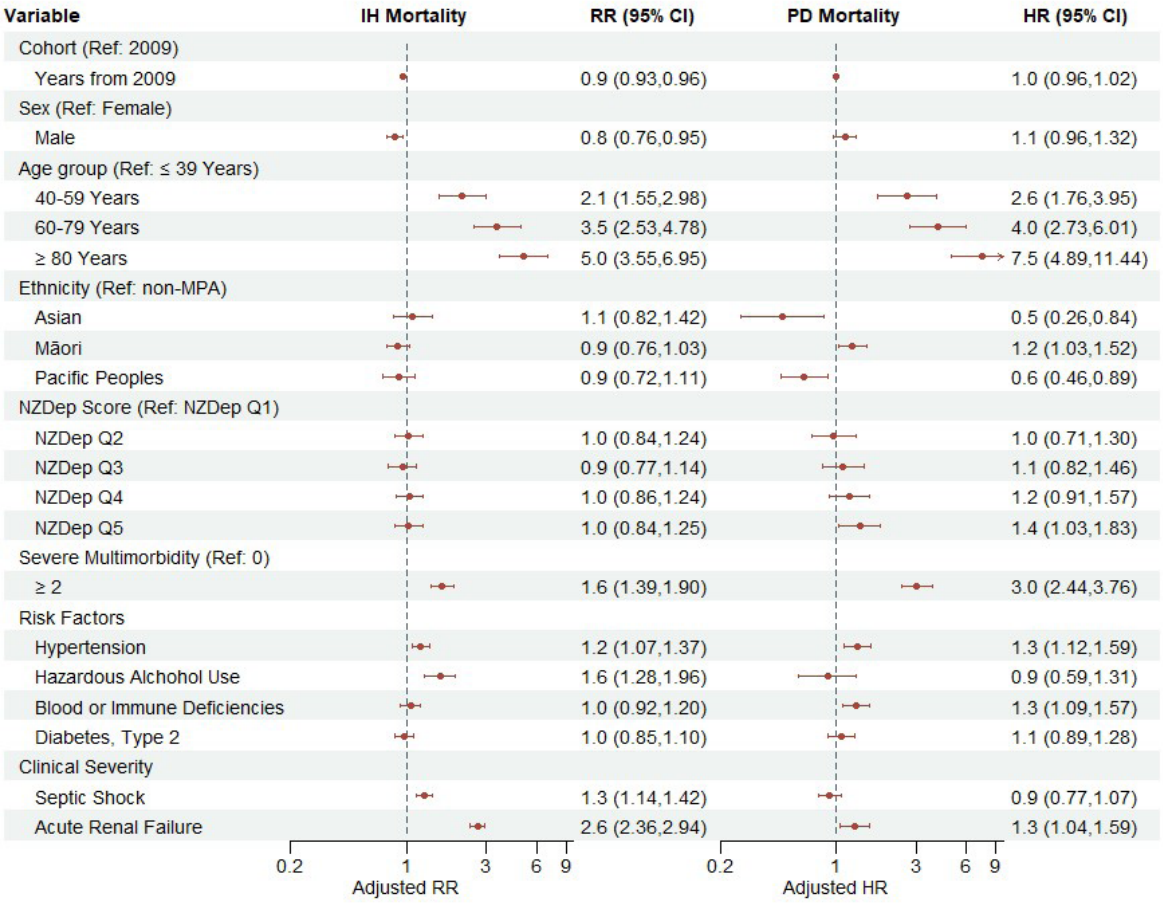
Similar to previous studies, we identified increasing age, hazardous alcohol use, blood or immune deficiencies, severe comorbidities and severe multimorbidity as strongly associated with in-hospital mortality.[25–27] We found no association between ethnicity or NZDep quintile and in-hospital mortality, consistent with studies conducted in Australia and the United Kingdom characterising sepsis mortality, where ethnicity and socio-economic deprivation were not associated with in-hospital mortality.[28,29] Our findings were also consistent with studies characterising overall ICU mortality by ethnicity in Aotearoa. A single-centre study conducted in Waikato over 15 years found no evidence of association between in-hospital mortality and ethnicity.[30] Similarly, a multicentre study characterising ICU patient outcomes for all patient populations admitted to 17 ANZICS-APD contributing sites in Aotearoa over 9 years found no evidence of associations between ethnicity and

Figure 3: Cox proportional-hazards plots indicating predicted average patient survival after an index intensive care unit admission due to community-acquired sepsis by ethnicity, NZDep quintile and severe comorbidity from hospital discharge to 365 days post-discharge.



Cox proportional-hazard models were used to predict the post-discharge survival of the average patient (male, 60–79 years) and to compare survival hazards among ethnic and socio-economic populations based on the degree of severe multimorbidity. Other covariates were set at mode levels (the most frequently occurring observations). The severity of severe multimorbidity was categorised as A: no severe comorbidities, B: one severe comorbidity and C: more than two severe comorbidities.

Figure 4: Association between patient characteristics (demographics, pre-existing conditions and risk factors) identifiable at or within 48 hours of intensive care unit (ICU) admission and in-hospital (IH) and post-discharge (PD) mortality.



Multivariable analysis of variables identifiable at ICU admission associated with IH and PD mortality. IH mortality risk is presented as rate ratio with 95% confidence interval; post-discharge mortality risk is presented as hazard ratio with 95% confidence interval. Both models are adjusted for year, sex, age, ethnicity, socio-economic deprivation and severe multimorbidity.

in-hospital mortality.[13]

We identified a significant risk of post-discharge mortality among patient populations with increasing age, chronic disease and severe multimorbidity, consistent with previous findings. Globally, significant post-discharge sepsis-associated mortality disparities are observable between patient populations, particularly populations with increasing age and/or those experiencing severe comorbidities and multimorbidity.[31,32] We also observed a similar level of severe comorbidity and multimorbidity in older patients living in areas of low socio-economic deprivation and younger patients living in areas of high socio-economic deprivation. Early onset of multimorbidity is strongly associated with socio-economic deprivation.[7,33] In Aotearoa, marginalised peoples—particularly patient populations of Māori ethnicity and those resident in high NZDep score areas—are disproportionately affected by chronic disease.[8,34] Patient populations of Māori ethnicity are significantly more likely to experience chronic comorbidities, and are more likely be resident in areas with high NZDep scores than non-Māori. This pattern may explain the increased risk of post-discharge mortality associated with patient populations of Māori ethnicity we observed and the decrease in post-discharge survival for Māori patient populations living in NZDep Q5 areas compared to non-MPA populations living in NZDep Q5 areas.

Our findings raise important public health concerns for patient populations usually resident in NZDep Q5 areas who develop CAS and

survive to hospital discharge in Aotearoa. We found substantial evidence that the prevalence of CAS requiring ICU admission in Aotearoa was not equitably spread across patient populations, particularly observable within those usually resident in NZDep Q5 areas. Secondly, although in-hospital mortality risk was equivalent, we observed clear post-discharge mortality risk disparities at 365 days following hospital discharge between patient populations, specifically those with severe comorbidities and/or severe multimorbidity residing in NZDep Q5 areas, particularly for those of Māori ethnicity. Our results strongly demonstrate that both ethnicity and socio-economic deprivation are associated with an increased mortality risk for hospital survivors. In addition, due to the constraints of the linked ANZICS-CORE-APD data and focussing only on ICU-admitted CAS events, our results may have under-estimated the strength of mortality risk associated with demographic, pre-existing conditions and clinical variables. Interventions that modify the major social determinants of health, such as socio-economic deprivation, could potentially decrease the incidence of CAS requiring ICU admission in Aotearoa. More specifically, interventions to reduce diabetes and improve tobacco smoking cessation may reduce the incidence of ICU-admitted CAS in Aotearoa. A more detailed study is needed of morbidities following an ICU-admitted sepsis event and post-discharge sepsis-associated mortality to identify interventions to reduce these significant post-discharge mortality risk disparities.

Strengths and limitations

Our study has several strengths. It was based on a large cohort of patient data from 17 ANZICS-CORE-APD contributing hospital sites across Aotearoa linked to the NMDS and MC for over 10 years. The linkage allowed us to follow patients post-discharge and compare in-hospital and post-discharge mortality. Linkage also allowed for a more in-depth characterisation of the ANZICS-CORE-APD patient cohort, particularly ethnicity, socio-economic deprivation and previously identified risk factors.

There are several limitations to our study. First, our results may not be generalisable to the wider population as the study was limited to patients admitted for intensive care in an ANZICS-CORE-APD contributing hospital site whose data could be linked to the NMDS and MC, and it is likely the true burden of treated and untreated CAS in Aotearoa is under-estimated. Second, the ANZICS-CORE-APD was designed to be a benchmarking database for quality improvement rather than an epidemiological database. As such, the ANZICS-CORE-APD does not collect data that we would find relevant to epidemiological studies characterising sepsis, such as differentiating between the site of infection for patients with complicated sepsis beyond describing sites as than genitourinary or other. Similarly, the ANZICS-CORE-APD has only recently started to collect data about patients' frailty before admission and does not currently collect data on health and quality of life before admission or on patient discharge, which would have improved the characterisation of the current cohort.

Conclusions

In Aotearoa, mortality following CAS-associated ICU admission remains high while in hospital and following discharge. The strong association between mortality risk, ICU-admitted CAS and the social determinants of health only becomes evident in the post-discharge period. This finding supports the need to identify and implement interventions to prevent sepsis, for early intervention to limit the necessity for ICU admission and to identify ways to address outcome disparities between patient populations following hospital discharge.

COMPETING INTERESTS
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Appendix

Appendix Table 1: APACHE-III-J diagnosis and sub-diagnosis sepsis or infectious disease codes identified in the current study population.

Diagnosis code group	APACHE-III diagnosis code	APACHE-III diagnosis sub-code*
Cardiovascular	109 – Other cardiovascular disease	109.06 – Endocarditis
Respiratory	210 – Parasitic pneumonia	210.02 – Pneumonia, parasitic (e.g., pneumocystis pneumonia)
	212 – Bacterial pneumonia	212.01 – Pneumonia, bacterial
		212.02 – Pneumonia, other
	213 – Viral pneumonia	213.01 – Pneumonia, viral
	1301 – Respiratory infection	1301.01 – Infection/abscess, other surgery for
Sepsis	501 – Sepsis, other than urinary	501.01 – Sepsis, cutaneous/soft tissue
		501.02 – Sepsis, gastrointestinal
		501.03 – Sepsis, gynaecologic
		501.04 – Sepsis, other
		501.05 – Sepsis, pulmonary
		501.06 – Sepsis, unknown
	502 – Sepsis of urinary tract origin	502.01 – Sepsis, renal/UTI (including bladder)
	503 – Sepsis with shock, other than urinary	503.01 – Sepsis with shock, not urinary tract
	504 – Sepsis of urinary tract origin with shock	504.01 – Sepsis with shock, urinary tract
Neurological	404 – Neurologic infection	404.01 – Abscess, neurologic
		404.02 – Encephalitis
		404.03 – Meningitis
	1506 – Other neurologic disease	1506.01 – Abscess/Infection-cranial, surgery for
Gastrointestinal	313 – Other GI inflammatory disease	313.01 – Cholangitis
		313.03 – GI abscess/cyst
		313.05 – Peritonitis
	1406 – Cholecystitis/cholangitis	1406.01 – Cholecystectomy/ cholangitis, surgery for (gallbladder removal)

Appendix Table 1 (continued): APACHE-III-J diagnosis and sub-diagnosis sepsis or infectious disease codes identified in the current study population.

	1409 – Fistula/abscess surgery	1409.01 – Fistula/abscess, surgery for (not inflammatory bowel disease)
	1412 – Peritonitis	1412.01 – Peritonitis, surgery for
Renal/genitourinary	901 – Renal disorders	901.04 – Renal infection/abscess
Skin & soft tissue	1102 – Cellulitis/soft tissue infection	1102.01 – Cellulitis & localised soft tissue infections
	1904 – Cellulitis/soft tissue infection	1904.01 Cellulitis and localised soft tissue infections, surgery for

*Not all patients in the current study had an APACHE-III-J sub-diagnosis code, but all had an APACHE-III-J diagnosis code.
UTI = urinary tract infection; GI = gastrointestinal.

Appendix Table 2A: Modified sequential organ failure assessment (mSOFA) scoring.

Clinical variable	Score: 0	Score: 1	Score: 2	Score: 3	Score: 4
PaO2/FIO2	≥400mmHg	<400mmHg	<300mmHg	<200mmHg with respiratory support	<100mmHg with respiratory support
Platelets	≥150×109/L	<150×109/L	<100×109/L	<50×109/L	<20×109/L
Bilirubin	<20mmol/L	20–32mmol/L	33–101mmol/L	102–204mmol/L	>204mmol/L
Cardiovascular	MAP ≥70mmHg	MAP <70mmHg	-	-	Any use of inotropes
Glasgow Coma Scale score	15 points	13–14 points	10–12 points	6–9 points	<6 points
Creatinine	<110mmol/L	110–170mmol/L	171–299mmol/L	300–400mmol/L	>440mmol/L
Urine output	-	-	-	<500mL/day	<200mL/day

Appendix Table 2B: Obstetric modified sequential organ failure assessment (omSOFA) scoring.

Clinical variable	Score: 0	Score: 1	Score: 2
PaO2/FIO2	≥400mmHg	300–400mmHg	<300mmHg
Platelets	≥150×109/L	100–150×109/L	<100×109/L
Bilirubin	<20mmol/L	20–32mmol/L	>32mmol/L
Cardiovascular	MAP ≥70mmHg	MAP <70mmHg	Use of intropes
Glasgow Coma Scale score	Alert	Rousable by voice	Rousable by pain
Creatinine	<90mmol/L	90–120mmol/L	>120mmol/L
Urine output	-	-	-

PaO2/FIO2 = ratio of arterial oxygen partial pressure to fractional inspired oxygen; MAP = mean arterial pressure.

Clinical alert: arrival of terbinafine resistant Trichophyton indotineae in New Zealand

Wendy P McKinney, Matthew R Blakiston, Sally A Roberts, Arthur J Morris

ABSTRACT

BACKGROUND: Over the past decade there has been a rapid emergence of a new dermatophyte species *Trichophyton indotineae* (*T. indotineae*) in the Indian subcontinent, with associated global spread. It is noted for extensive recalcitrant infections and high rates of terbinafine resistance that are changing treatment paradigms for tinea infection.

AIM: To report on the epidemiology of dermatophyte infections from the National Mycology Reference Laboratory at Auckland City Hospital and the arrival of *T. indotineae* in New Zealand.

METHODS: This was a retrospective review of laboratory data from January 2017 to August 2024. Antifungal susceptibility was performed by disc testing. Species identification was performed by phenotypic methods and for a limited number of isolates by DNA sequence analysis.

RESULTS: There were 961 dermatophytes identified. *Trichophyton rubrum* was the most common species, accounting for 72% of all isolates. There were 85 (9%) confirmed or probable *T. indotineae* identified from 63 individuals. These included both Auckland isolates and isolates referred from laboratories around the country. Of the 49 *T. indotineae* isolates that had antifungal susceptibility testing performed, only 30 (61%) were susceptible to terbinafine, while 45 (92%) were susceptible to itraconazole.

CONCLUSIONS: Terbinafine resistant *T. indotineae* has arrived in New Zealand. To assist appropriate management, practitioners encountering extensive tinea infection, particularly if failing terbinafine treatment, should request culture, asking for full dermatophyte identification and susceptibility testing. Itraconazole is the recommended treatment for *T. indotineae*, and up to 12 weeks duration may be required.

Dermatophytosis is one of the most common fungal infections worldwide.[1] It is caused by a group of keratinolytic filamentous fungi known as dermatophytes that infect superficial tissues such as the stratum corneum, hair and nails.[1] Anthropophilic and zoophilic species in the genera *Trichophyton*, *Epidermophyton* and *Microsporum* are responsible for most infections.[1,2]

Dermatophyte epidemiology displays significant geographic and temporal variation.[1,2] Epidemiological changes have included the emergence of *Trichophyton rubrum* (*T. rubrum*) as a globally widespread pathogen associated with tinea pedis and onychomycosis in the 1940–1950s. Similarly, *Trichophyton tonsurans* (*T. tonsurans*) replaced *Microsporum canis* (*M. canis*) as the dominant cause of tinea capitis in the United Kingdom at the end of the twentieth century.[1–3] Over the past decade, *Trichophyton indotineae* (*T. indotineae*) (previously called *Trichophyton mentagrophytes* genotype VIII) has replaced *T. rubrum* in India in association with an epidemic of tinea corporis/cruris.[4–6] *T. indotineae* is now also being isolated in regions outside the Indian subcontinent.[7–9] In New Zealand, *T. rubrum* was the most common species reported in two studies from Wellington (1975–1979) and Auckland (1999–2002).[10,11]

Antifungal resistance has not historically been a concern in the treatment of dermatophytes. However, this paradigm is shifting, with increasing reports of resistance to the first line anti-dermatophyte agent terbinafine. Most notable has been the emergence of *T. indotineae* associated with recalcitrant infections and high rates of terbinafine resistance (up to 71%).[12–15] A proportion of these isolates also have decreased susceptibility to the triazoles.[15] Terbinafine resistance has also been observed less frequently in *T. rubrum*.[13,15] Treatment-resistant *T. indotineae* has recently been reported in Australia, but there are no published data on its presence in New Zealand.[16]

We have examined the laboratory data from the National Mycology Reference Laboratory at Auckland City Hospital with the aims of reporting on the current epidemiology of dermatophyte infections and the arrival of *T. indotineae* in New Zealand.

Methods

We searched our laboratory information system for the period January 2017 to August 2024 to identify dermatophyte positive specimens and referred isolates from other New Zealand laboratories. For each isolate we extracted data on the specimen site, location of referring laboratory and susceptibility results. Dermatophytes were primarily identified by standard microscopic and macroscopic characteristics. Since 2017, we have encountered atypical strains of *Trichophyton interdigitale* (*T. interdigitale*) that were urease negative (*T. interdigitale* is urease positive) and that had abundant macroconidia (none or sparse for *T. interdigitale*). We have reported these as "atypical *T. interdigitale*". If these were speciated by molecular methods, we reported as *T. indotineae*. For this report we refer to the isolates as *T. indotineae*/probable *T. indotineae* based either on DNA sequencing or the atypical morphology described above. Molecular identification was performed on two isolates, one resistant and one with intermediate terbinafine susceptibility. The isolates' internal transcribed spacer (ITS) region was amplified using PCR Buffer and Taq DNA polymerase. The amplified products were sequenced twice in both directions (forwards and reverse). The sequences were then compared to the ITS sequences of all fungal isolate accessions in the National Center for Biotechnology Information GenBank database.

Susceptibility testing is not performed routinely on dermatophytes; however, requests have been increasing in recent years associated primarily with dermatologists managing recalcitrant infections. Disc diffusion antifungal susceptibility testing (AFST) is performed locally for dermatophytes following the disc manufacturer methods.[17] Briefly, the isolates are sub-cultured at 30 degrees Celsius for 4–15 days (until sporulation confirmed); the inoculum (conidial suspension) is then prepared in sterile saline, adjusted to a 0.5 McFarland standard and inoculated onto Mueller–Hinton agar with 2% glucose and 0.5μg/mL methylene blue. Antifungal discs (Neo-Sensitabs™, Rosco Diagnostica A/S, Taastrup, Denmark) are placed onto the inoculated agar. These discs include terbinafine (30μg), fluconazole (25μg), itraconazole (10μg) and voriconazole (1μg). Plates are incubated at 30 degrees Celsius in ambient air with reading on day 4 (and up to 7 days for slow growing organisms). Interpretive criteria recommended by the manufacturer for local (topical) treatment of *Candida* species are used; for fluconazole and terbinafine, susceptible, intermediate and resistant zone sizes are ≥20mm, 12–19mm and ≤11mm respectively. For itraconazole, the zone sizes are ≥15mm, 10–14mm and no zone.[18] The manufacturer has no recommendation for voriconazole, and the fluconazole zone sizes are used.

Results

From January 2017 to August 2024, we isolated or identified 961 dermatophytes (Table 1). *T. rubrum* was the most common isolate (688, 72%) and was the most frequent species from all body sites except the scalp. Scalp infections were mostly caused by the well-recognised causes of tinea capitis, *M. canis* and *T. tonsurans* (Table 2). Feet and nails (mostly toenails) were the most common sites of infection (Table 2).

Since 2017 we have identified 85, molecularly confirmed (2) or probable (83), *T. indotineae* isolates. These included 24 from our own specimens, 22 from the local community laboratory, 17 from other Auckland hospital laboratories and 22 referred isolates from laboratories outside Auckland. From 2021 there have been more confirmed or probable *T. indotineae* than *T. interdigitale* identified (Table 1). The 85 *T. indotineae* isolates were from 63 patients, 50 with one isolate, seven with two, four with three, one with four and one with five isolates. The most common sites of infection were groin 28%, thighs 13%, feet 12% and arms 12% (Table 2). The median time between isolates for the six patients with cultures separated in time was 6 months, ranging from 1 to 18 months.

Available antifungal susceptibility results for 49 confirmed or probable *T. indotineae* and 24 *T. rubrum* are summarised in Table 3. Itraconazole was the most active agent, with 92% and 100% of *T. indotineae* and *T. rubrum* isolates testing susceptible respectively. For terbinafine only 61% and 92% of *T. indotineae* and *T. rubrum* tested susceptible respectively. Fluconazole was the least active agent (Table 3). All terbinafine resistant isolates had no zone of inhibition around the discs. It was also notable that there was a difference in the disc zone sizes for terbinafine susceptible strains of *T. rubrum* and *T. indotineae*: 21 of the 22 (95%) susceptible *T. rubrum* isolates had zone sizes ≥40mm, whereas only 19 of the 30 (63%) susceptible *T. indotineae* had zone sizes ≥40mm.

Discussion

Our laboratory data show that the local epidemiology of the common dermatophytes is similar to past reports, with *T. rubrum* the most common species at all sites except the scalp.[11] The notable exception is the emergence of *T. indotineae* that made up 9% of isolates. This, however, is likely a much higher proportion than an unbiased community sample, due to the reference laboratory's selective receipt of isolates from recalcitrant infections for antifungal susceptibility testing. Of the *T. indotineae* isolates, only 61% were terbinafine susceptible. Consistent with prior reports, a greater proportion, including terbinafine resistant isolates, were susceptible to itraconazole.[9,12] This local emergence of terbinafine resistant *T. indotineae* threatens to complicate tinea treatment locally, as it is doing in many areas globally.

There are limitations to the data, including the formal molecular identification of only two *T. indotineae* isolates, although the phenotype features, and resistance, of the probable *T. indotineae* isolates make their identity highly likely. Another limitation is that we did not use a standardised technique to determine antifungal minimum inhibitory concentrations (MICs), preventing in-depth comparisons with other susceptibility reports. However, others have shown that disc testing methodology (using different antifungal concentrations than locally) for dermatophytes generates reproducible zone diameters, and zone sizes correlate to MICs.[19–21] It is likely the utilised zone diameter cut-offs to define susceptibility in this report are suboptimal, and the difference observed for susceptible *T. indotineae* versus *T. rubrum* isolates suggests we may be underestimating terbinafine resistance. Our finding that terbinafine resistant isolates were susceptible to itraconazole is consistent with sizeable studies reporting on *T. indotineae* isolates for which the terbinafine MICs were elevated (>2mg/L and many >32mg/L) having low itraconazole MICs (≤0.03mg/L).[9,12] As this was a laboratory-based study, we have no information on travel history, ethnicity, the extent of infection or response to treatment. Some patients did, however, have infection for some time, with positive cultures separated by up to 18 months.

We are planning a more in-depth analysis on our isolates using molecular methods to confirm species identity, detect squalene epoxidase (SQLE) mutations known to confer resistance to terbinafine and perform MIC measurements. This testing will allow better determination of isolates susceptibility and reveal how terbinafine disc zone sizes correlate to MICs and SQLE mutations.

In the meantime, however, we alert clinicians in primary care to be aware of the possibility of *T. indotineae* in persons with extensive long-standing tinea corporis and/or tinea cruris, particularly in those of Indian or other South Asian ethnicities that have failed terbinafine treatment. In this setting, we recommend that culture for dermatophytes is specifically requested of the local laboratory, and that if an atypical isolate is recovered that the initial laboratory refers the isolate for susceptibly testing and formal identification. Faced with a likely clinical history, it would be reasonable to initiate itraconazole treatment. The optimal dosing regimen and treatment duration have not been established, but 200–400mg daily for 2–12 weeks tailored to patient response (resolution of skin lesions) has been recommended.[7,8,22,23] The addition of a topical antifungal agent to systemic therapy may be considered; however, data are lacking on whether this improves therapeutic outcome.[8,23] The use of topical steroids should be avoided.

Conclusions

Terbinafine resistant *T. indotineae* can be added to the list of antifungal resistant fungi, including *Candida auris* and azole-resistant *Aspergillus fumigatus*, which are now being encountered in New Zealand.[24,25] To enable appropriate management, practitioners encountering extensive tinea infection, particularly if failing terbinafine treatment, should request culture, asking for full dermatophyte identification and susceptibility testing. Itraconazole is the recommended treatment for *T. indotineae*, and up to 12 weeks duration may be required.

Table 1: Dermatophyte isolates January 2017–August 2024: Auckland City Hospital National Mycology Reference Laboratory.

	Year of isolation									
Dermatophyte groups	**2017**	**2018**	**2019**	**2020**	**2021**	**2022**	**2023**	**2024**	**Total**	
Epidermophyton floccosum	-	3	2	1	2	-	2	1	11	1%
Microsporum canis	4	2	3	5	2	1	2	-	19	2%
Microsporum other[1]	1	1	-	1	-	1	-	2	6	0.6%
Trichophyton indotineae[2]	8	1	6	10	24	14	10	12	85	9%
Trichophyton interdigitale	21	23	12	14	6	9	10	5	100	11%
Trichophyton other[3]	3	9	4	4	1	3	4	-	28	3%
Trichophyton rubrum	80	112	81	107	106	67	72	63	688	72%
Trichophyton tonsurans	2	4	7	1	3	4	1	2	24	2%
Total	119	155	115	143	144	99	101	85	961	100%

[1]Includes: *Lophophyton (Microsporum) cookei* (1), *Microsporum audouinii* (1) and *Nannizzia gypsea* (*Microsporum gypseum*) (4).
[2]Comprises two confirmed isolates identified by molecular sequencing and 83 probable isolates based on phenotypic characteristics.
[3]Includes: *Arthroderma insingulare* (*Trichophyton terrestre*) (3), *Trichophyton equinum* (1), *Trichophyton mentagrophytes* (7), *Trichophyton verrucosum* (2), *Trichophyton violaceum* (7) and *Trichophyton* species not further identified (8).

Table 2: Sites of dermatophyte infection for 961 isolates, January 2017–August 2024.

	Site of dermatophyte infection							
Dermatophyte groups	**Body**	**Groin**	**Foot**	**Nail**	**Scalp**	**Unknown**	**Total**	
Epidermophyton floccosum	2	1	6	2	-	-	11	1%
Microsporum canis	5	-	1	-	13	-	19	2%
Microsporum other[1]	2	-	-	2	2	-	6	0.6%
Trichophyton indotineae[2]	40[4]	24	10	4	-	7	85	9%
Trichophyton interdigitale	12	8	47	29	-	4	100	11%
Trichophyton other[3]	13	1	1	3	9	1	28	3%
Trichophyton rubrum	172	117	218	159	2	20	688	72%
Trichophyton tonsurans	1	-	-	-	22	1	24	2%
Total	247	151	283	199	48	33	961	100%

[1]Includes: *Lophophyton* (*Microsporum*) *cookei* (1), *Microsporum audouinii* (1) and *Nannizzia gypsea* (*Microsporum gypseum*) (4).
[2]Comprises two formally identified by molecular sequencing and 83 probable isolates based on phenotypic characteristics.
[3]Includes: *Arthroderma insingulare* (*Trichophyton terrestre*) (3), *Trichophyton equinum* (1), *Trichophyton mentagrophytes* (7), *Trichophyton verrucosum* (2), *Trichophyton violaceum* (7) and *Trichophyton* species not further identified (8).
[4]Body sites were thigh (11), upper limb (10), chest/back (7), abdomen (5), face/neck (5) and leg (2).

Table 3: Antifungal susceptibility of *Trichophyton indotineae* and *Trichophyton rubrum*.[1]

Organism	Terbinafine			Fluconazole			Itraconazole			Voriconazole		
	S	I	R	S	I	R	S	I	R	S	I	R
Trichophyton indotineae (N=49)[2]	30 (61%)	11 (22%)[3]	8 (16%)[3]	10 (21%)	3 (7%)	34 (72%)	45 (92%)	2 (4%)	2 (4%)	27 (73%)	1 (3%)	9 (24%)
Trichophyton rubrum (N=24)	22 (92%)	2 (8%)[4]	-	17 (81%)	2 (10%)	2 (10%)	24 (100%)	-	-	17 (100%)	-	-

[1]S = susceptible; I = intermediate; R = resistant. Disc susceptibility results.
[2]Comprises two formally identified by DNA sequencing and 47 probable isolates based on phenotypic characteristics.
[3]All isolates with intermediate susceptibility and seven (88%) of the eight terbinafine resistant isolates were susceptible to itraconazole.
[4]Both isolates susceptible to itraconazole.

COMPETING INTERESTS
Nil.

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The historical and projected prevalence of dysphagia in Aotearoa New Zealand

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ABSTRACT

AIM: To estimate the current prevalence of dysphagia in the Aotearoa New Zealand population and to project its prevalence to 2073.

METHODS: The current prevalence of dysphagia in Aotearoa New Zealand is computed from the prevalences of the aetiologies of dysphagia combined with the rates at which the aetiologies result in dysphagia. Projected dysphagia rates use autoregressive integrated moving average forecasting techniques combined with population projections from Statistics New Zealand and estimates of current and past prevalence rates of dysphagia.

RESULTS: The prevalence of dysphagia in Aotearoa New Zealand is estimated to have been approximately 1.78% in 2020, with the biggest aetiological contributors being stroke, Alzheimer's disease and other dementias, and gastroesophageal reflux disease. These three causes made up 81.5% of all estimated dysphagia cases in 2019. The prevalence rate of dysphagia in Aotearoa New Zealand is projected to rise to 2.54%, reflecting the ageing population.

CONCLUSION: An increased prevalence of dysphagia will result in an increased healthcare burden, both from resources spent on treating dysphagia and complications stemming from undiagnosed and thus untreated dysphagia. Estimating the full extent of this increased burden is hampered by the absence of systematic, extensive and reliable records available relating to cases of dysphagia in Aotearoa New Zealand.

Dysphagia is a potentially life-threatening condition that can have severe complications, such as aspiration pneumonia, malnutrition and dehydration. Many risk factors that cause dysphagia are associated with increasing age.[1] Since the median age of the Aotearoa New Zealand population is projected to increase from the current 37 years to 47 years by 2073, this will disproportionately increase conditions such as stroke and Parkinson's disease that can cause dysphagia.[2–4] While age-related health spending will increase significantly as the population ages, what is not clear is what will happen to the economic burden from specific conditions, such as dysphagia. Delineation of the economic implications of dysphagia will offer a valuable foundation on which to forecast service delivery costs and meet the health needs of patients with this condition.

Currently, the only estimates of the general prevalence rate for dysphagia are based on a few isolated sub-group studies. One study found that the risk of dysphagia among older people in the Aotearoa New Zealand district health board community was 3.5%, with the risk increasing to 32.1% for patients in aged residential care.[5] Another found a higher risk of dysphagia in a similar cohort of aged residential care patients in Aotearoa New Zealand, at 37.1%.[6] A further study concluded that the prevalence of dysphagia in older patients newly admitted to an Aotearoa New Zealand hospital was 29.5%.[7] An Australian and New Zealand Society for Geriatric Medicine study found a lower prevalence estimate of between 7% and 21% in the community.[8] While dysphagia commonly occurs from conditions associated with the elderly, it also results from traumatic brain injuries or congenital disorders, which occur in younger age groups. As much of the literature focusses on the elderly, these figures are therefore inadequate to estimate the prevalence of dysphagia in Aotearoa New Zealand's general population. Global studies are also of little generality to Aotearoa New Zealand as they tend to be from specific population sub-groups within specific conditions known to cause dysphagia.[9–11]

This paper estimates the historical prevalence of dysphagia in Aotearoa New Zealand's population and uses this to forecast this prevalence rate over a 50-year timespan. The result of this work is available to be used to calculate projections of future clinical resource needs to treat dysphagia and to calculate projections of the economic costs

of dysphagia in an ageing Aotearoa New Zealand population.

Method

Conventional methods estimate the prevalence of a medical condition using recorded cases or estimate the number of cases and therefore the prevalence rate from representative population samples.[12–14] These are not applicable to Aotearoa New Zealand as there exists no detailed public information on the number of dysphagia cases or age-specific incidence rates of dysphagia. Similarly, little information exists about the prevalence of dysphagia in Aotearoa New Zealand representative groups. In response, the prevalence rate is estimated using the prevalences of the underlying conditions that cause dysphagia. These are then used to indirectly compute the number of historical dysphagia cases in a method similar to Brookmeyer and Gray.[12]

Method for estimating the historical prevalence rate of dysphagia

Historical case numbers of dysphagia are estimated using a flow-based model. Each year, individuals can potentially develop a condition that could cause dysphagia at a time-varying prevalence rate, with an associated time invariant probability of then developing dysphagia from that condition. The resulting numbers of dysphagia cases across all conditions are then aggregated to get a total figure. This is combined with historical population figures to calculate the annual prevalence rate of dysphagia.

This approach allows for changing demographics to affect the underlying conditions that cause dysphagia. This is because the impacts of demographic movements are reflected in the prevalence rates and case numbers of the underlying conditions that cause dysphagia, which are allowed to vary over time as demographics change. The constant condition-specific prevalence rates of dysphagia effectively imply that dysphagia developed as a secondary result of a condition is independent of demographic population changes.

Data for the prevalence of causes

Data concerning the prevalence and case numbers of conditions that cause dysphagia in Aotearoa New Zealand, except for traumatic brain injuries, are obtained from the 2019 Global Burden of Disease (GBD) Study.[15] GBD data can also be used to calculate 95% upper and lower bound estimates for each condition prevalence around their midpoint estimate, which are then used to perform a sensitivity analysis of the dysphagia prevalence estimates.[16] Another study is used to determine the number of traumatic brain injury cases in Aotearoa New Zealand each year.[17–18] This study finds that the Aotearoa New Zealand–specific age-standardised rate of existing traumatic brain injuries is 534 per 100,000, with 95% upper and lower bound estimates of 561 per 100,000 and 508 per 100,000. This rate is applied to the population each year to compute the number of traumatic brain injury cases, assuming a constant population age-standardised prevalence rate for traumatic brain injury between 1990 and 2019.

Cause-specific dysphagia prevalence data

Most of the condition-specific prevalence rates of dysphagia are obtained from a 2018 literature review on causes of dysphagia among different age groups.[19] Simple averages of the upper and lower bounds from the study are used to form the midpoint prevalence rates for each condition. These are used to form the central estimates from the method and models. Another study is used in the same way for the traumatic brain injury–specific prevalence rate of dysphagia.[10] Table 1 includes the cause of dysphagia, the GBD condition that cause is related to and the upper, lower and midpoint estimates of the condition-specific rate of dysphagia prevalence. In situations where conditions that cause dysphagia are a subcategory of a larger condition in the GBD study, a simple average prevalence rate of the subcondition rates is used to form an overall prevalence rate for that condition. For example, in the 2019 GBD Study, head and neck cancer (HNC) has one prevalence measure even though multiple forms of HNC occur and each have their own dysphagia prevalence rate.

Another important condition that causes dysphagia is gastroesophageal reflux disease (GRD).[20] This condition can cause swallowing difficulties and result in dysphagia in severe or long-term cases of GRD.[21] The 2019 GBD Study shows that GRD is relatively common in Aotearoa New Zealand, with an estimated 534,050 cases or 10.5% of the 2019 population. The GBD study unfortunately uses a broad definition of GRD and includes many mild cases that have a low risk of causing dysphagia.[22] Therefore, the GRD-specific rate of dysphagia is assumed to be represented

Table 1: Midpoint estimate of the prevalence of dysphagia among different causes with upper and lower bounds.

Cause	Associated Global Burden of Disease condition	Lower prevalence rate (%)	Upper prevalence rate (%)	Midpoint prevalence rate (%)
Stroke[19]	Stroke	25	81	53
Alzheimer 's disease[19]	Alzheimer's disease and other dementias	7	29	18
Frontotemporal dementia[19]	Alzheimer's disease and other dementias	19	57	38
Parkinson's disease[19]	Parkinson's disease	15	87	51
Multiple sclerosis[19]	Multiple sclerosis	24	34	29
Amyotrophic lateral sclerosis[19]	Motor neurone disease	86	86	86
Reflux disease[19]	Gastroesophageal reflux disease	6	50	28
Head and neck cancer (pre-treatment)[19]	Head and neck cancer	9.2	67	38.1
Head and neck cancer (post-treatment)[19]	Head and neck cancer	23	100	61.5
Oesophageal squamous cell carcinoma[19]	Oesophageal cancer	62	93	77.5
Oesophageal adenocarcinoma[19]	Oesophageal cancer	53	79	66
Anaplastic thyroid cancer[19]	Thyroid cancer	40	40	40
Traumatic brain injury[10]	Traumatic brain injury	27	30	28.5

by the reported lower estimate of 6% to avoid over-estimating the number of dysphagia cases from this condition.

Population data

Estimates of Aotearoa New Zealand's historical population are available using Statistics New Zealand's (Stats NZ) Infoshare tool[23] in each discrete year for the period from 1990 until 2019.

Method for projecting the prevalence of dysphagia

Once the historical case numbers and the prevalence rates of dysphagia have been estimated, we use an autoregressive integrated moving average (ARIMA) model to project dysphagia cases into the future.[24–26] A constant growth rate model, a linear model and a quadratic model are estimated as robustness checks.

Each model is fitted to historical data, with the number of dysphagia cases in each year as

the dependent variable and discrete time as the independent variable. This captures any impacts of changing demographics within the trend of each model through the historical case numbers and prevalence of the underlying conditions that cause dysphagia, and the rate at which individuals contract these conditions. As demographic changes are reflected in these variables, the past behaviour of the dysphagia case numbers also includes these changes. The results for each model contain the forecast of dysphagia case numbers for a particular year.

The ARIMA framework allows many attributes of a time series to be represented in a single model. The autoregressive term determines the number of lagged values of the dependent variable to include and captures how much the current value depends on what has happened in the past. The order of integration specifies the number of times the series is differenced to achieve stationarity to ensure validity of the statistical methods used to forecast the variable. The Kwiatkowski–Phillips–Schmidt–Shin (KPSS) test is used to check for the presence of a unit root.[27] This is complemented with a visual analysis of the autocorrelation function to determine the degree of stationarity. The minimum Akaike information criterion (AIC) determines the level of differencing required to achieve stationarity. When forecasting the number of dysphagia cases, any future error terms are replaced with zero and the previous steps are used to determine the number of lagged values of the dependent variable and the error term, which are used with the computed regression coefficients to provide a forecasted value at each step.

The first comparison model uses the historical growth rate of dysphagia case numbers to compute the geometric average growth rate in the dysphagia case numbers that have occurred historically. The second uses historical dysphagia cases as a dependent variable with discrete time as the independent variable. Estimates from this linear model are then used to forecast the prevalence rate of dysphagia by extrapolation of the linear trend into the future for which population projections exist. The quadratic regression comparison model uses ordinary least squares (OLS) fitted to historical dysphagia cases with linear and quadratic time independent variables. This incorporates any potential quadratic trend resulting from the growth in the number of dysphagia cases. Extrapolation uses estimates of the coefficients from the quadratic model as well as the future time period parameters for forecasting.

Finally, the model results are combined with population projections from Stats NZ to estimate the future prevalence rates of dysphagia. Aotearoa New Zealand population projections are available for 2020, 2023 and every 5 years following 2023 until 2073 using Stats NZ's NZ.Stat tool.[2]

Results

The results are expressed as estimates of the number of dysphagia cases and of the prevalence rate of dysphagia. While these are linked, the rate of prevalence for dysphagia is based on forecasts of the underlying case numbers in order to capture demographic changes rather than the rate of prevalence itself. Thus, output and regression coefficients for each model correspond to changes in the number of dysphagia cases over time.

Historical results

The estimated historical Aotearoa New Zealand dysphagia prevalence rate shows a steady increase over time, as shown in Figure 1. Dysphagia is estimated to have affected 55,162 individuals in 1990 (a prevalence rate of 1.58%) increasing to 89,253 individuals by 2019 (a prevalence rate of 1.76%). The estimated number of cases has risen by 61.8% and the prevalence rate increased by 0.18 percentage points. Yearly growth in the number of cases varies between 0.93% and 2.07%.

A 5-year breakdown of the estimated number of dysphagia cases and the prevalence rate is

Table 2: Five-year breakdown of historical dysphagia cases and prevalence.

Year	1990	1995	2000	2005	2010	2015	2019
Number of dysphagia cases	55,162	58,676	63,656	69,253	75,952	82,700	89,253
Dysphagia prevalence rate (%)	1.58	1.58	1.64	1.66	1.73	1.77	1.76

Figure 1: Estimated historical dysphagia prevalence rate and case numbers in Aotearoa New Zealand.

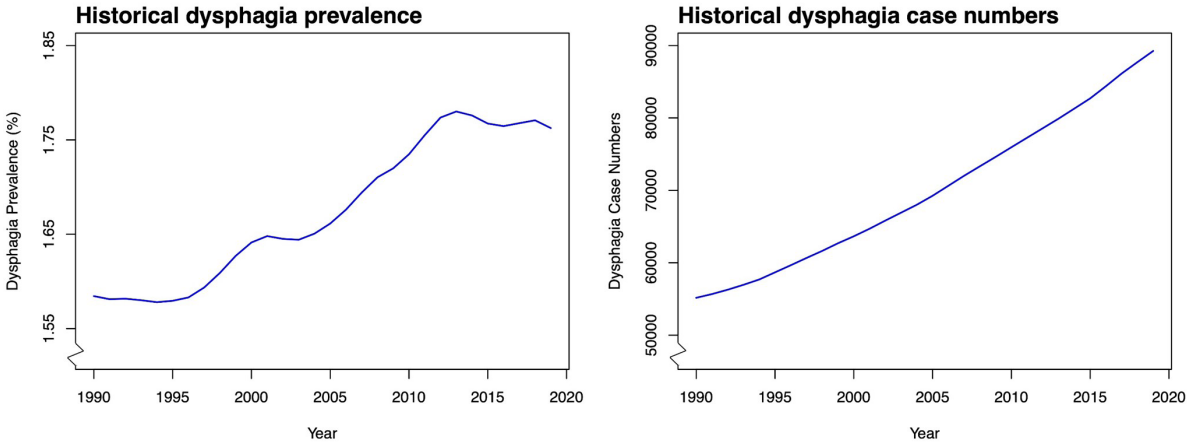


Figure 2: Forecasts of dysphagia prevalence rate and case numbers in Aotearoa New Zealand.

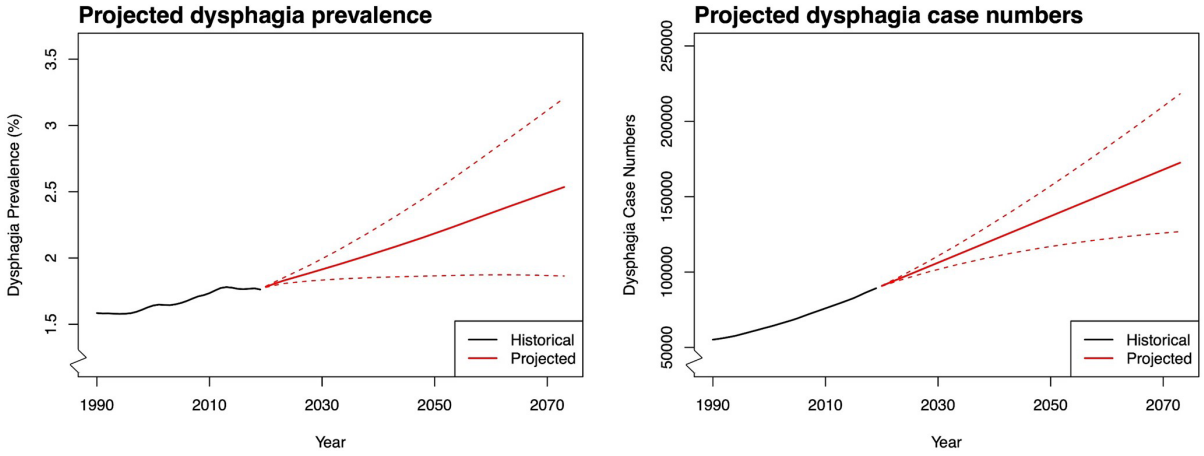


Figure 3: Forecasts of dysphagia prevalence rates and case numbers by model.

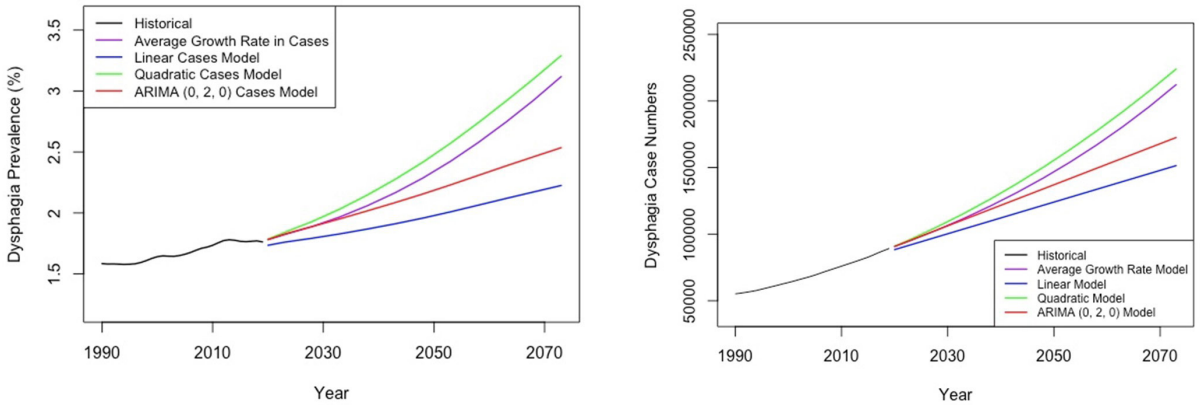
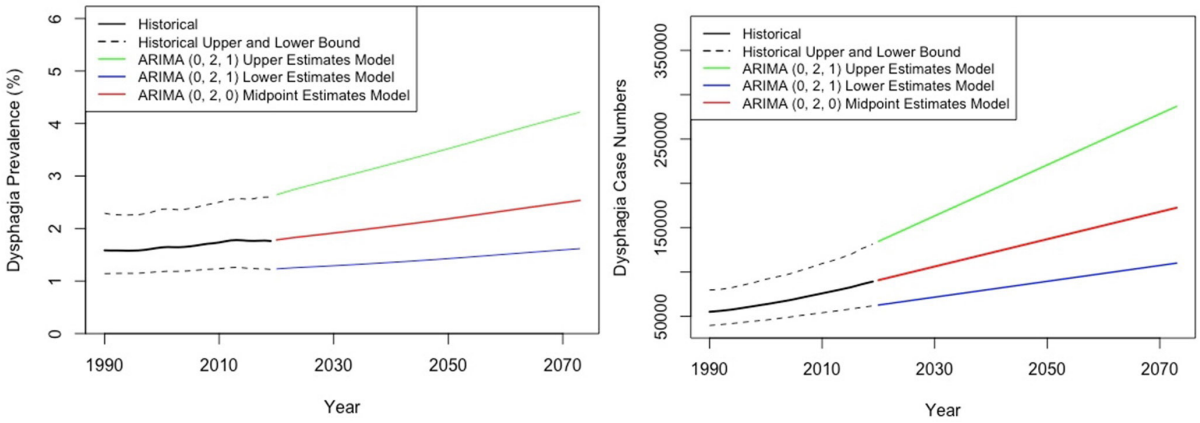


Figure 4: Forecasts of dysphagia prevalence rates and case numbers using ARIMA models on lower, midpoint and upper values of independent variables.



shown in Table 2. While the estimated number of past dysphagia cases shows an exponential trend, the historical population growth rate in Aotearoa New Zealand varies over time. This results in the rate of dysphagia prevalence rising over certain periods and remaining relatively stable during others.

Forecasted results

The ARIMA model is the main model used for forecasting the number of dysphagia cases. In testing the historical case numbers for stationarity, the KPSS test is only accepted (p-value >0.1) at the second difference, which is confirmed by analysis of the autocorrelation function. Therefore, a second difference (order 2) ARIMA model is used for forecasting. Furthermore, the AIC is lowest (AIC=339.56) with no moving average or autoregressive terms.

Figure 2 displays the forecasted prevalence rate and case numbers of dysphagia, plus 95% uncertainty intervals (dashed lines), from the fitted ARIMA (0, 2, 0) model. Forecasted case numbers and prevalence rate values are in Table 3. The prevalence rate is forecast to rise to approximately 2.2% by 2050, with over 130,000 individuals affected by dysphagia. This rises to an estimated 172,529 individuals by 2073, or just over 2.5% of the general Aotearoa New Zealand population. This represents an increase of 93.3% over the current number and a 0.78 percentage point increase in the prevalence rate. The case numbers display exponential growth, similar to what is seen historically. The uncertainty intervals become wider as time progresses, owing to the longer time horizon over which forecasting takes place.

The forecasts from the other three models show a similar pattern for both the forecast numbers and prevalence rates of dysphagia. Figure 3 shows a comparison of the projected prevalence rate and case numbers of the main ARIMA model with the alternative models (Appendix Table 1 and 2 contain side-by-side comparisons of the numbers of cases and prevalence rates).

There is little difference in projected prevalence rates between each model for the first 5–10 years. However, the difference between the forecasted prevalence rates widens as the forecast horizon lengthens. The quadratic model produces the highest forecast estimates and is distinctly non-linear in nature. The average growth rate model shows similar characteristics. Both models produce a forecast of the prevalence rate above the ARIMA model, especially later in the time horizon. In contrast, the linear model produces lower predictions for the future prevalence rate of dysphagia in Aotearoa New Zealand than the ARIMA model.

Sensitivity analysis of the ARIMA forecasts of the prevalence rate of dysphagia

Sensitivity analysis is used to assess the robustness of the forecasts of dysphagia obtained from the main ARIMA model. This involves recalculating historical dysphagia case numbers, fitting new ARIMA models and then making new forecasts based on them. This uses the 95% confidence lower and upper bounds for the historical case numbers for each condition causing dysphagia provided in the 2019 GBD data. The most efficient model for all scenarios based on the AIC involves two orders of differencing. However, each now includes one lagged error term. Forecasts of the number of dysphagia cases and prevalence rates with their upper and lower bounds are calculated

Table 3: ARIMA (0, 2, 0) forecast of dysphagia case numbers and prevalence rate (95% lower and upper bounds in brackets).

Year	2020	2023	2028	2033	2038	2043	2048	2053	2058	2063	2068	2073
Forecasted number of dysphagia cases	90,795 (90,598–90,992)	95,421 (94,344–96,499)	103,132 (99,811–106,453)	110,843 (104,576–117,110)	118,554 (108,777–128,330)	126,264 (112,494–140,035)	133,975 (115,780–152,170)	141,686 (118,673–164,699)	149,397 (121,203–177,590)	157,108 (123,394–190,821)	164,818 (125,266–204,371)	172,529 (126,835–218,224)
Forecasted dysphagia prevalence rate (%)	1.78 (1.78–1.79)	1.83 (1.81–1.85)	1.89 (1.83–1.95)	1.95 (1.84–2.06)	2.02 (1.85–2.18)	2.09 (1.86–2.31)	2.16 (1.86–2.45)	2.23 (1.87–2.60)	2.31 (1.87–2.74)	2.39 (1.87–2.90)	2.46 (1.87–3.05)	2.54 (1.86–3.21)

for each estimated model, shown in Figure 4. Appendix Table 3 contains the numbers of cases and prevalence rates.

Each scenario predicts that the prevalence of dysphagia in Aotearoa New Zealand will steadily increase. Additionally, the sensitivity analysis shows that the results corresponding to the lower bounds of the explanatory variables are closer to the midpoint outcomes than the results corresponding to the upper bounds. This is a result of the non-symmetrical 95% confidence intervals reported in the GBD study.

Discussion

This study has addressed a major shortcoming about dysphagia in Aotearoa New Zealand—a lack of information about its general prevalence, and about its historical and likely future trends. We estimate the prevalence of dysphagia in Aotearoa New Zealand to be approximately 1.78% in 2020. Over 81.5% of the total number of estimated dysphagia cases are due to Alzheimer's disease and other dementias, and GRD. The analysis shows that the historical prevalence rate has been increasing and is likely to increase significantly over the next 50 years. This trajectory reflects an ageing Aotearoa New Zealand population, leading to the fastest growing causes of dysphagia being thyroid cancer, oesophageal cancer and Alzheimer's disease and other dementias.

In terms of related literature, a recently published related study found similar forecast outcomes, although it used a different approach.[28] One point of difference is that our approach allows for estimates of historical case numbers and prevalence rates of dysphagia. Another key difference is that our method results in higher forecasted New Zealand dysphagia case numbers and prevalence rates out to the mid-2040s. This is because our approach covers more conditions that cause dysphagia, and thus incorporates more complete effects of population demographic changes. After this period, the impact of an ageing population dominates other factors and our forecasts are similar.

While our study is an important first step, its limitation is that it estimates the dysphagia prevalence indirectly. We used an indirect method to estimate the prevalence of dysphagia because there exist no systematic, extensive and reliable records about dysphagia in Aotearoa New Zealand. This suggests a need for a common national data framework for defining relevant medical conditions and practices, for collecting and storing data of all medical conditions and practices and for making data available to researchers to analyse trends and needs within the Aotearoa New Zealand health system.

Regardless of whether the actual rate is a bit above or below our estimate, the overall magnitude and trend of the prevalence rate are still valid. The finding that the prevalence rate of dysphagia in Aotearoa New Zealand is likely to increase significantly highlights that the associated healthcare burden will likely increase substantially. Some of this will be in terms of resources required for the treatment of dysphagia, in which case advancing treatment technologies and methods now could avoid significant treatment costs in the future. Some of the burden will be from treating complications in patients from conditions resulting from undiagnosed dysphagia, such as aspiration pneumonia. A 2018 meta-analysis by Attrill et al. documented that a dysphagia case created a further burden on healthcare costs of 40.36%.[29] Undiagnosed dysphagia creates an even higher eventual burden per case. Investing resources to better recognise and diagnose dysphagia would allow for saving resources from avoidance of complications caused from undiagnosed dysphagia. Wilson and Howe investigated cost-effectiveness of the videofluoroscopic swallowing study compared to clinical methods for evaluation of swallowing related to stroke. Incorporation of an early radiographic exam for dysphagia was more effective and less costly than clinical swallowing evaluation alone.[30] Finally, some of this burden will be borne through a lower quality of life and premature death if dysphagia is undiagnosed or treatment is delayed. Developing better ways to recognise and diagnose dysphagia and advancing treatment technologies and methods would mean those affected have a higher quality of life and longer lifespan.

COMPETING INTERESTS
MLH is a founding Board Member of SwalTech Ltd and a Board Member of Capistrano Charitable Trust.

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Appendix

Appendix Table 1: Forecasted dysphagia case numbers for ARIMA, linear, quadratic and historical growth models.

Year	2020	2023	2028	2033	2038	2043	2048	2053	2058	2063	2068	2073
ARIMA	90,954	96,126	105,373	115,406	126,223	137,824	150,211	163,382	177,338	192,079	207,605	223,915
Linear	88,359	91,930	97,881	103,833	109,785	115,736	121,688	127,639	133,591	139,542	145,494	151,445
Quadratic	90,954	96,126	105,373	115,406	126,223	137,824	150,211	163,382	177,338	192,079	207,605	223,915
Historical growth	90,696	95,167	103,114	111,724	121,054	131,162	142,115	153,982	166,840	180,772	195,867	212,223

Appendix Table 2: Forecasted dysphagia prevalence rates for ARIMA, linear, quadratic and historical growth models.

Year	2020	2023	2028	2033	2038	2043	2048	2053	2058	2063	2068	2073
ARIMA	1.78	1.82	1.89	1.97	2.06	2.17	2.29	2.42	2.58	2.74	2.92	3.12
Linear	1.73	1.76	1.79	1.83	1.87	1.91	1.96	2.01	2.06	2.12	2.17	2.23
Quadratic	1.79	1.84	1.93	2.03	2.15	2.28	2.42	2.57	2.74	2.92	3.1	3.29
Historical growth	1.78	1.82	1.89	1.97	2.06	2.17	2.29	2.42	2.58	2.74	2.92	3.12

Appendix Table 3: Forecasts of dysphagia case numbers and prevalence rates using ARIMA models on midpoint, lower and upper values of independent variables.

Year	2020	2023	2028	2033	2038	2043	2048	2053	2058	2063	2068	2073
Midpoint case numbers forecast (prevalence)	90,795 (1.78%)	95,421 (1.83%)	103,132 (1.89%)	110,843 (1.95%)	118,554 (2.02%)	126,264 (2.09%)	133,975 (2.16%)	141,686 (2.23%)	149,397 (2.31%)	157,108 (2.39%)	164,818 (2.46%)	172,529 (2.54%)
Lower case numbers forecast (prevalence)	55,759 (1.09%)	58,149 (1.11%)	62,134 (1.14%)	66,118 (1.16%)	70,103 (1.19%)	74,087 (1.22%)	78,071 (1.26%)	82,056 (1.29%)	86,040 (1.33%)	90,024 (1.37%)	94,009 (1.40%)	97,993 (1.44%)
Upper case numbers forecast (prevalence)	135,306 (2.66%)	143,907 (2.76%)	158,242 (2.90%)	172,576 (3.04%)	186,911 (3.18%)	201,245 (3.32%)	215,580 (3.47%)	229,914 (3.62%)	244,249 (3.77%)	258,583 (3.93%)	272,918 (4.07%)	287,252 (4.22%)

Hepatitis C virus seroprevalence in defined populations in New Zealand: data from a general practice–based screening programme

Ho Tuan Tiong, Arlo Upton, Angelle Lockie, Kirsty Moore, Catherine A M Stedman

ABSTRACT

AIM: To assess the hepatitis C virus (HCV) seroprevalence data for defined regions in New Zealand.

METHODS: Email or mobile phone text invitations were sent out to adults enrolled with three participating general practices in different parts of New Zealand. Patients who provided informed consent were instructed to self-present for HCV blood tests. Patients with positive HCV antibodies had reflex testing of HCV antigen and ribonucleic acid (RNA) viral load.

RESULTS: In total, 26,247 invitations were issued. Of these, 1,368 (5.2%) people gave informed consent and 1,021 patients (3.9%) had HCV blood tests. Ten out of 1,021 (0.98%; 95% confidence interval [CI] 0.51–1.82%) tested positive for HCV antibodies, of whom two (0.2%; 95% CI <0.01–0.76%) had positive antigen and elevated RNA viral load. The proportion of NZ Māori and Pacific people was low, at 3.8% and 0.4%, respectively. Volunteers with a high deprivation index were under-represented (3% from New Zealand Index of Deprivation deciles 9 and 10).

CONCLUSIONS: The HCV viraemia prevalence in this general practice–based screening programme is 0.2%, which is lower than previous estimates. This may have implications for appropriate resource allocations and the determination of the best strategies to find new HCV infections. Participation rates of people with high deprivation indexes or who were NZ Māori and Pacific people were low, suggesting that a tailored screening approach is needed.

Chronic hepatitis C virus (HCV) infection results in significant increases in morbidity and mortality from end-stage liver disease and hepatocellular carcinoma (HCC), as well as extrahepatic manifestations including cryoglobulinaemic vasculitis, chronic lethargy, skin conditions and increased risk of diabetes mellitus and lymphoma. In New Zealand, chronic HCV infection has been a leading indication for liver transplantation.[1]

Oral direct-acting antiviral therapies can cure almost all people with chronic HCV infection.[2] These medicines are significantly more tolerable, have shorter durations and are more efficacious than past therapies, making elimination of HCV infection from New Zealand a possibility, with major benefits for both individual health and the overall health system. New Zealand is a signatory to the World Health Organization's (WHO) goal of eliminating viral hepatitis by 2030.

To achieve HCV elimination, all individuals with HCV infection need to be identified and treated. In an individual with positive HCV antibody, the presence of HCV antigen and HCV (ribonucleic acid) RNA confirms active chronic HCV infection; absence of HCV antigen and HCV RNA indicates past infection.[3] New Zealand currently has no universal screening programme for HCV infection; testing is usually performed based on a risk factor assessment. Important risk factors associated with chronic HCV infection include history of injecting drug use, unsafe therapeutic injections, transfusion of blood products and organ transplantation from infected donors and occupational exposure to blood (primarily contaminated needle sticks).[4] However, this approach is missing some people with infection, as demonstrated by data from New Zealand's national tertiary HCC service, where 28% of patients with HCC related to chronic HCV received the diagnosis of advanced HCC prior to diagnosis of HCV.[5] Universal screening has been shown to be cost-effective in other healthcare settings,[6] but it is unclear if this is the case for New Zealand. There is a lack of robust epidemiological data for New Zealand, so a comprehensive evaluation of the potential economic and public health costs and benefits of universal screening cannot be undertaken. We also have no registry for chronic HCV;

therefore, the retesting of people with known past infection would reduce cost effectiveness of any screening programme.

The global prevalence of individuals with HCV viraemia from a 2020 modelling study was reported at 0.7%.[7] The same modelling study estimated a New Zealand viraemic prevalence of 0.9% in 2020. This number is similar to modelling undertaken by local experts in 2014, equating to roughly 45,000 individuals with HCV infections in New Zealand.[8] However, there is evidence these numbers may be an over-estimate. For instance, only 29 cases of acute HCV were detected by laboratories and notified nation-wide in 2020.[9] Also, unpublished Auckland community laboratory data indicate that approximately two-thirds of patients with positive HCV antibody tests have previous positive tests (personal communication, in an email from Dr A Upton, clinical microbiologist, Southern Community Laboratories, 10 June 2020). This raises the following possibilities: firstly, patients with chronic HCV infection are not accessing healthcare, and the current testing is targeting the wrong population; and/or secondly, the estimate of 45,000 infected New Zealanders is an over-estimate. Both these scenarios will result in inappropriate estimation and misallocation of resources for HCV elimination in New Zealand.

In contrast, a 2015 study in Dunedin, New Zealand, among patients aged 40–59 years presenting for community and hospital blood tests, found an HCV antibody seroprevalence of 4%. The study included a questionnaire about HCV infection that found significant gaps in knowledge among randomly selected individuals in Dunedin.[10] The finding of relatively high antibody seroprevalence among the age groups studied is consistent with the current understanding of HCV epidemiology. In addition, the findings may point to variable prevalence in different regions of New Zealand. However, this study did not measure HCV viraemia to separate active chronic infection from past infections. Also, data from a recent study using point-of-care HCV antibody testing on a group of construction workers in Christchurch, New Zealand showed an HCV antibody prevalence of 1.3% out of the 234 participants, all of whom also had positive HCV RNA.[11]

The current study has been designed to assess the prevalence of HCV infection based on community screening in defined regions to improve estimates of the HCV burden in New Zealand. The study also evaluates the screening uptake of a primary care–based HCV screening approach that utilises phlebotomy. These data could help determine appropriate methods to identify HCV-infected people in New Zealand, inform appropriate future resource allocation and contribute to overall strategies for HCV elimination.

Methods

The study design is a cross-sectional observational study where all adults enrolled with participating general practices were invited to have a phlebotomy for HCV antibody testing with reflex HCV RNA and antigen testing for antibody positive cases. Three general practices participated in this study.

In order to minimise introduction of bias due to location, socio-economic factors and ethnicity, we identified three large medical practices located in areas that serve a mixed population, incorporating regional, urban and suburban populations (Christchurch and Motueka in the South Island and New Plymouth in the North Island) and avoiding practices with potentially enriched at-risk populations (e.g., those providing opioid substitution services). Practices were also required to have the appropriate IT support and capacity to manage the additional study-related workload.

Standardised email or mobile phone text invitations were sent to all enrolled adult clients aged 18 and above in the participating practices. They were provided links to an electronic patient information sheet and consent form on an electronic data capture system software (REDCap). Those who provided consent were instructed to self-present to a local laboratory for a phlebotomy after they completed the consent form. Additionally, posters were displayed in practice waiting areas to allow the option of enrolment of casual (non-enrolled) patients who may be attending the practice for healthcare, and paper-based consent forms were available if requested by patients. An email reminder was sent 1 month after the initial invitation to people who had provided consent but had not yet presented for a phlebotomy.

HCV antibody serology was performed on all participant samples in the study, regardless of prior test results. Testing was performed on the Abbott ARCHITECT platform in a two-step immunoassay, using chemiluminescent microparticle immunoassay technology, for the qualitative detection of anti-HCV in human serum and plasma. Where the HCV antibody was positive (reactive), the samples were reflexed

to HCV antigen testing utilising the ARCHITECT HCV Ag assay, which uses chemiluminescent microparticle immunoassay for the quantitative determination of hepatitis C core antigen in human serum and plasma. HCV RNA viral load testing was also performed on samples with a positive HCV antibody. No further testing was performed on samples with a negative HCV antibody result.

All results were entered into laboratory test repositories, as per usual practice, and were communicated by electronic notification to general practitioners. Additional specific communication was undertaken to general practitioners about positive HCV viral load results to ensure that the general practitioner would arrange appropriate assessment and HCV antiviral treatment for the participant according to standard of care protocols. Results were communicated to study participants via a unique password-protected email, with individual access details provided to participants when they presented for the blood test. There was no further follow-up from the study for participants with negative HCV antibody results, or those with positive HCV antibody but with negative HCV antigen and negative HCV viral load results.

For data analysis, the primary end point was the percentage of positive HCV antibody and/or HCV RNA results in the participating general practice populations. The secondary end point was the percentage of screening uptake in these populations. Basic demographic data were collected from the general practices and the New Zealand Ministry of Health statistics database. Participants were included in the analysis if they were 1) adults aged 18 years or older enrolled in or attending the participating primary care practices, and 2) provided consent for phlebotomy and HCV testing. People were excluded if they were unable or unwilling to provide informed consent.

It was planned to invite a minimum of 10,000 individuals with provision to invite up to 30,000 individuals from three medical practices, with a scheduled data analysis after a minimum enrolment of 1,000 individuals for HCV antibody testing. Enrolment was planned to be allowed to continue for 12 months to a maximum of 5,000 individuals. The minimum sample size of 1,000 enrolments was based on the stated sensitivity of the test as 99.1% and specificity of 99.6%.[12] For an estimated prevalence in the population tested of 1%, at a 95% confidence level (CI), the precision estimate interval width would be 0.013 (giving a lower limit of 0.005 and upper limit of 0.018 for the prevalence).

This study was approved by the New Zealand Health and Disability Ethics Committee (approval reference: 20/NTB/261).

Results

Between February 2021 and August 2022, a total of 26,247 invitations were issued from the three participating general practices. The duration of recruitment was extended beyond the planned 12 months because of disruption to primary healthcare systems caused by the COVID-19 pandemic. A total of 1,368 (5.2%) individuals provided electronic consent, and 1,021 (3.9%) underwent a phlebotomy (Figure 1). No patients participated utilising written paper consent. Of the 1,021 who presented for phlebotomy and make up the population of interest, 10 (0.98%; 95% CI 0.51–1.82%) tested positive for HCV antibody. Two patients (0.2%; 95% CI <0.01–0.76%) tested positive for HCV RNA and HCV antigen and eight (0.8%) tested negative for HCV RNA (Figure 1). Out of the eight who tested negative for HCV RNA, three were previously known to have a positive HCV antibody.

The majority of participants were female (59.4%) in the 50–79-year age group (68.2%) with a median age of 59 years (Figure 2). Participants overwhelmingly self-identified as NZ European or Other European (83.2%), with the proportion identifying as NZ Māori or Pacific low at 3.8% and 0.4%, respectively (Figure 3). New Zealand Index of Deprivation deciles (NZDep) data are shown in Figure 4, demonstrating a low representation of participants with a high deprivation index (3% from deciles 9 and 10).

Discussion

The prevalence of positive HCV antibody in the combined group of participants from all three participating general practices was 0.98% (95% CI 0.51–1.82%) with 0.2% (95% CI <0.01–0.76%) positive HCV antigen and viraemia rate. This is lower than the estimates of HCV viraemia reported by the modelling performed by Polaris Observatory, at 1.1% and 0.9% in 2015 and 2020, respectively.[7] Similarly, this rate of positive HCV antibody is lower than results from the 2015 study in Dunedin, New Zealand, which tested patients aged 40–59 years presenting for community and hospital blood tests and found an antibody seroprevalence of 4%.[10] However, as noted, the

Figure 1: Study flowchart.

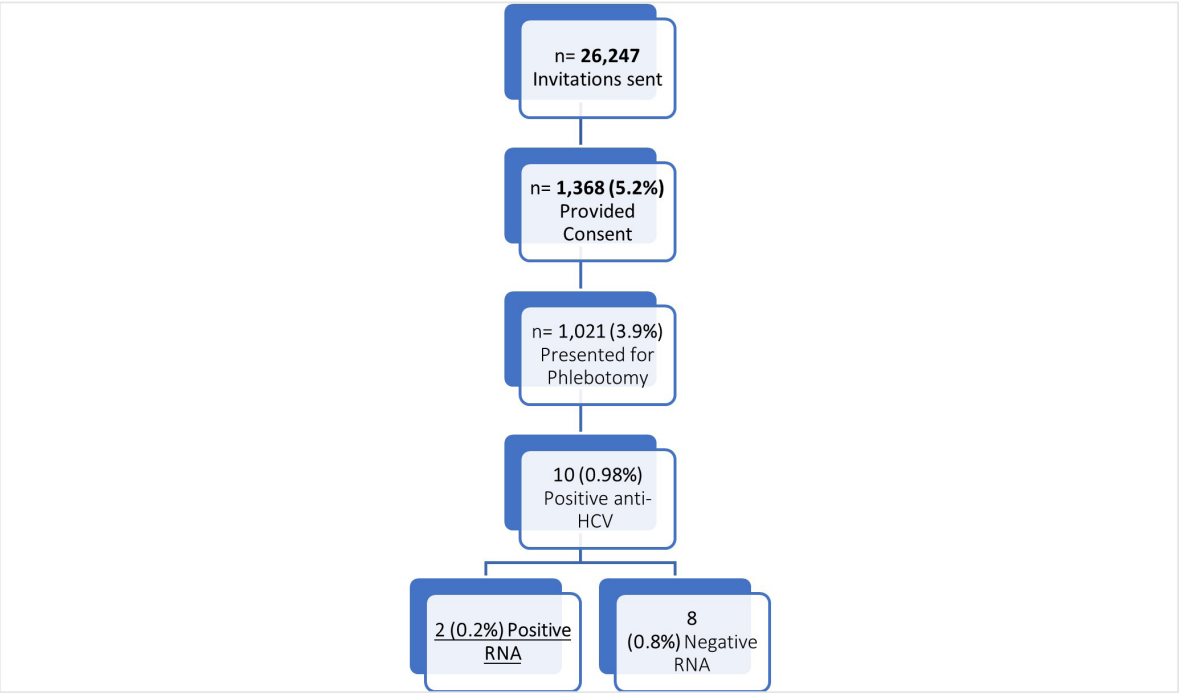


Figure 2: Age of participants (n=1,021).

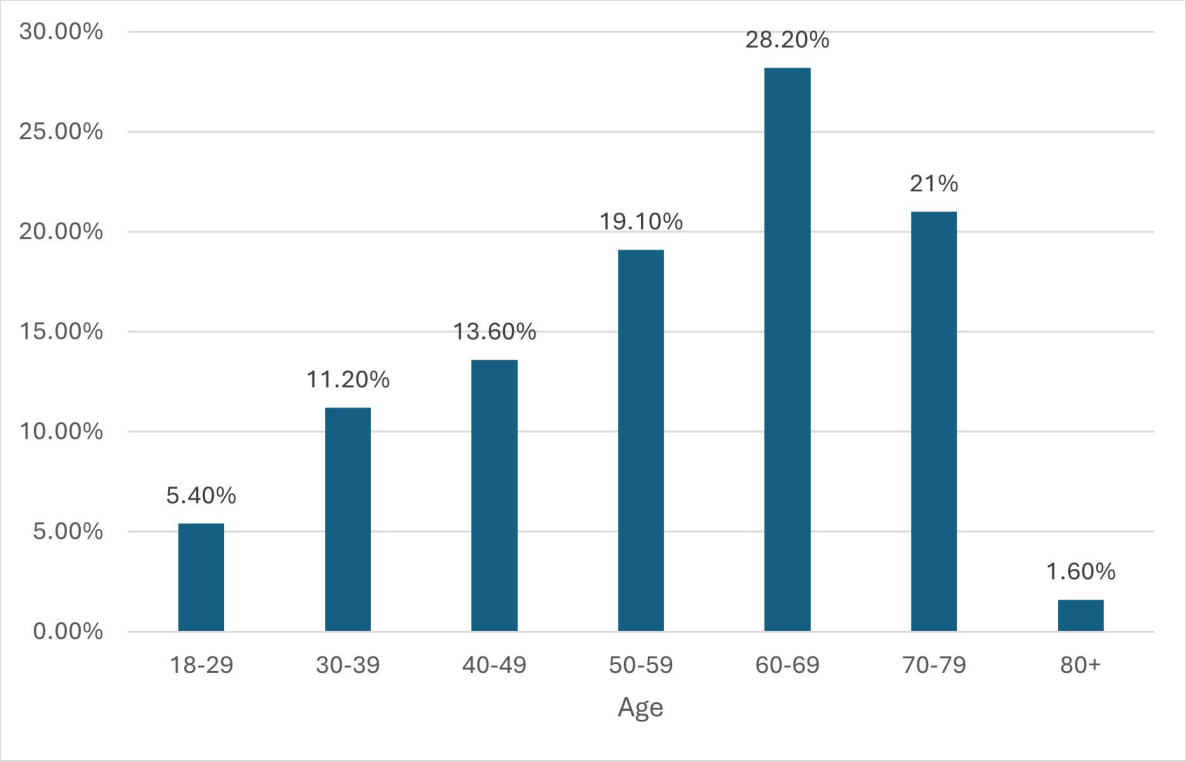


Figure 3: Ethnicity of participants (n=1,021).

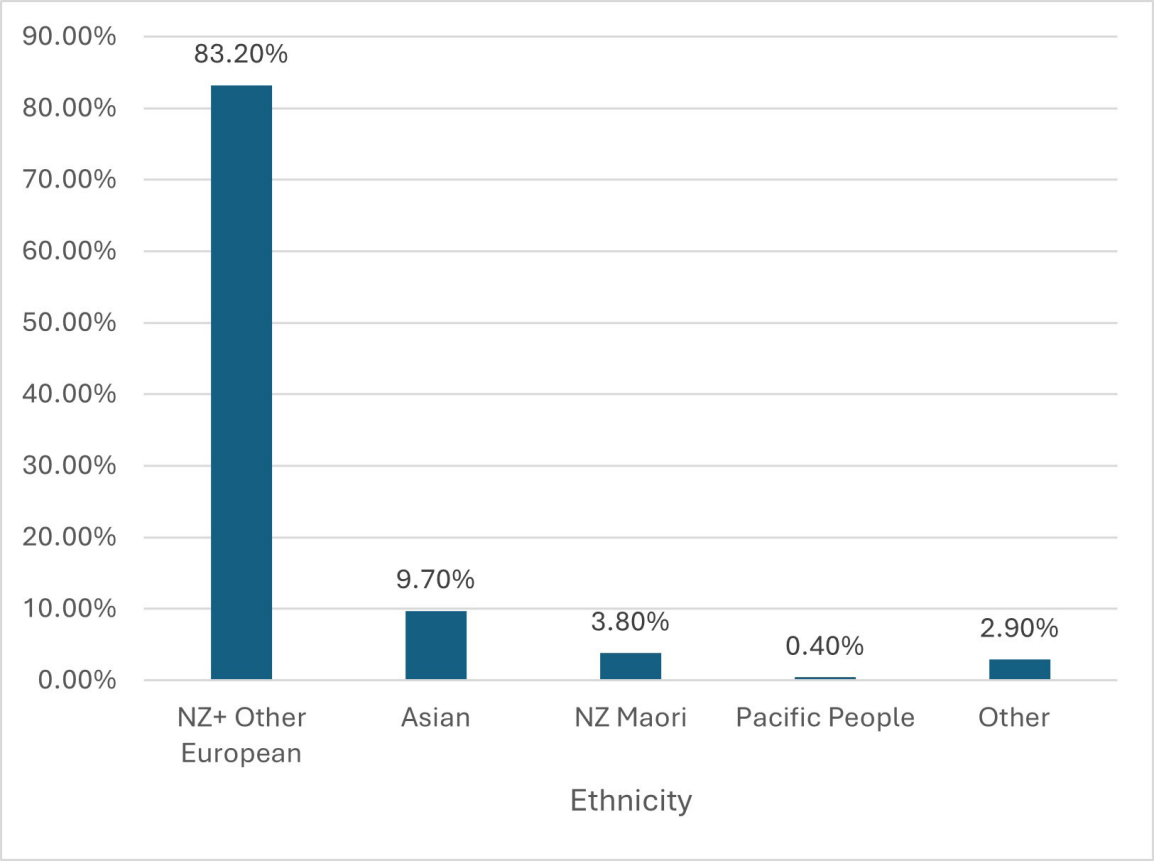
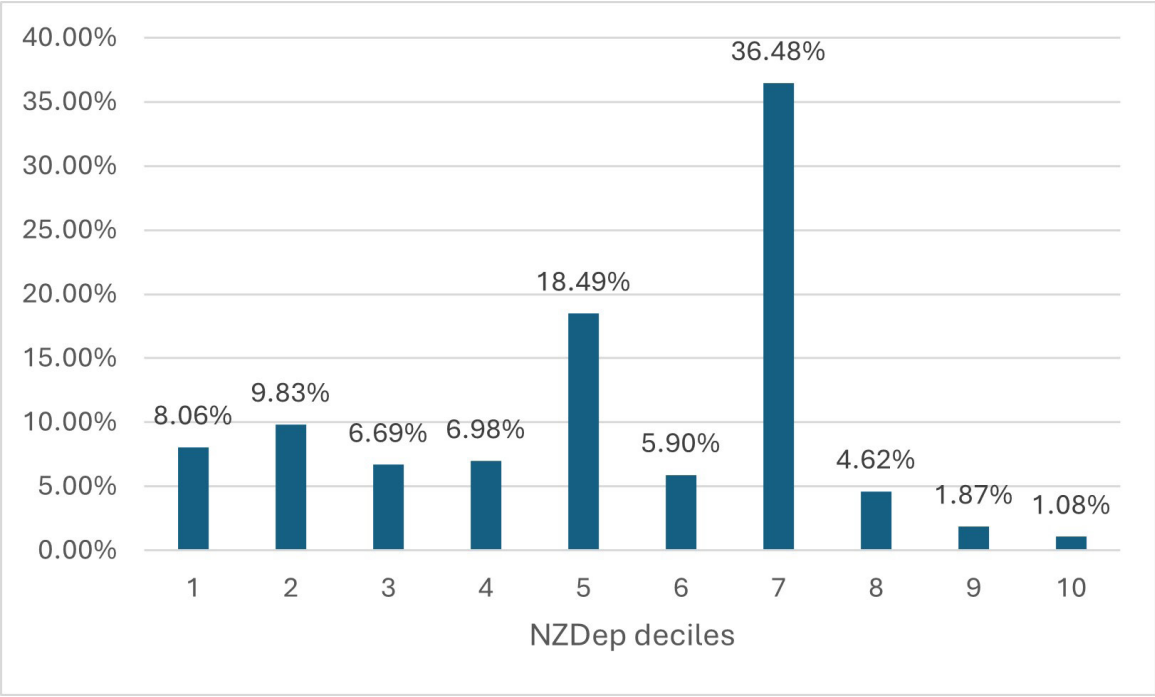


Figure 4: New Zealand Index of Deprivation deciles of participants (n=1,021).



Dunedin study did not test for the HCV antigen or viraemia so would be expected to over-estimate of the prevalence of active infection, and the study population selection differed from our study by focussing on a specific age group of people who were presenting for blood tests for other reasons.

This is the first study in New Zealand to estimate the HCV prevalence from an unselected adult population via primary care. We obtained real-world data from a group of participants, regardless of risk factors, rather than focussing on high-risk groups (e.g., prison populations, age cohort screening). We recruited participants from three general practices across different regions of New Zealand to obtain a broad representation of the general New Zealand population.

However, caution is required to interpret our data as there are limitations. Foremost, the overall participation rate from everyone who received email and text invitations is low at 3.9%. Potential reasons for this include the requirement for phlebotomy, potential for stigma associated with a hepatitis study, and also an individual's perception that they are not at risk for hepatitis C. The low participation rate could affect the representativeness of our volunteer group to the general New Zealand population. There is potential this could be an enriched group including participants who are aware they have risk factors for HCV infection and may therefore be more likely to volunteer for this study. Alternatively, the study could be affected by healthy volunteer bias, where those who volunteered were at a lower risk of having chronic HCV compared to the general population; further, evidence from some studies suggests people who inject drugs have low rates of engagement with primary care;[13,14] therefore, they would be unlikely to be captured in a study through general practice and would be less represented in our study. Although this study was moderately effective in targeting the age cohort of 50–79 years, which made up more than two-thirds of our volunteer population, and overseas data has suggested that this age cohort (people born between 1945 and 1965) made up the majority of people with chronic HCV infections,[15] the HCV prevalence is still low in our participants. However, more recent United States Centers of Disease Control and Prevention (CDC) data suggest that the infection rate is also high within the age group of 20–39 years.[16] Overall, it is difficult to predict what the net effect on our HCV estimate is from the alternatives and combination of the different factors mentioned above.

Secondly, some demographic groups are under-represented in our volunteer population. With regards to ethnicity, representation of NZ Māori and Pacific people was low at 3.8% and 0.4%, respectively. This is lower than the estimated proportion of these ethnicities in these regions as reported by the 2018 New Zealand Census, which ranged from 8.7% to 27.6% for NZ Māori and 1.5% to 3.8% for Pacific people.[17,18] With respect to the deprivation index, there is a low representation of participants with high deprivation index, with only 3% of participants from deciles 9 and 10. This is not an unexpected finding as one of the three general practices included provided the deprivation index data for their patients, which showed only 8.15% of their patients were from the two most deprived deciles (no further deprivation index data were available from the other general practices).

This study provides the first real-world New Zealand data of HCV screening uptake in response to electronic (email and text) and poster invitations for phlebotomy using a primary care–based universal invitation to patients from selected general practices. Lower screening uptake among NZ Māori and Pacific people and a low participation rate from people with high deprivation index suggest that a more targeted screening approach is needed to engage these groups of people. This may include utilising community-based point-of-care testing methods and partnership with local iwi (Māori tribes) or community leaders.

Conclusion

The HCV viraemia prevalence in this general practice–based screening programme is 0.2%, which is lower than previous estimates of New Zealand HCV infection prevalence. However, the prevalence estimate needs to be interpreted with caution, due to the risk of bias affecting the estimate.

These data may have implications for appropriate resource allocations and the determination of the best strategies to find undiagnosed HCV infections in New Zealand. A cost-effective analysis needs to be carried out to determine if universal screening is cost-effective in the New Zealand healthcare setting.

Low participation rates of people with high deprivation index, NZ Māori and Pacific people suggest that a tailored screening approach is needed to engage these populations.

COMPETING INTERESTS
HT has no relevant interests to declare. CS has received Speaker bureau fee from AbbVie. AL is an employee of AbbVie and owns AbbVie stock.
AbbVie sponsored the study, contributed to the design, participated in writing, reviewed and approved of the final version of this manuscript. No honoraria or payments were made for authorship. Abbott provided the diagnostic kits for hepatitis C virus antigen testing.

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A descriptive observational study of B12 testing during pregnancy and infancy in New Zealand and suggested guidance for testing and treatment

Asher Henry, Natasha Heather, Campbell Kyle, Teresa Gudex, Dianne Webster, Callum Wilson

ABSTRACT

AIMS: Severe B12 deficiency is harmful to infants. This study describes the recent detection and treatment rates of antenatal and infant B12 deficiency in the Auckland–Northland region.

METHOD: Regional laboratory data on serum B12 levels were analysed. B12 deficient infants and pregnant women were identified and paired with their corresponding mother or infant, followed by a review of electronic health records.

RESULTS: Testing incidence was low in infants (5 per 1,000 infants per year). Among 529 infants tested over 5 years, 6% exhibited B12 deficiency (<148pmol/L). Antenatal B12 deficiency was found in 16% of 6,365 pregnant women tested over 1 year, with *high-risk* deficiency (<100pmol/L) found in 2%. Both infants and mothers with B12 deficiency had suboptimal rates of adequate treatment. Among infants of *high-risk* B12 deficient pregnancies, only 1% had serum B12 tested despite being at high risk of infant B12 deficiency.

CONCLUSION: Current guidelines and testing practices in Auckland–Northland inadequately detect and treat B12 deficiency in pregnancy and infancy. A risk-based screening approach is best suited to detect infants at risk of severe deficiency. Antenatal and postnatal recommendations for B12 testing and treatment of mothers and infants are made, along with nutritional advice in pregnancy and infancy.

B12 is an essential vitamin crucial to human neurodevelopment that is obtained almost exclusively from dietary animal products, fortified foods or supplementation. The mother is an infant's sole source of B12, provided antenatally via active transport across the placenta, and postnatally in breastmilk, until B12-rich foods or fortified milk formula are introduced to the infant's diet.[1] Low maternal serum B12 status correlates with increased risk of infant B12 deficiency.[1,2]

The classic infant presentation of B12 deficiency occurs in the exclusively breastfed infant of a B12 deficient mother, manifesting between 4 and 9 months old as the infant's low B12 stores, already inadequate at birth following deficiency *in utero*, are steadily depleted and not replaced in the diet. In severe deficiency, the infant may present with anaemic pallor and fatigue, developmental delay, irritability, gastrointestinal symptoms, feeding difficulty and faltering growth. A high index of suspicion is required by the clinician, as these symptoms are common and nonspecific in infants, but the diagnosis is easily confirmed by identifying low serum B12. Deficiency is treated with supplementation, and symptoms rapidly resolve with early intervention, but if left untreated the neurological consequences can be irreversible.[1]

There is no gold standard definition of B12 deficiency at any age, and serum B12 levels alone are an imperfect measure of body stores. Various measurement methods of serum B12 are employed, including bacterial inhibition assays and various immunoassays, and these differing measurement techniques between laboratories may influence local deficiency thresholds. Defining antenatal B12 deficiency is further complicated by the gradual decline in measured serum B12 levels during pregnancy due to a combination of factors unrelated to B12 stores, especially a 20–30% reduction in the major B12 binding protein (haptocorrin) caused by increased oestrogens, along with haemodilution and increased glomerular filtration rate.[1,2] The most commonly cited threshold for deficiency in pregnancy and infancy is a serum B12 <148pmol/L (200pg/mL), which is the third standard deviation value in non-pregnant North American adults as per

the National Health and Nutrition Examination Survey (NHANES).[3] Global prevalence estimates of antenatal B12 insufficiency are approximately 25%, increasing up to 65% in ethnic groups where a vegetarian or vegan diet is common.[4] A retrospective cohort study in Vancouver reported a prevalence of antenatal B12 deficiency (serum B12 <148pmol/L) in the first and second trimesters at 20.1% and 20.4% respectively and in women with South Asian ancestry 30.2% and 35.8% respectively.[5]

The prevalence of antenatal B12 deficiency in New Zealand is unknown. Recent estimates of the prevalence of vegetarian diet in New Zealand adults vary between 2–19%, with higher rates in women compared to men.[6,7] The *2008/09 New Zealand Adult Nutrition Survey* reported inadequate dietary B12 intake using dietary questionnaires in 22.8% of women respondents aged between 19–30 and 16.1% of women aged between 31–50, along with B12 deficiency (<148pmol/L) in 2% of the subset of non-pregnant adults who had serum B12 measured, increasing to 3% among those of South Asian and NZ European ethnicity.[8,9] The ethnic communities at highest risk of B12 deficiency in New Zealand are South Asians (defined as people with ancestral origins in the Indian subcontinent including India, Afghanistan, Pakistan, Sri Lanka, Nepal, Bangladesh, Bhutan and the Maldives) and Fijian Indians, related to cultural and religious dietary practices with the key dietary determinant being the consumption of red meat.[8] Current New Zealand antenatal guidelines do not recommend routine B12 supplementation or measurement; however, they include dietary advice that encourages intake of lean meat and dairy products while recommending those with a vegan diet orally supplement B12 while pregnant and breastfeeding.[10]

The prevalence of symptomatic B12 deficiency among New Zealand infants is unknown. However, reports of the late detection of severely affected infants along with recently published findings of very low B12 levels (<50pmol/L) in the cord blood of otherwise healthy newborns in South Auckland suggests that deficiency may be under-recognised.[11,12] Prevalence estimates of newborn B12 deficiency in demographically similar European countries range between 1:2,000 and 1:5,000.[13,14] Assuming these estimates are comparable to New Zealand, with 60,000 births annually in New Zealand, this may represent a significant number of affected infants who could benefit from early detection and treatment.

Methods

Aims

The aims of this descriptive observational study were to describe the recent detection and treatment rates of B12 deficiency in the Auckland–Northland region among pregnant mothers and infants who had serum B12 measured.

Study design

Awanui Labs (formerly Labtests Auckland [LTA]) provides almost all community laboratory services in the Auckland–Northland region. LTA provided data on serum B12 levels for analysis, along with approximate testing rates in the general population for comparison.[15] Two patient cohorts were identified with the following inclusion criteria:

1. Infant cohort: infants aged less than 12 months who had B12 measured between 01/01/2017–01/06/2022 in the Auckland–Northland region. Infants with B12 deficiency (serum B12 <148pmol/L) were paired with the maternal national health index (NHI), and the electronic health record (EHR) of both mother and infant were reviewed. The longer timeframe was chosen to compensate for the lower rate of testing in this cohort.
2. Antenatal cohort: pregnant women who had B12 tested between 01/04/2021–01/04/2022 in the Auckland–Northland region. Mothers at highest risk of B12 deficiency (serum B12 <100pmol/L) were paired with the infant(s') NHI, and the EHR was reviewed.

Data collection categories included serum B12 levels of mother and infant, treatment prescribed and qualitative review of clinical records.

The EHR contains all prescriptions and laboratory test results for the study participants, along with documentation from hospital clinicians in the Auckland–Northland region. It includes antenatal documentation for women with complex pregnancies, but does not contain primary care documentation by community midwives or general practitioners providing care for women with low-risk pregnancies.

The New Zealand Ministry of Health – Manatū Hauora maternity database paired mothers and infants. Population statistics, including live births and city populations by year, were sourced from Statistics New Zealand.[16] The number of live births

in 2022 represented completed pregnancies that followed antenatal blood tests collected between 01/04/2021 and 01/04/2022. Exclusion criteria were incomplete or duplicate records, non-liveborn babies and patients likely incorrectly coded as antenatal (male, <15 years old, >50 years old).

B12 deficiency and treatment thresholds

This study used the NHANES definition of B12 deficiency (<148pmol/L) for ease of comparison with other literature, but acknowledges this definition's limitations, particularly in the unique physiological states of pregnancy and infancy.[1,2] Pregnant women in the study cohort with serum B12 <100pmol/L were deemed to have the highest likelihood of clinically significant B12 deficiency and are referred to here as *high-risk* pregnancies.

This study defined adequate treatment as "B12 treatment at any dose administered within 3 months of diagnosis, and if pregnant administered prior to delivery". Dietary advice alone did not meet this threshold. Both enteral and parenteral B12 administration were considered appropriate treatment modalities. In the absence of documented treatment, a subsequent rise in serum B12 level to >400pmol/L on repeat testing was considered evidence that treatment was administered by alternative means, such as during a hospital admission or using a non-prescribed B12 supplement, as serum B12 is unlikely to spontaneously rise to this extent.

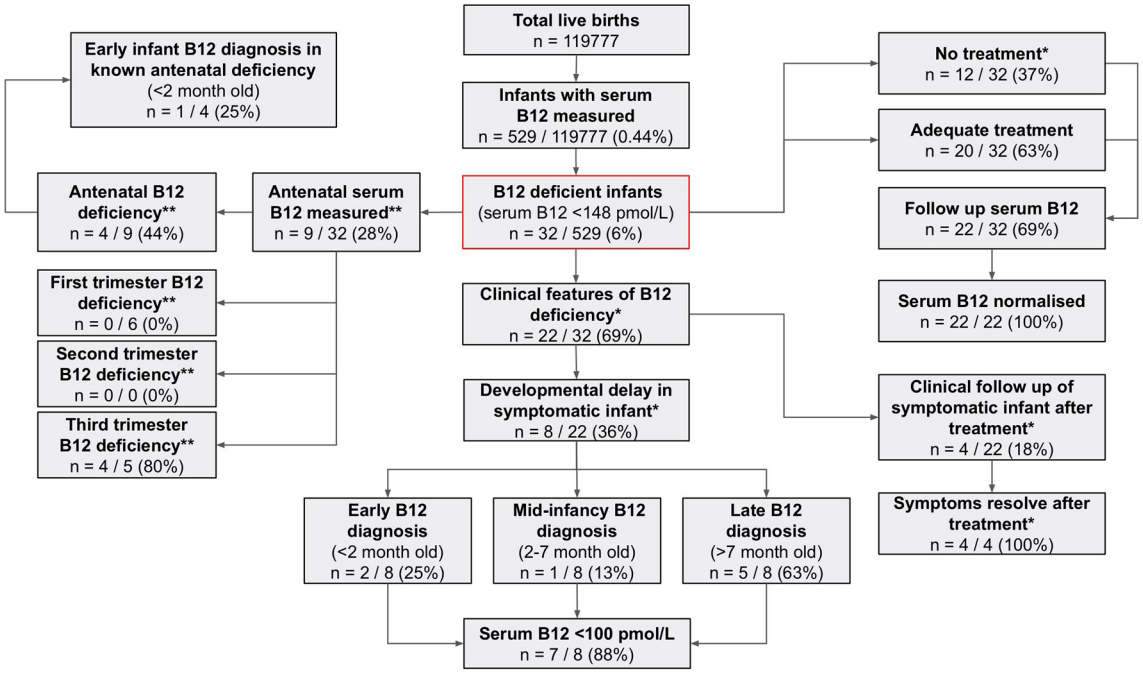
Biochemical analysis

Serum B12 was measured at LTA using the Siemens ADVIA Centaur between January 2017 and November 2020. From December 2020, the Roche cobas platform was used. The two assays closely correlate in accuracy in the normal and low range of serum B12; however, the Roche assay has a negative bias for very low levels compared to the Siemens method (e.g., Roche 100pmol/L approximated to Siemens 138pmol/L).

Ethics

This study was approved by the Auckland Health Research Ethics Committee (reference number AH25382).

Figure 1: Flowchart summary of infant cohort results.



*As documented in the electronic health record (EHR).
**Serum B12 levels were measured at varying gestations (see Table 3) and without important contextual information, which affects their interpretation. Normal antenatal B12 levels decline over time and antenatal B12 deficiency thresholds are debated.

Results

Infant cohort

In the 5-year period between 01/01/2017 and 31/12/2021 there were 119,777 live births registered in the Auckland–Northland region. Serum B12 was measured in 529 infants during this period (approximately 4 per 1,000 infants per year, or 0.44%), with 105 of these infants tested at 6 months of age or younger (approximately 1 per 1,000 infants per year, or 0.09%) (Figure 2). By comparison, 22% of the greater Auckland population had serum B12 measured at least once by LTA in 2022 (227 per 1,000 persons per year).[15]

B12 deficiency was found in 32 (6%) of tested infants, 22 of whom had clinical features documented in the EHR that may be caused by B12 deficiency (Table 1). The testing indication and/or symptoms of the remaining 10 infants were unavailable.

Seven out of the eight developmentally delayed infants had a serum B12 level less than 100pmol/L. Only two of these eight infants had B12 deficiency diagnosed in early infancy (<2 months old), with five diagnosed in late infancy (>7 months) (Table 2).

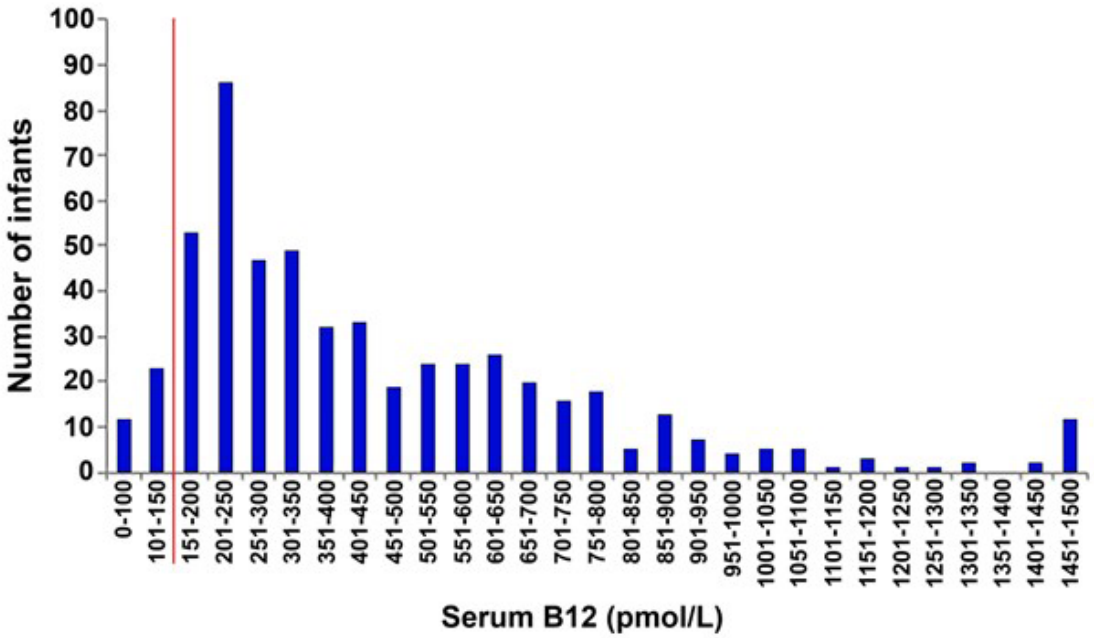
Among the 32 infants with B12 deficiency, 20 (63%) had evidence of adequate treatment. The dose varied widely, from low dose over-the-counter B12 drops in one infant to a cumulative 24mg of intramuscular B12 in another infant. The remaining 12 infants had no recorded treatment, but they may have been given dietary advice or over-the-counter B12 treatment.

A follow-up serum B12 level was checked at least 6 weeks after the initial test in 22 (69%) of the deficient infants. All B12 levels normalised on repeat measurement, including in two infants without documented treatment.

Four symptomatic treated infants had clinical follow-up documented in the EHR. All reported improved symptoms within 1 month of treatment, including rapid neurodevelopmental progress. One had long term follow-up that described normal neurodevelopment at age 2 years despite initial high-risk B12 deficiency (74pmol/L) at 10 months old. The remaining infants may have had clinical follow-up in primary care.

Nine of the 32 mothers of infants with B12 deficiency had serum B12 measured during the pregnancy and four had B12 deficiency antenatally (<148pmol/L), each in the third trimester. In each case, contextual information including the reason for antenatal testing, the presence of antenatal risk factors for B12 deficiency and antenatal

Figure 2: Serum B12 levels of tested infants (n=529) born between 01/01/2017 and 01/06/2022 in Auckland and Northland.



*The red line indicates the approximate B12 deficiency threshold (<148pmol/L).

Table 1: Proportion of symptomatic B12 deficient infants with the corresponding clinical feature of B12 deficiency.*

Symptom	n/22 (%)
Feeding difficulties	15 (68%)
Faltering growth	13 (59%)
Developmental delay	8 (36%)
Anaemia and/or macrocytosis	5 (23%)
Raised urinary methylmalonic acid	1 (5%)
Tremor	1 (5%)

*As per available electronic health record (EHR) documentation. Some infants had several symptoms.

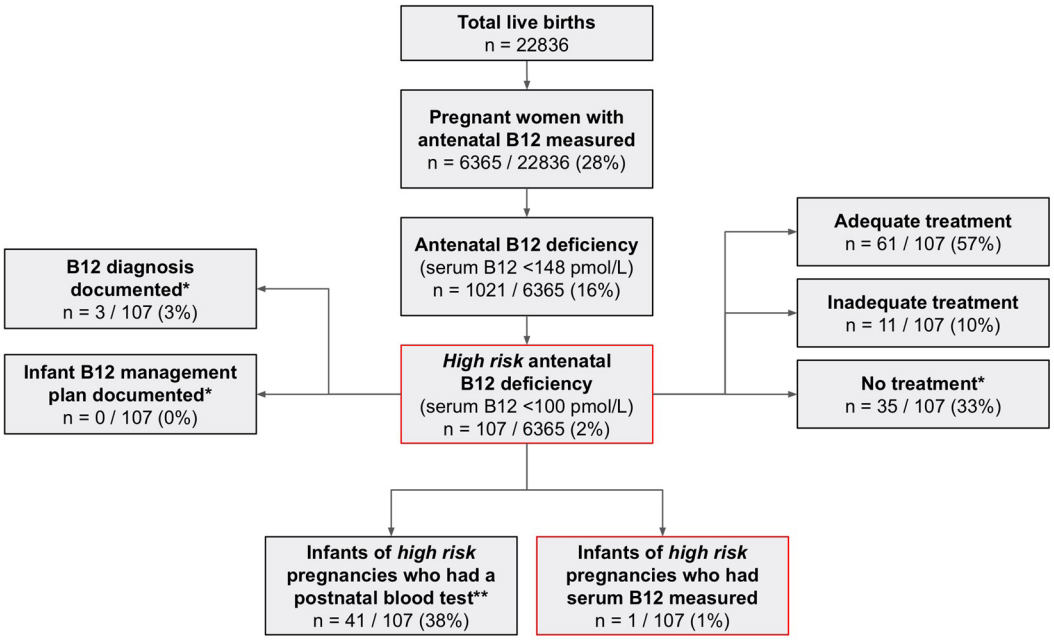
Table 2: Age of diagnosis and serum B12 level of B12 deficient infants with developmental delay.

Case number	Age at diagnosis (days)	B12 level (pmol/L)
1	212	52
2	322	74
3	319	74
4	347	74
5	148	83
6	37	94
7	48	99
8	345	143

Table 3: Age at diagnosis and maternal antenatal B12 levels of infants with B12 deficiency.

Case number	First trimester	Second trimester	Third trimester	Infant serum B12 (pmol/L)	Infant age at diagnosis (days)
1	219	-	-	92	240
2	-	-	219	94	37
3	-	-	92	97	291
4	165	-	-	99	164
5	198	-	111	101	240
6	-	-	126	111	32
7	347	-	133	119	310
8	385	-	-	132	121
9	172	-	-	145	205

Figure 3: Flowchart summary of antenatal cohort results.



*As documented in the electronic health record (EHR).
**Excluding newborn metabolic screen and blood sugar testing.

B12 treatment or supplementation could not be accurately determined from the EHR. Only one of these four infants was diagnosed in early infancy (<2 months) (Table 3).

Antenatal cohort

A total of 6,365 pregnant women in the Auckland–Northland region between 01/04/2021 and 01/04/2022 had serum B12 levels tested, which is approximately 28% of the 22,836 live births in Auckland and Northland in 2022. Antenatal B12 deficiency (<148pmol/L) was found in 1,021 (16%) of these women, with *high-risk* deficiency (<100pmol) in 107 (2%) of these pregnancies.

Among the *high-risk* pregnancies, 61 (57%) had evidence of adequate treatment. All but one were treated with intramuscular B12 with the cumulative dose ranging between 1 and 8mg. The remaining person was prescribed an oral multivitamin containing B12. Thirty-five women (33%) had no recorded treatment, but they may have been given dietary advice or over-the-counter B12 treatment. Eleven women (10%) were prescribed inadequate treatment; seven had treatment delayed either by >3 months after diagnosis or until postpartum, three had persistent deficiency on post-treatment follow-up testing but did not receive further treatment, and two were prescribed a multivitamin that did not contain B12.

A clinician documented the diagnosis of antenatal B12 deficiency in three (3%) of the *high-risk* pregnancies. There was no documented plan in any *high-risk* pregnancy to screen the infant for B12 deficiency after birth, but there may have been documentation in primary care.

Of the 109 children born of *high-risk* pregnancies only one (1%) had serum B12 measured in infancy. By comparison, 41 (38%) had blood tests (not including newborn metabolic screening or blood sugar testing) performed in infancy unrelated to B12.

Discussion

This study found that serum B12 was measured in over a quarter of pregnancies despite not being recommended as a routine screening test. However, when pregnant women were diagnosed with B12 deficiency they were frequently under-treated and there was little testing of their at-risk infants. Serum B12 was measured 50-fold less frequently in infants than in the general population. B12

deficient infants were usually not diagnosed until late infancy. When neurodevelopmental delay was present in a B12 deficient infant, it was almost exclusively in those with the lowest B12 levels (<100pmol) and resolved with supplemental B12 treatment where developmental data was available. Despite the known causal link between antenatal and infant B12 deficiency, it was uncommon to find cases where a mother and infant both had serum B12 measured. These findings suggest there may be an unrecognised burden of treatable B12 deficiency in infants in the Auckland–Northland region.

The key strengths of this study lie in the large study population from which the B12 deficient cohorts were identified. During the study period LTA was effectively the sole provider of the test in the region; therefore, this large dataset was a representative sample and allowed for focussed analysis of a significant number of *high-risk* pregnancies and infants. However, there were significant limitations. Database linkage analysis may have incompletely or inaccurately identified patient records. The EHR is not a comprehensive medical record and therefore relevant clinical information recorded elsewhere would have been overlooked. Interpretation of paired antenatal–infant B12 levels were particularly confounded by this limitation. The study contained participants in the Auckland–Northland region and due to demographic differences, as well as potential regional differences in clinical and laboratory practice, these findings may not apply to other regions of New Zealand. Furthermore, these data cannot determine the prevalence or effect of B12 deficiency on infant neurodevelopment, as they are confounded by the absence of randomisation, the low testing incidence and the comparatively high prevalence of developmental delay in infants.

Infants of B12 deficient mothers were rarely tested for deficiency, and the reason is unclear. A large proportion of these infants had blood tests performed for other reasons, and thus a reluctance by clinicians to test due to the painful nature or technical difficulty of blood sampling in infancy cannot be the sole explanation. The disruption to care continuity during the transition from pregnancy to infancy may be contributory. There is usually no single practitioner that oversees both the pregnancy and infancy in New Zealand. Antenatal and early postnatal care is led by the lead maternity carer (LMC), usually a midwife. As B12 deficiency is asymptomatic in the first weeks of life, there may be no clinical concerns when the mother and baby's care is transferred to a general practitioner at 4–6 weeks postnatally. By the time they present to primary care with neurodevelopmental symptoms in later infancy, the antenatal risk factor may be overlooked or assumed not to be relevant.

Several large prospective cohort studies and small randomised trials have suggested that mild to moderate B12 deficiency either antenatally or in infancy may have a detrimental effect on infant neurodevelopment.[17–21] However, a recent large randomised controlled trial of antenatal B12 supplementation in a Nepalese population with endemic B12 deficiency demonstrated no difference in infant neurodevelopment outcomes between the treated and untreated groups despite improved B12 status in the treated group.[22] These latter findings support the current World Health Organization (WHO) recommendation against routine antenatal B12 supplementation.[23]

However, there remains a threshold of severity where B12 deficiency becomes unequivocally and irreversibly harmful to an infant. The New Zealand National Metabolic Service is notified of between one and three such cases annually in New Zealand, typically presenting with severe anaemia and neurological impairment, which can be life-threatening.[24] These infants remain a priority for early detection and treatment, particularly when comparing the relative ease and low cost of treatment against the high cost of neurodevelopmental impairment to both the patient and the healthcare system over a lifetime.

The New Zealand Newborn Metabolic Screening Programme (NMSP) occasionally detects incidental B12 deficiency via raised propionylcarnitine (C3) levels while screening for methylmalonic and propionic acidaemia, which has led to NMSP considering implementation of universal newborn screening (NBS) in New Zealand.[24] Several European NBS centres have recently published pilot studies implementing systematic newborn B12 bloodspot screening by adapting the screening thresholds of the B12 metabolites classically used to detect these acidaemias. They reported an unexpectedly high prevalence of B12 deficiency (1:1989–1:5355); however, the approach appears limited by suboptimal sensitivity and specificity.[13,14,25]

Since universal newborn screening appears impractical, targeted screening must be considered. However, symptoms of infant B12 deficiency such as poor feeding and irritability are common and non-specific in infancy, and there is a high

prevalence of developmental delay in New Zealand children.[26,27] Using the third percentile cutoff for developmental milestones, approximately 2,000 of the 60,000 infants born annually in New Zealand will be expected to have some degree of developmental delay. Symptomatic B12 deficiency will rarely be the cause of these symptoms, particularly in populations with regular dietary intake of animal products, thereby rendering indiscriminate testing of serum B12 of these infants inefficient and impractical.

Targeted testing of B12 status in infants and their mothers based on risk factors for deficiency is therefore recommended. If B12 deficiency is diagnosed in either group, it should be managed primarily with the goal of reducing the infant's risk of severe deficiency and neurodevelopmental harm. If a mother and infant are at risk of B12 deficiency, this must be included in the handover of care between antenatal and primary care providers. The following screening recommendations aim to guide the management of at-risk pregnant women and infants while increasing awareness of this complex issue among clinicians.

COMPETING INTERESTS
DW is Vice President of the International Society for Neonatal Screening (ISNS).

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URL
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Appendix

There are currently no formal consensus screening or treatment guidelines in managing the risk of B12 deficiency in the infants of B12 deficient mothers. This shortfall may be contributing to the results described in this study. The recommendations that follow are not systematic guidelines, but rather intend to provide pragmatic advice to the clinician managing a pregnancy or infancy at risk of B12 deficiency in New Zealand based on the local context described in this study and other recent emerging evidence.

These recommendations specifically target infants at high risk of B12 deficiency; they do not provide comprehensive guidance regarding the investigation and management of B12 deficiency in pregnant women. For systematic guidelines regarding the management of B12 deficiency in adults, refer to the National Institute for Care and Excellence (NICE) guideline *Vitamin B12 deficiency in over 16s: diagnosis and management*.[28]

A) Screening recommendations

Recent evidence suggests that the vast majority of infants at risk of B12 deficiency will experience normal neurodevelopment with no medical consequences, including those who are mild–moderately deficient.[22] However, B12 deficiency that is severe and prolonged can cause irreversible neurological harm to an infant. The goal of these recommendations is to identify these infants with the highest risk for severe deficiency, and to effectively reduce their risk through dietary and pharmacological intervention both before and after birth. Where dietary/supplementation advice is recommended, refer to *B) Nutrition and treatment recommendations*. Allowing for the margin of error of the laboratory assay and the lack of consensus definition for deficiency, thresholds have been rounded up to the nearest 10pmol/L for simplicity.

Pregnancy (see Appendix Figure 1)

1. **Take a medical and dietary history in the first trimester to identify risk factors for deficiency**. See Appendix Table 1 and *Appendix—B) Nutrition and treatment recommendations*.
2. **If a woman has no risk factors, then testing is not recommended**. Most women do not require B12 testing or supplementation in pregnancy.
3. **If a woman has any risk factor for B12 deficiency, provide dietary/supplementation advice and measure serum B12 alongside other routine antenatal screening blood tests at the first booking appointment (ideally in the first trimester)**. Antenatal serum B12 levels trend downwards as gestation progresses due to normal physiological changes in pregnancy; therefore, early antenatal serum B12 levels are a more representative screening test for deficiency in the mother.[1,2]
4. **Recommended management according to antenatal serum B12 level (ideally measured first trimester):**
   A. >400pmol/L: no further testing or treatment is recommended due to the low risk for infant deficiency.[2]
   B. 150–400pmol/L: reiterate diet/supplementation advice. Further testing or treatment has not been shown to improve infant neurodevelopmental outcomes.[22]
   C. 100–149pmol/L: recommend antenatal oral or intramuscular B12 treatment to reduce the infant's risk of deficiency. Reiterate diet/supplementation advice.
   D. <100pmol/L: recommend administration of intramuscular B12 treatment to reduce the infant's risk of deficiency. Reiterate diet/supplementation advice.
5. **If B12 deficiency is appropriately treated antenatally, then follow-up testing of the mother is not required.**
6. **If serum B12 level is <150pmol/L at any gestation, refer to the "Infancy" recommendations to guide management of the infant** (see Appendix Figure 2). Refer to the NICE Guidelines for advice regarding investigation of the underlying cause of B12 deficiency in pregnant adults.[28]

Infancy (see Appendix Figure 2)

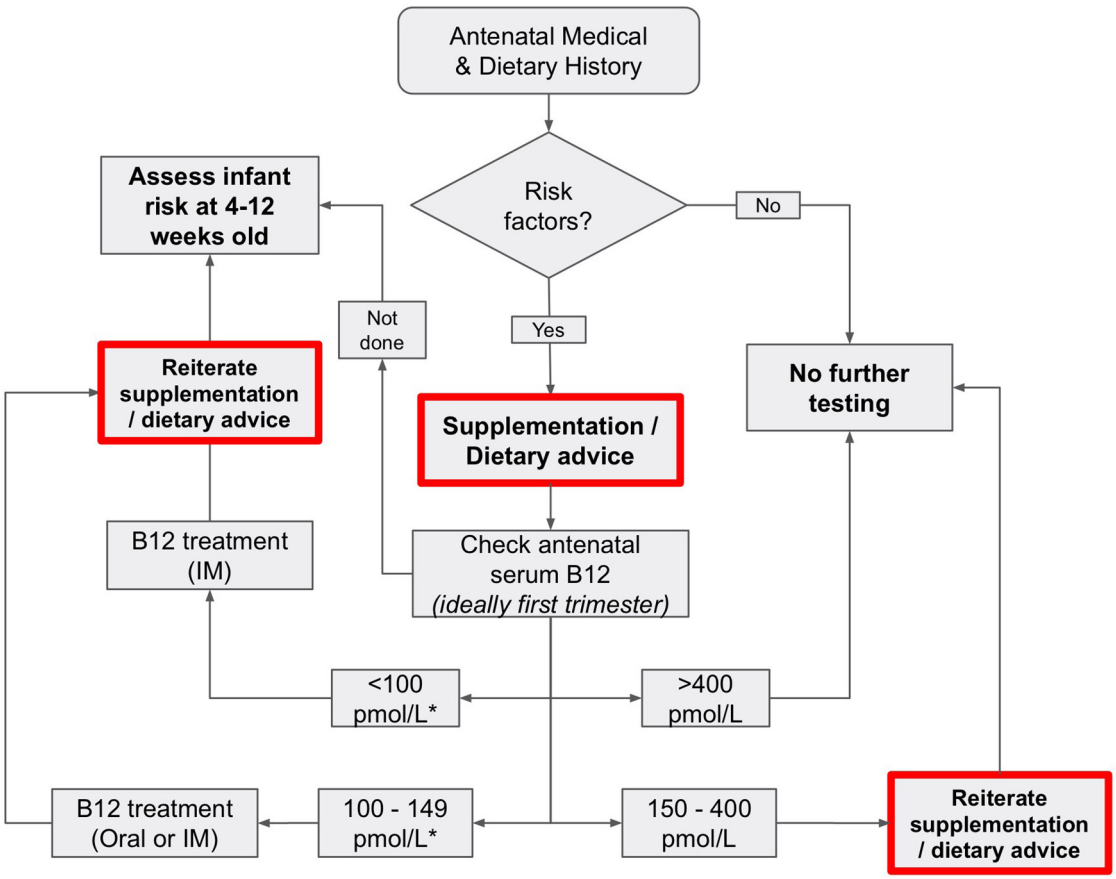
1. **If antenatal serum B12 was <150pmol/L at any gestation, or if any maternal risk factors for deficiency were present but antenatal serum B12 levels were not measured, then the infant is at risk of B12 deficiency.** Provide dietary/supplementation advice. This risk factor must be included in any handover of care from antenatal care to primary care (e.g., general practitioner).
2. **Reassess infant risk between 4–12 weeks old** (e.g., at time of discharge from lead

Appendix Table 1: Maternal risk factors for infant B12 deficiency.[1,8]

Previous antenatal B12 deficiency
Previous child with B12 deficiency
Limited consumption of animal products, particularly red meat (vegetarian/vegan diet, socio-economic factors, eating disorders)*
Gastrointestinal condition causing B12 malabsorption (pernicious anaemia, significant disease or surgery affecting the stomach, ileum or pancreas, inflammatory bowel disease)
Unexplained or macrocytic anaemia
Genetic disorder of B12 metabolism
Chronic use of medications/substances that affect B12 absorption or metabolism (e.g., metformin, proton pump inhibitor, H2-receptor antagonists, excess alcohol)
History of autoimmune disease (e.g., Coeliac, autoimmune thyroiditis, type 1 diabetes)

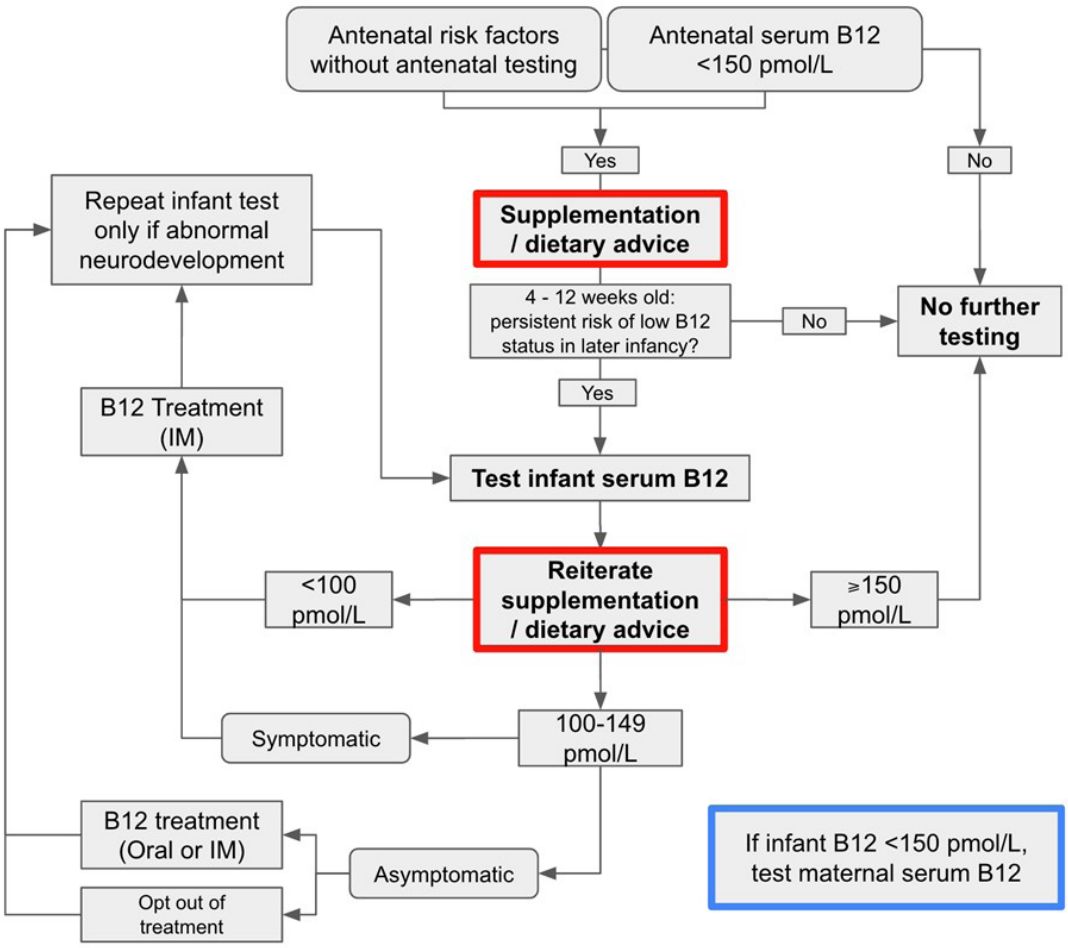
*See Appendix—*B) Nutrition and treatment recommendations*.

Appendix Figure 1: Antenatal recommendations flowchart.



*Refer to NICE guidelines regarding investigation of cause of B12 deficiency.[28]

Appendix Figure 2: Infant recommendations flowchart.



maternity carer [LMC] care, or during the "6-week infant check" in primary care). If a risk reduction strategy has been put in place (e.g., infant/maternal B12 supplementation, plan for prioritised introduction of animal products into diet when the infant starts solids—see *Appendix*), then no further testing is needed. However, if no risk reduction strategy is in place, the infant remains at risk of B12 deficiency; **test serum B12 in these selected infants while reiterating dietary/supplementation advice.**

3. **Recommended management according to infant serum B12 level:**
   A. <100pmol/L: strongly recommend B12 treatment via the intramuscular route.
   B. 100–149pmol/L: if symptomatic, treat as per (A) above. If asymptomatic, provide treatment based on family preference. If they opt out of treatment, monitor the infant clinically for symptoms of B12 deficiency, particularly abnormal neurodevelopment.
   C. ≥150pmol/L: no treatment is required.
4. **Follow-up testing is not required in most infants, regardless of treatment.** The exception is when specific symptoms develop in later infancy suggestive of severe B12 deficiency, particularly abnormal neurodevelopment.
5. **If an infant's serum B12 is <150pmol/L, measure the B12 status of the mother.** If she is also found to be B12 deficient, treat as per NICE guidelines.[28]

B) Nutrition and treatment recommendations

Diet is the most important determinant of a person's B12 status. The consumption of red meat is the main dietary factor correlating to serum B12 concentration in the New Zealand population.[8] When taking an antenatal dietary history,

specifically ask about consumption of animal products, with particular attention in patients of South Asian (defined as people with ancestral origins in the Indian subcontinent including India, Afghanistan, Pakistan, Sri Lanka, Nepal, Bangladesh, Bhutan and the Maldives) and Fijian Indian ethnicities, where reduced animal product consumption is more prevalent due to cultural and religious practices.[8] Other factors causing food restriction (such as socio-economic deprivation or eating disorders) may also limit a person's ability to regularly consume animal products or B12 supplementation.[1]

The antenatal recommended daily intake (RDI) for B12 is 2.6mcg/day (increased from 2.4mcg/day for non-pregnant adults due to placental and foetal demand), and further increases to 2.8mcg/day when breastfeeding.[29] Pregnant women with a diet inclusive of animal products will usually meet this requirement by following the Ministry of Health guidance on *Safe and healthy eating in pregnancy*, consuming at least three servings per day from the following food groups: lean meat, poultry, seafood, eggs, nuts, seeds and legumes, while prioritising the consumption of animal products.[10] If a pregnant woman is vegetarian or vegan, they are recommended to take an oral supplement providing at least the RDI of vitamin B12 due to the variable levels of B12 in fortified food products.[10] There are numerous inexpensive oral vitamin supplements containing B12 that are commercially available in New Zealand, although none are currently subsidised for pregnant women or infants.

In infants with risk factors or a confirmed diagnosis of B12 deficiency, do not delay introducing solids beyond 6 months of age, and consider introduction of solids from 4 months of age if the infant is developmentally ready. Prioritise B12-rich foods such as well-cooked and pureed meat, seafood and egg. B12 supplementation is recommended in children older than 6 months who transition to a diet that restricts animal products, or have a malabsorptive medical condition, or have not introduced solids or fortified milk formula into the diet. Refer to a New Zealand Registered Dietitian for individualised advice.

If treatment doses of B12 are required for either a mother or infant, both oral and parenteral B12 are considered equally effective unless enteral dosing is contraindicated (e.g., pernicious anaemia or other malabsorptive condition).[30] B12 has minimal risk of toxicity even in large doses.[1,30] In severe deficiency, considering the potential for neurodevelopmental impairment, we have advised intramuscular B12 be given in alignment with NICE guidelines as it guarantees adherence, has high bioavailability and is subsidised.[28,30] Refer to the New Zealand Formulary for intramuscular dosing. Alternatively, high dose oral B12 can be given; there is no standard dose, but a several week course of high dose oral B12 at 500–1,000mcg per day can be safely administered in both women and infants.[1,13,28,30]

Measuring follow-up serum B12 levels within 3 months of intramuscular B12 treatment is not useful as these levels are often misleadingly elevated and do not accurately reflect body stores.[28]

Consequences of COVID-19 protection measures on children's respiratory health in Aotearoa New Zealand

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ABSTRACT

AIM: To explore the impact of COVID-19 protection measures on children's respiratory health in Aotearoa New Zealand.

METHOD: Annual hospitalisation rates (2017/2018 to 2022/2023) for specific respiratory illnesses in children under age 15 years were calculated. Comparisons were made across time and age/sex/ethnicity groups.

RESULTS: Hospitalisation rates for respiratory illnesses were lower for all children in the years when COVID-19 protection measures were strictly enforced, followed by an increase in rates in subsequent years. There was an excess of hospitalisations for tamariki Māori and for Pacific children compared with non-Māori, non-Pacific children. Inequities in influenza that were present before the pandemic re-emerged rapidly following the relaxation of COVID-19 protection measures.

CONCLUSION: Reducing the burden of respiratory illness in children is a key challenge for health delivery in Aotearoa New Zealand. The re-appearance of inequities across outcomes and age groups following the relaxation or removal of COVID-19 protection measures indicates the need for an effective strategy that embeds learnings from our pandemic response.

Various non-pharmaceutical interventions (NPIs) were used to manage the risk of COVID-19 in Aotearoa New Zealand. These included international border controls; social distancing and national and regional "lockdowns"; test, trace and isolate procedures; mask wearing and enhanced hygiene measures; and a comprehensive public information campaign. Their effects were heralded in the literature as resoundingly successful during the early phases of the pandemic.[1–3]

In addition to keeping rates of COVID-19 at among the lowest levels of any country in 2020 and 2021, these measures resulted in lower rates of other respiratory viral infections and associated respiratory illnesses, as well as disruptions to the seasonal patterns of these virus-associated illnesses.[4–8] It has been proposed that one consequence of these disrupted patterns is the so-called "immunity debt", where a larger proportion of the population becomes susceptible to a disease following an extended period of reduced exposure.[9,10] For young children, who have not been exposed to maternal antibodies or viral infection in infancy, this immunity gap raises concerns of future and potentially more severe respiratory illnesses as NPIs are relaxed or discontinued worldwide.

Aotearoa New Zealand's own COVID-19 protection measures began on 3 February 2020 with a ban on foreigners arriving from mainland China, and on 19 March the border was closed to everyone except citizens and permanent residents. A four-tiered Alert Level system was introduced to eliminate COVID-19 on 21 March, and on 25 March the country moved to Alert Level 4—full lockdown—until 27 April 2020. During this period, the public was advised to stay at home in their "bubble" with no travel except for necessities. Gatherings were banned and public and education facilities were closed, along with all businesses except for essential services.[2] A timeline infographic of key events for COVID-19 in Aotearoa New Zealand that covers the period January 2020 to October 2022 plots the subsequent shifts in national and regional alert levels alongside "All-of-Government" and other public sector activities that characterised the ongoing response to the pandemic.[11] On 2 December 2021 the Alert Level system ended, and there was a shift to the COVID-19 Protection Framework (with three "traffic light" settings of red, orange and green). This framework ran from 2 December 2021 to 12 September 2022 and set rules around face masks, capacity limits, local protections and lockdowns for different settings to firstly suppress the Delta variant wave of infection, and subsequently manage the impact of Omicron in

Aotearoa New Zealand.[11]

Following the implementation of a COVID-19 elimination strategy in March 2020, there was a dramatic reduction in the circulation of seasonal respiratory viruses, with a 99.9% reduction in influenza virus detections and a 98.0% reduction in respiratory syncytial virus (RSV) detections during winter 2020 compared with the 2015–2019 reference period.[12] At Kidz First Children's Hospital in South Auckland, a marked reduction in hospitalisations for lower respiratory tract infection (LRTI) among children <2 years of age was observed following the national lockdown, and cases of RSV and influenza plummeted.[13] Hatter et al. highlighted the absence of a seasonal epidemic of national hospital admissions for bronchiolitis in 2020 for children aged 0–4 years.[14] Further, analysis of national rates of children treated in hospital for a range of acute respiratory conditions revealed that hospital admissions halved in 2020.[15]

In 2021, however, a very different pattern emerged. Following the border with Australia reopening in late April 2021, the Institute of Environmental Science and Research's weekly data reports showed a return of RSV, with a rapid increase in cases documented in June 2021.[16] Provisional national data for children aged 0–4 years revealed a peak in hospital discharges for bronchiolitis that was three times higher than average peaks during 2015–2019.[14] Resurgences of RSV infections, including out-of-season peaks, have also been documented across several Northern and Southern hemisphere countries following the removal of COVID-related NPIs.[8,17–19]

In Aotearoa New Zealand, the hospitalisation of young children due to LRTI is both high relative to other developed countries and unequal, with a disproportionate burden of respiratory illness being borne by tamariki Māori, Pacific children and those living in the most deprived households.[15,20,21] In 2020, hospitalisation rates of children and adolescents for respiratory conditions decreased for all ethnic groups and across levels of socioeconomic deprivation; however, rates then increased in 2021.[15]

To explore the impact of the introduction, then later removal, of NPIs on the inequitable burden of respiratory illness, we describe trends from 2017/2018 to 2022/2023 in hospitalisation rates for respiratory infections among children in Aotearoa New Zealand.

Method

Data on numbers of hospitalisations by age, sex and ethnicity were obtained from the Ministry of Health – Manatū Hauora (MOH) for specific respiratory illnesses, based on the International Classification of Diseases, 10th version (ICD-10). These were extracted from the National Minimum Dataset (NMDS), a national collection of public hospital discharge data, on 10 November 2023. The NMDS records a new entry for each admission–discharge event for encounters including emergency department visits lasting ≥3 hours in duration. The data supplied covered the years 2017/2018 to 2022/2023, with each 12-month period pertaining to a July to June year.

Data in the NMDS are recorded by each individual person's unique National Health Index (NHI) number. Ethnic group was classified using the prioritisation system,[22] in which individuals are allocated to a single ethnic group in an order of priority if they have identified with more than one ethnic group. The first two prioritised groups are Māori then Pacific peoples. All others were included in the non-Māori, non-Pacific group. Thus, if someone identifies as Māori and Samoan, they are reported as Māori only. Discussion of the limitations of this approach is included below.

Population data were obtained from the MOH and were based on annual population projections estimated by Statistics New Zealand using 2018 as the base. These projections are based on post-enumeration surveys to produce population estimates. The same prioritisation of ethnic group was applied to the population data.

Annual hospitalisation rates by age group (0–4 years, 5–9 years and 10–14 years), sex (male and female) and ethnic group (Māori, Pacific, non-Māori/non-Pacific) were calculated by dividing the number of hospitalisations by the population estimates. Eleven events of people with unrecorded sex were excluded from all analyses. Rate ratios with associated 95% confidence intervals (CIs) were calculated over time, using 2017/2018 as the reference year. These were stratified by age group (0–4 years, 5–9 years and 10–14 years) and sex. Further analyses were conducted by ethnic group, using non-Māori, non-Pacific children as the reference group, similarly stratified by age group and sex.

Discharges were grouped by the ICD code on discharge using the following illness categories: acute upper respiratory infections (URTIs; J00-J06); influenza (J09-J11); selected pneumonia, bronchitis and bronchiolitis (J12-J16, J18, J20-J21), referred to as LRTIs; asthma and wheeze (J45-J46, R06.2). Selection of ICD codes for inclusion was based on Cure Kids' *State of Child Health in Aotearoa New Zealand 2022* report.[15]

Results

The total number and crude rate of hospitalisations in each of the four illness categories across all years of the study are shown in Table 1. In all years other than 2020/2021, the most frequent hospitalisation illness category was LRTIs. The 2020/2021 years were when NPIs were enforced most strictly; during that period, URTIs and asthma/wheeze accounted for a greater number of hospitalisations than LRTIs, and there were virtually no instances of hospitalisation for influenza in 2020/2021. In the latter 2 years the most noticeable increase was for LRTIs and influenza, although in 2022/2023 hospitalisation rates were higher for each outcome than in any of the previous years studied.

The relative hospitalisation rates across time for the four illness categories, by age and sex group, are shown in Table 2. For all children, there was a marked absence of influenza, and significantly lower rates of LRTIs in 2020/2021. For LRTIs, these low rates persisted among children aged 5–14 into 2021/2022. For influenza, the rates increased in all age/sex groups in 2021/2022 to very high rates in 2022/2023. For URTIs, there was an overall pattern of lower rates in 2019/2020 to 2021/2022, with an increase in 2022/2023 to rates that were higher than 2017/2018 in children aged 0–9 years, but not older children. Overall, hospitalisations for asthma/wheeze showed less variation over time, although compared with 2017/2018, rates from 2019/2020 to 2020/2021 were lower, and these remained low for children aged 10–14 years into 2021/2022. In 2022/2023, the rates for children aged 0–9 years were the highest they had been over the 6-year period.

Patterns of hospitalisation rates for the four illness categories, by ethnic group and sex for children aged 0–4 years, 5–9 years and 10–14 years, are shown in Figures 1–4. In virtually all age groups and periods, the rates among Pacific children were higher than among non-Māori, non-Pacific children, other than for influenza in 2020/2021 when there was a near-total absence of the illness in all age and ethnic groups. Among tamariki Māori, the rates were generally higher than in non-Māori, non-Pacific children for asthma/wheeze across all age groups, and for influenza and LRTIs in children aged 0–4 years.

Table 1: Hospital discharges among children aged 0–14 years in Aotearoa New Zealand, 2017/2018–2022/2023.

	2017/2018	2018/2019	2019/2020	2020/2021	2021/2022	2022/2023
Acute upper respiratory infections						
Number	7,238	7,734	5,426	6,852	6,050	8,500
Rate per 10,000	76.5	80.9	55.9	70.7	62.7	88.5
Influenza						
Number	384	1,638	686	14	1,089	2,091
Rate per 10,000	4.1	17.1	7.1	0.1	11.3	21.8
Selected pneumonia, bronchitis, bronchiolitis						
Number	9,970	9,147	7,573	4,080	7,887	11,612
Rate per 10,000	105.4	95.7	78.0	42.1	81.8	120.9
Asthma/wheeze						
Number	6,788	6,598	5,556	5,135	6,597	8,572
Rate per 10,000	71.7	69.0	57.2	53.0	68.4	89.3

Due to random rounding at the most detailed level, from which the totals have been calculated, the figures in this table may contain small errors.

Table 2: Relative rates of hospital discharges among children aged 0–14 years in Aotearoa New Zealand, 2017–2023.

		0–4 years (F)	0–4 years (M)	5–9 years (F)	5–9 years (M)	10–14 years (F)	10–14 years (M)
		RR (95% CI)	RR (95% CI)	RR (95% CI)	RR (95% CI)	RR (95% CI)	RR (95% CI)
Influenza	**2017/2018**	1	1	1	1	1	1
	2018/2019	4.47 (3.60–5.55)	4.29 (3.54–5.20)	4.94 (3.51–6.97)	4.39 (3.33–5.80)	2.56 (1.65–3.95)	3.62 (2.39–5.50)
	2019/2020	2.14 (1.69–2.71)	1.63 (1.31–2.03)	1.83 (1.24–2.70)	1.75 (1.28–2.40)	1.28 (0.79–2.09)	1.41 (0.88–2.28)
	2020/2021	0.01 (0.00–0.07)	0.04 (0.02–0.10)	*	0.08 (0.03–0.20)	0.07 (0.02–0.28)	0.03 (0.00–0.24)
	2021/2022	3.10 (2.47–3.88)	2.58 (2.11–3.17)	3.26 (2.27–4.67)	2.54 (1.89–3.42)	3.08 (2.02–4.70)	2.70 (1.76–4.15)
	2022/2023	5.29 (4.27–6.55)	4.82 (3.98–5.83)	8.42 (6.04–11.74)	6.50 (4.96–8.52)	3.04 (1.99–4.64)	5.21 (3.49–7.79)
URTI	**2017/2018**	1	1	1	1	1	1
	2018/2019	1.04 (0.98–1.09)	1.05 (1.00–1.10)	1.22 (1.06–1.40)	1.26 (1.12–1.41)	0.94 (0.76–1.15)	1.09 (0.89–1.35)
	2019/2020	0.72 (0.68–0.77)	0.77 (0.73–0.81)	0.66 (0.56–0.78)	0.73 (0.64–0.84)	0.63 (0.50–0.79)	0.73 (0.58–0.92)
	2020/2021	0.93 (0.88–0.98)	1.08 (1.03–1.13)	0.56 (0.47–0.66)	0.69 (0.61–0.79)	0.51 (0.40–0.65)	0.55 (0.43–0.71)
	2021/2022	0.86 (0.81–0.91)	0.90 (0.86–0.94)	0.59 (0.50–0.70)	0.69 (0.60–0.78)	0.63 (0.50–0.79)	0.59 (0.46–0.75)
	2022/2023	1.16 (1.10–1.22)	1.22 (1.16–1.27)	1.20 (1.05–1.39)	1.21 (1.08–1.36)	0.98 (0.80–1.20)	0.93 (0.75–1.15)
LRTI	**2017/2018**	1	1	1	1	1	1
	2018/2019	0.90 (0.86–0.94)	0.92 (0.89–0.96)	1.02 (0.86–1.21)	0.84 (0.71–0.99)	0.91 (0.70–1.19)	1.07 (0.83–1.39)
	2019/2020	0.73 (0.70–0.77)	0.77 (0.74–0.80)	0.76 (0.64–0.91)	0.78 (0.66–0.92)	0.71 (0.53–0.94)	0.62 (0.46–0.84)
	2020/2021	0.37 (0.35–0.40)	0.44 (0.42–0.46)	0.31 (0.24–0.40)	0.35 (0.28–0.44)	0.39 (0.27–0.55)	0.40 (0.28–0.56)
	2021/2022	0.83 (0.79–0.87)	0.82 (0.79–0.85)	0.48 (0.39–0.59)	0.45 (0.37–0.55)	0.41 (0.29–0.57)	0.46 (0.33–0.63)
	2022/2023	1.20 (1.15–1.25)	1.19 (1.14–1.23)	1.15 (0.97–1.35)	0.90 (0.77–1.06)	0.89 (0.68–1.16)	0.89 (0.68–1.16)

Table 2 (continued): Relative rates of hospital discharges among children aged 0–14 years in Aotearoa New Zealand, 2017–2023.

		0–4 years (F)	0–4 years (M)	5–9 years (F)	5–9 years (M)	10–14 years (F)	10–14 years (M)
		RR (95% CI)	RR (95% CI)	RR (95% CI)	RR (95% CI)	RR (95% CI)	RR (95% CI)
Asthma/ wheeze	**2017/2018**	1	1	1	1	1	1
	2018/2019	0.95 (0.88–1.01)	1.01 (0.96–1.06)	0.98 (0.88–1.09)	0.96 (0.88–1.05)	0.74 (0.62–0.87)	0.92 (0.78–1.09)
	2019/2020	0.77 (0.72–0.83)	0.83 (0.78–0.87)	0.86 (0.77–0.97)	0.82 (0.75–0.90)	0.62 (0.52–0.73)	0.89 (0.75–1.05)
	2020/2021	0.73 (0.68–0.78)	0.84 (0.79–0.88)	0.68 (0.60–0.77)	0.69 (0.62–0.76)	0.47 (0.39–0.56)	0.75 (0.63–0.89)
	2021/2022	1.02 (0.96–1.09)	1.09 (1.03–1.14)	0.85 (0.76–0.96)	0.91 (0.83–1.00)	0.45 (0.37–0.54)	0.66 (0.55–0.79)
	2022/2023	1.36 (1.28–1.44)	1.34 (1.28–1.41)	1.20 (1.08–1.33)	1.25 (1.15–1.37)	0.72 (0.61–0.85)	0.90 (0.76–1.06)

RR = rate ratio; 95% CI = 95% confidence interval; URTI = upper respiratory tract infection; LRTI = lower respiratory tract infection.
*No cases of influenza among females aged 5–9 years were reported in 2020/2021.

For other illness categories and age groups the patterns were mixed.

The hospitalisation rates for influenza were generally greater for children ≤5 years old compared with older children (Figure 1). Among all age groups, influenza hospitalisation rates, which had peaked in 2018/2019, were virtually zero in 2020/2021. In 2021/2022, these rates rose again, and reached a higher rate in 2022/2023 in most groups than in previous outbreaks—particularly noticeable among Pacific children. Notably, the rise was steeper for Māori and Pacific children aged 0–4 years compared with non-Māori, non-Pacific children, meaning inequities in influenza that were present prior to the pandemic re-emerged rapidly when COVID-19 protection measures were relaxed or discontinued.

Broadly, for children aged 0–9 years similar patterns were seen for hospitalisations for LRTIs (Figure 2). Although the 2020/2021 figures show a narrowing of inequities as the rates decreased in these younger children, the rates increased again subsequently, and for Pacific children were higher than the pre-pandemic rates. For older children (aged 10–14 years), the increase in 2022/2023 of LRTI rates was only evident for Pacific children.

For URTIs, males in each ethnic group aged 0–9 years tended to have higher hospitalisation rates than females. In 2019/2020, hospitalisation rates fell. In the youngest age group, these increased in 2020/2021 and between 2021/2022 and 2022/2023; in Pacific males, rates reached a level not seen in the previous 5 years. In children aged 5–9 years, rates plateaued from 2019/2020 to 2021/2022, and then increased in 2022/2023. In older children, there was a downwards trend from a peak in 2017/2018 and 2018/2019, until 2022/2023 when rates showed a modest increase (Figure 3).

Hospitalisations for asthma or wheeze showed a rather different pattern to influenza and LRTIs (Figure 4). For most age/ethnic groups, there were modest reductions in hospitalisation rates from 2017/2018 to 2020/2021, with these being more marked for older children (aged 10–14 years) and proportionally smaller for younger children. Data on Māori males aged 10–14 years contradicted this pattern. In 2021/2022 and 2022/2023, hospitalisation rates for asthma or wheeze increased for children aged 0–4 and 5–9 years but showed little change for 10–14-year-olds. Pacific children and tamariki Māori had higher hospitalisation rates for these conditions than non-Māori, non-Pacific children.

Hospitalisation rates for tamariki Māori compared to non-Māori, non-Pacific children are shown in Table 3. For all illness categories, there is an excess of hospitalisations for tamariki Māori under 5 years. These inequities are most marked for LRTIs in this youngest group of children, and extend across all age/sex groups for influenza rates in 2021/2022 and across all age/sex groups and time periods for asthma/wheeze.

Hospitalisation rates for Pacific children compared to non-Māori, non-Pacific children are shown in Table 4. The inequities shown are particularly striking for pre-school–aged children, with relative rates for Pacific children over twice that of non-Māori, non-Pacific children in each year for influenza, LRTIs and asthma/wheeze. Inequities in URTIs are also evident in this age group, but to a lesser degree. Of note is the high relative rate of hospitalisation for influenza in older Pacific children compared to non-Māori, non-Pacific children in 2019/2020, which reduced to virtually none in 2020/2021, but reappeared the following year. Inequities in LRTI rates for older Pacific children have increased over time, being particularly stark in the most recent years (2021/2022 to 2022/2023).

Discussion

The data presented show changing patterns of hospitalisations for respiratory conditions over a 6-year period, including the years during which COVID-related NPIs were enforced. The dip in rates in 2019/2020 and/or 2020/2021 was seen for each of the four illness categories but was most marked for influenza and least marked for asthma/wheeze and URTIs. For each of influenza, LRTIs and URTIs, the changing trends were most marked for younger children.

This study includes all public hospital discharges across the country for a 6-year period. In Aotearoa New Zealand, all acute infectious disease–related admissions are to public hospitals. A significant limitation of the data for Pacific children arises from the use of prioritised ethnicity.[22] Although this has been used as a mechanism to allow comparison between groups without overlapping categories and causes no issues for the interpretation of Māori data, it results in significant under-counting of Pacific children. We have calculated that in the 2018 Census, of the 125,967 Pacific children aged under 15 years, 30% also reported Māori ethnicity (calculated from https://explore.data.stats.govt.nz/). Thus, the data presented here will be an under-estimate of the

Figure 1: Rates of hospital discharges for influenza.

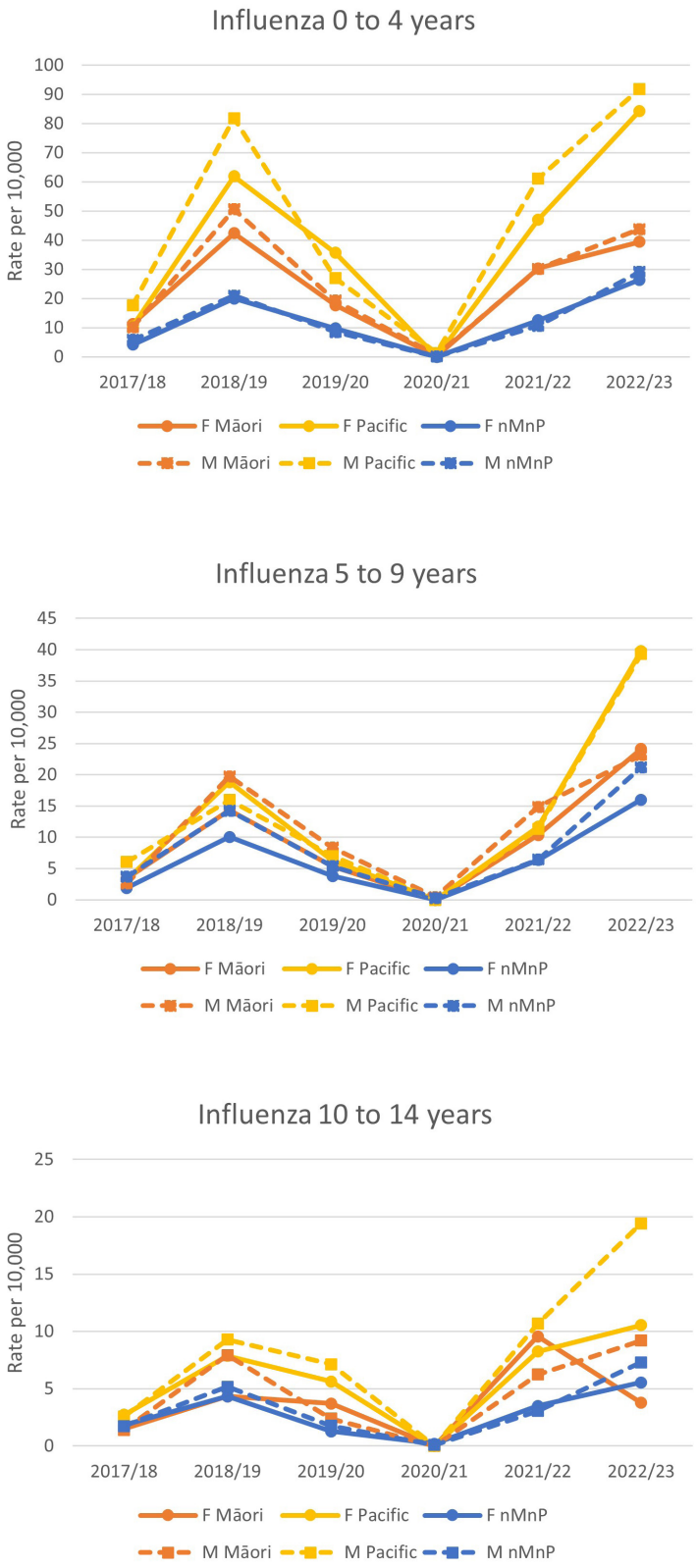

Figure 2: Rates of hospital discharges for lower respiratory tract infections.

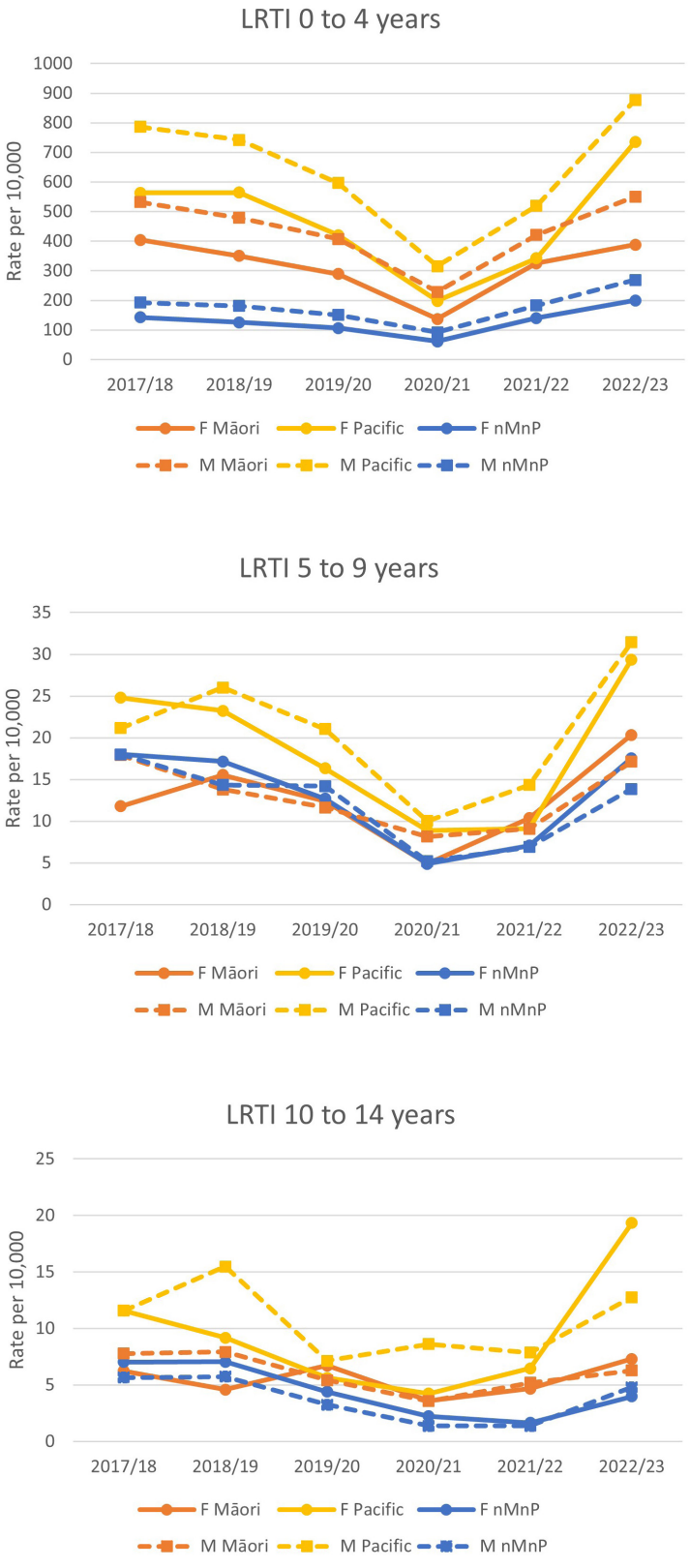

Figure 3: Rates of hospital discharges for acute upper respiratory tract infections.

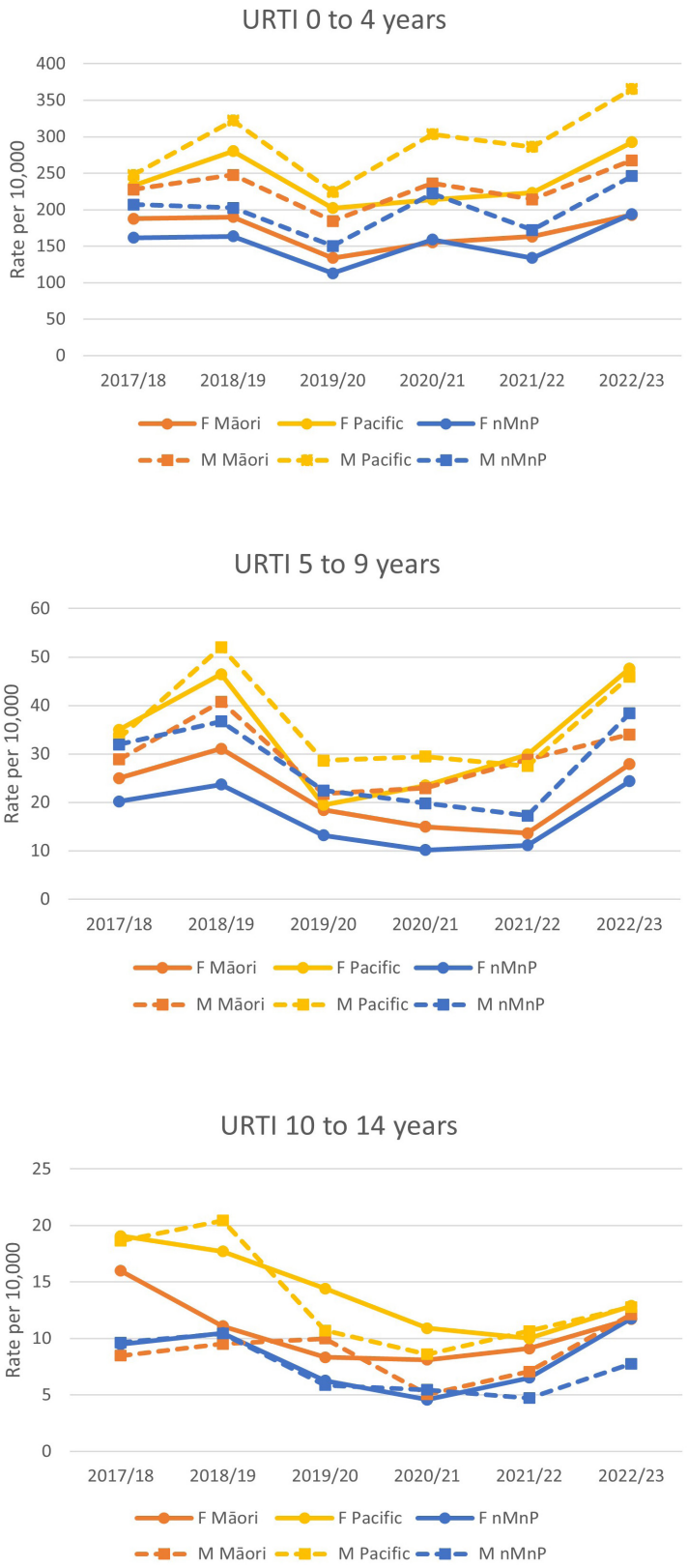

Figure 4: Rates of hospital discharges for asthma/wheeze.

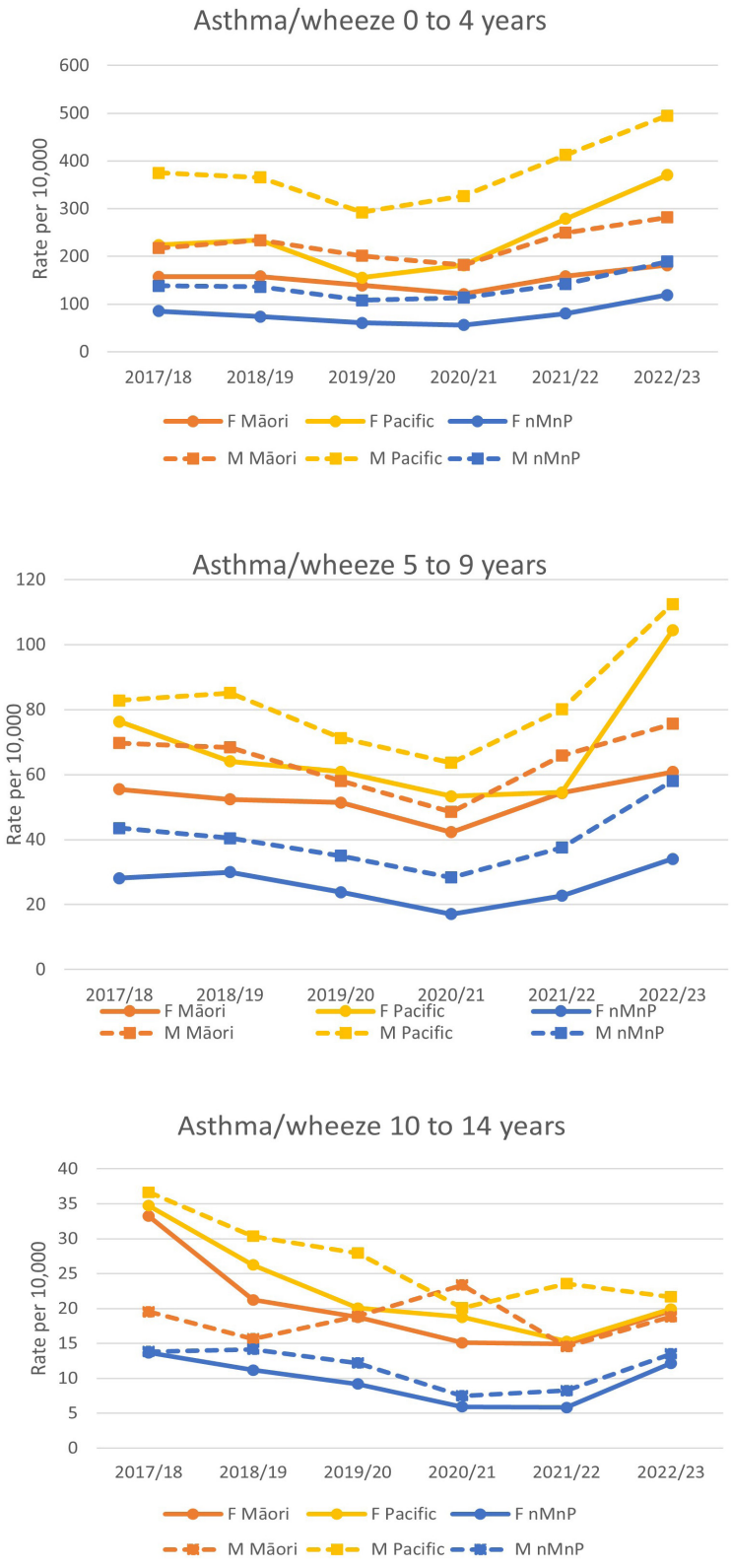

Table 3: Relative rates of hospital discharges for Māori compared to non-Māori, non-Pacific children aged 0–14 years in Aotearoa New Zealand, 2017/2018–2022/2023.

		0–4 years (F)	0–4 years (M)	5–9 years (F)	5–9 years (M)	10–14 years (F)	10–14 years (M)
		RR (95% CI)	RR (95% CI)	RR (95% CI)	RR (95% CI)	RR (95% CI)	RR (95% CI)
Influenza	**2017/2018**	2.70 (1.76–4.13)	1.75 (1.18–2.59)	1.84 (0.93–3.61)	0.71 (0.37–1.36)	0.82 (0.32–2.06)	0.81 (0.32–2.03)
	2018/2019	2.12 (1.72–2.60)	2.41 (2.00–2.92)	1.43 (1.04–1.96)	1.38 (1.07–1.79)	1.00 (0.58–1.74)	1.54 (1.00–2.35)
	2019/2020	1.81 (1.33–2.46)	2.26 (1.67–3.05)	1.41 (0.84–2.36)	1.55 (1.03–2.34)	2.91 (1.40–6.05)	1.35 (0.64–2.84)
	2020/2021*						
	2021/2022	2.42 (1.88–3.12)	2.83 (2.19–3.66)	1.63 (1.11–2.39)	2.31 (1.65–3.25)	2.73 (1.75–4.25)	2.04 (1.25–3.35)
	2022/2023	1.49 (1.23–1.82)	1.51 (1.25–1.81)	1.51 (1.17–1.93)	1.09 (0.86–1.38)	0.68 (0.39–1.17)	1.26 (0.87–1.82)
URTI	**2017/2018**	1.16 (1.07–1.27)	1.10 (1.02–1.19)	1.24 (0.98–1.56)	0.90 (0.74–1.10)	1.68 (1.23–2.32)	0.88 (0.60–1.29)
	2018/2019	1.16 (1.07–1.26)	1.22 (1.14–1.31)	1.31 (1.06–1.62)	1.11 (0.93–1.32)	1.06 (0.75–1.50)	0.91 (0.64–1.30)
	2019/2020	1.19 (1.07–1.31)	1.23 (1.13–1.34)	1.40 (1.06–1.85)	0.97 (0.77–1.22)	1.33 (0.88–2.00)	1.70 (1.17–2.49)
	2020/2021	0.98 (0.89–1.07)	1.06 (0.99–1.14)	1.47 (1.08–2.02)	1.16 (0.92–1.46)	1.77 (1.15–2.74)	0.93 (0.58–1.49)
	2021/2022	1.22 (1.11–1.34)	1.24 (1.15–1.35)	1.23 (0.89–1.69)	1.67 (1.33–2.09)	1.40 (0.95–2.06)	1.50 (0.97–2.31)
	2022/2023	0.99 (0.91–1.08)	1.09 (1.02–1.17)	1.15 (0.92–1.43)	0.89 (0.74–1.07)	1.00 (0.72–1.38)	1.56 (1.12–2.19)
LRTI	**2017/2018**	2.83 (2.63–3.04)	2.77 (2.61–2.94)	0.65 (0.48–0.89)	1.00 (0.77–1.29)	0.89 (0.56–1.40)	1.10 (0.73–1.67)
	2018/2019	2.79 (2.59–3.01)	2.65 (2.49–2.82)	0.90 (0.68–1.20)	0.96 (0.72–1.29)	0.65 (0.39–1.08)	1.12 (0.75–1.69)
	2019/2020	2.72 (2.51–2.96)	2.71 (2.53–2.90)	0.98 (0.71–1.34)	0.82 (0.60–1.12)	1.52 (0.96–2.43)	1.23 (0.76–2.01)
	2020/2021	2.24 (1.99–2.51)	2.48 (2.27–2.71)	1.01 (0.60–1.68)	1.57 (1.04–2.39)	1.61 (0.85–3.05)	1.60 (0.85–2.99)
	2021/2022	2.33 (2.16–2.51)	2.31 (2.16–2.46)	1.46 (1.00–2.13)	1.32 (0.90–1.93)	2.82 (1.49–5.35)	3.14 (1.70–5.82)
	2022/2023	1.94 (1.82–2.07)	2.05 (1.94–2.16)	1.16 (0.89–1.50)	1.24 (0.94–1.63)	1.83 (1.16–2.90)	1.57 (0.98–2.52)

Table 3 (continued): Relative rates of hospital discharges for Māori compared to non-Māori, non-Pacific children aged 0–14 years in Aotearoa New Zealand, 2017/2018–2022/2023.

		0–4 years (F)	0–4 years (M)	5–9 years (F)	5–9 years (M)	10–14 years (F)	10–14 years (M)
		RR (95% CI)	RR (95% CI)	RR (95% CI)	RR (95% CI)	RR (95% CI)	RR (95% CI)
Asthma/ wheeze	**2017/2018**	1.85 (1.67–2.05)	1.57 (1.45–1.71)	1.97 (1.66–2.34)	1.60 (1.39–1.85)	2.43 (1.91–3.09)	1.41 (1.08–1.85)
	2018/2019	2.15 (1.93–2.39)	1.72 (1.59–1.87)	1.75 (1.47–2.07)	1.69 (1.46–1.96)	1.90 (1.43–2.51)	1.10 (0.83–1.47)
	2019/2020	2.30 (2.05–2.58)	1.86 (1.70–2.03)	2.16 (1.80–2.59)	1.66 (1.42–1.94)	2.04 (1.51–2.74)	1.55 (1.18–2.03)
	2020/2021	2.16 (1.92–2.45)	1.60 (1.46–1.75)	2.47 (2.01–3.05)	1.71 (1.44–2.03)	2.54 (1.80–3.59)	3.12 (2.35–4.16)
	2021/2022	1.98 (1.78–2.19)	1.76 (1.62–1.90)	2.39 (1.99–2.87)	1.75 (1.51–2.04)	2.55 (1.80–3.62)	1.77 (1.29–2.42)
	2022/2023	1.52 (1.39–1.67)	1.49 (1.39–1.60)	1.78 (1.52–2.10)	1.30 (1.14–1.49)	1.62 (1.24–2.13)	1.40 (1.07–1.82)

Figures displayed are rate ratios for Māori children compared with the reference category of 1.0 for non-Māori, non-Pacific children.
RR = rate ratio; 95% CI = 95% confidence interval; URTI = upper respiratory tract infection; LRTI = lower respiratory tract infection.
*Very few cases of influenza in 2020/2021 precluded the calculation of RRs.

Table 4: Relative rates of hospital discharges for Pacific children compared to non-Māori, non-Pacific children aged 0–14 years in Aotearoa New Zealand, 2017/2018–2022/2023.

		0–4 years (F)	0–4 years (M)	5–9 years (F)	5–9 years (M)	10–14 years (F)	10–14 years (M)
		RR (95% CI)	RR (95% CI)	RR (95% CI)	RR (95% CI)	RR (95% CI)	RR (95% CI)
Influenza	**2017/2018**	2.51 (1.38–4.55)	3.05 (1.93–4.82)	1.68 (0.63–4.51)	1.64 (0.82–3.29)	1.48 (0.50–4.38)	1.47 (0.50–4.33)
	2018/2019	3.10 (2.41–3.99)	3.90 (3.12–4.87)	1.87 (1.25–2.81)	1.12 (0.74–1.69)	1.82 (0.96–3.44)	1.80 (1.01–3.18)
	2019/2020	3.65 (2.59–5.13)	3.16 (2.18–4.59)	1.65 (0.82–3.31)	1.30 (0.70–2.42)	4.43 (1.89–10.37)	4.04 (1.96–8.32)
	2020/2021*						
	2021/2022	3.76 (2.78–5.08)	5.73 (4.33–7.59)	1.84 (1.09–3.10)	1.77 (1.06–2.94)	2.35 (1.27–4.36)	3.49 (1.99–6.14)
	2022/2023	3.19 (2.56–3.97)	3.15 (2.57–3.87)	2.49 (1.85–3.34)	1.86 (1.41–2.45)	1.90 (1.12–3.23)	2.66 (1.79–3.97)
URTI	**2017/2018**	1.44 (1.28–1.62)	1.20 (1.07–1.33)	1.73 (1.29–2.33)	1.04 (0.78–1.38)	2.01 (1.32–3.07)	1.93 (1.28–2.92)
	2018/2019	1.71 (1.54–1.91)	1.59 (1.44–1.75)	1.96 (1.51–2.55)	1.42 (1.13–1.79)	1.69 (1.11–2.58)	1.96 (1.33–2.89)
	2019/2020	1.79 (1.57–2.04)	1.50 (1.33–1.68)	1.48 (1.00–2.18)	1.27 (0.94–1.73)	2.30 (1.43–3.70)	1.83 (1.08–3.08)
	2020/2021	1.35 (1.19–1.52)	1.37 (1.24–1.51)	2.31 (1.59–3.37)	1.49 (1.09–2.03)	2.38 (1.38–4.10)	1.58 (0.90–2.78)
	2021/2022	1.67 (1.48–1.89)	1.66 (1.50–1.85)	2.69 (1.91–3.79)	1.59 (1.15–2.20)	1.54 (0.90–2.61)	2.26 (1.34–3.83)
	2022/2023	1.51 (1.36–1.67)	1.48 (1.36–1.63)	1.95 (1.50–2.54)	1.20 (0.94–1.53)	1.10 (0.70–1.72)	1.65 (1.04–2.61)
LRTI	**2017/2018**	3.95 (3.62–4.30)	4.09 (3.81–4.39)	1.38 (0.98–1.95)	1.17 (0.82–1.68)	1.64 (0.97–2.80)	1.64 (0.98–2.76)
	2018/2019	4.50 (4.12–4.91)	4.10 (3.81–4.41)	1.35 (0.95–1.93)	1.81 (1.30–2.53)	1.30 (0.73–2.31)	2.19 (1.39–3.46)
	2019/2020	3.96 (3.58–4.37)	3.97 (3.66–4.30)	1.29 (0.85–1.96)	1.48 (1.03–2.13)	1.28 (0.63–2.62)	1.62 (0.86–3.06)
	2020/2021	3.23 (2.80–3.72)	3.42 (3.07–3.82)	1.82 (1.01–3.30)	1.93 (1.12–3.33)	1.89 (0.81–4.41)	3.85 (2.01–7.37)
	2021/2022	2.45 (2.21–2.71)	2.85 (2.62–3.09)	1.29 (0.72–2.28)	2.08 (1.31–3.30)	3.92 (1.83–8.36)	4.75 (2.34–9.64)
	2022/2023	3.68 (3.42–3.96)	3.26 (3.06–3.48)	1.67 (1.20–2.32)	2.27 (1.65–3.11)	4.85 (3.07–7.67)	3.20 (1.92–5.34)

Table 4 (continued): Relative rates of hospital discharges for Pacific children compared to non-Māori, non-Pacific children aged 0–14 years in Aotearoa New Zealand, 2017/2018–2022/2023.

		0–4 years (F)	0–4 years (M)	5–9 years (F)	5–9 years (M)	10–14 years (F)	10–14 years (M)
		RR (95% CI)	RR (95% CI)	RR (95% CI)	RR (95% CI)	RR (95% CI)	RR (95% CI)
Asthma/ wheeze	**2017/2018**	2.63 (2.31–2.99)	2.71 (2.46–2.99)	2.71 (2.19–3.35)	1.90 (1.57–2.30)	2.54 (1.84–3.51)	2.65 (1.95–3.60)
	2018/2019	3.18 (2.79–3.62)	2.69 (2.44–2.96)	2.14 (1.71–2.67)	2.11 (1.75–2.54)	2.34 (1.63–3.36)	2.14 (1.55–2.96)
	2019/2020	2.57 (2.20–2.99)	2.71 (2.43–3.02)	2.56 (2.02–3.24)	2.04 (1.66–2.50)	2.18 (1.46–3.25)	2.29 (1.64–3.20)
	2020/2021	3.24 (2.79–3.76)	2.87 (2.59–3.19)	3.12 (2.40–4.04)	2.24 (1.80–2.79)	3.16 (2.05–4.87)	2.68 (1.81–3.99)
	2021/2022	3.48 (3.08–3.93)	2.91 (2.65–3.19)	2.40 (1.87–3.08)	2.13 (1.75–2.59)	2.62 (1.66–4.15)	2.86 (1.99–4.13)
	2022/2023	3.11 (2.81–3.45)	2.62 (2.41–2.84)	3.06 (2.54–3.70)	1.94 (1.64–2.28)	1.64 (1.12–2.39)	1.61 (1.13–2.29)

Figures displayed are rate ratios for Pacific children compared with the reference category of 1.0 for non-Māori, non-Pacific children.
RR = rate ratio; 95% CI = 95% confidence interval; URTI = upper respiratory tract infection; LRTI = lower respiratory tract infection.
*Very few cases of influenza in 2020/2021 precluded the calculation of RRs.

true acute respiratory illness burden experienced by Pacific children. Furthermore, we based our data on the ICD codes used in the 2022 Cure Kids report.[15] We note that J22 (unspecified acute lower respiratory infection) was not included in the 2022 report but is included in the recently published 2023 report. This omission could affect our results if there is differential use of the code across age/sex/ethnicity groups; we are unable to assess the impact of this within the current study.

Given the nature of our study design, we were unable to ascribe hospitalisations to a causative agent (cf. Trenholme et al. 2021).[13] Moreover, given that the data pertain to a July to June year, winter peaks cannot be easily ascribed to one year or another, since the winter period overlaps these. An important observation in Aotearoa New Zealand is the changing pattern of RSV infections, which has been previously described.[12,20] In our study, most RSV infections would likely have been captured in the LRTI group, which includes pneumonia, bronchitis and bronchiolitis; this category will also include non-RSV diseases. In addition, RSV can lead to URTI or the exacerbation of asthma/wheeze, particularly viral wheeze in preschool children. Patterns of causative agents of respiratory infections (both community and hospital) in 2020/2021 in Australia and Aotearoa New Zealand have recently been described, including peaks of RSV and rhinovirus activity and an absence of influenza.[23]

It is important to consider non-causal reasons for the observed trends. These could include changes in the threshold for admissions based on the severity of illnesses due to health sector pressures. The changes in viral panel testing during the pandemic could also have differentially affected clinical diagnoses. Furthermore, lower access to primary healthcare, both due to concerns of accessing health services while COVID-19 was a threat[24,25] as well as the more recent issues of closed books[26] and inability to get general practitioner appointments, could have affected rates of hospital admissions for respiratory illnesses among children.

Importantly, we demonstrate the reappearance of pre-existing inequities in respiratory health in the years following the relaxation or removal of COVID-related NPIs. The inequities in respiratory disease for tamariki Māori identified in our study are consistent with previous research that illustrates the significant health inequities Māori experience across multiple health domains.[27] The inequities are driven by the ongoing experience of colonisation and the harm caused by societal structures that systematically disadvantage Māori.[28] The causal mechanisms between colonisation and health inequities have been identified, beginning with the basic causes of racism and discrimination through to medial drivers of socio-economic opportunities and health systems.[29] Across this pathway Māori experience systemic racism,[30] barriers to accessing care[31] and fewer socio-economic resources[32] than non-Māori, non-Pacific. The re-emergence of pre-existing respiratory inequities is therefore unsurprising given COVID-related NPIs reduced the spread of infection but did little to address the underlying basic causes.

For Pacific children, who had higher rates of respiratory illnesses prior to the pandemic, the re-appearance of inequities is even more stark, with hospitalisation rates in 2022/2023 for many age/sex/illness categories being higher than in pre-COVID years. We postulate that this could be due to a combination of factors. The broader socio-economic determinants of health affect respiratory health, including living in crowded and poorly insulated houses.[33] Pacific children are disproportionately more likely to be living in households experiencing material hardship, food insecurity or housing issues, including household crowding,[34,35] all factors which may have been exacerbated by the current cost of living crisis. However, the higher rates of respiratory disease for Pacific peoples are not fully explained by area-level deprivation.[36] The health challenges experienced by Pacific peoples are also influenced by systemic racism, discrimination and unconscious biases within healthcare structures.[37–39] These biases may extend to children through their caregivers, as caregivers often engage with health services on behalf of their children.[40] Each of these factors, either individually or in combination, could be potential explanations for the observed patterns that we demonstrate.

The higher rates of hospitalisations in young children for illnesses due to infectious causes seen in our results are consistent with the concept of immunity debt.[9,10] For example, the absence of RSV circulation for one season when COVID-related NPIs were in place has been argued to have resulted in a change in population immunity, with absence of exposure to RSV resulting in a waning in immunity and hence more severe disease when re-exposure occurred. While this concept has been discussed predominantly in relation to infants and young children, a recent

paper examining temporal changes in RSV epidemiology in Aotearoa New Zealand in the post-COVID era showed that this effect was seen across the whole population.[41]

Results for asthma/wheeze showed persisting inequities in hospitalisations, which is consistent with previous findings.[42] Preschool wheeze is the most common cause of hospital admission in the preschool age group in Aotearoa New Zealand.[43] It is frequently a recurring problem with affected children having multiple hospital presentations. An excessive inflammatory response to a respiratory viral infection is the central underlying process leading to recurrent disease. That wheeze admissions have increased in this age group since COVID-19 is another indicator of changes in immune system function in the post-COVID era. Lower access to primary care in the post-COVID era is another potential explanation for the increase in asthma-related admissions.[26]

The national immunisation schedule includes vaccines for respiratory health, specifically against pertussis, pneumococcal disease and *Haemophilus influenzae* type b, along with a targeted influenza vaccine for high-risk children—although in 2022/2023 this was briefly funded for all children aged 3–12 years, and then 6 months–12 years. However, vaccine coverage has never been equitable in Aotearoa New Zealand. Coverage for tamariki Māori has been consistently lower than for all other ethnic groups; prior to the onset of the COVID-19 pandemic, Pacific children had high immunisation rates at 12 and 24 months, though not at 6 months.[44] However, since the 2020 lockdowns the rates for tamariki Māori and for Pacific children have fallen substantially.[25,44] Strengthening support for both Māori and Pacific providers to address declining levels of vaccine coverage is likely to reverse the worrying trends.

The adverse impacts of the cost of living and health service crises in the recent years are likely to have impacted on childhood hospitalisations. Māori and Pacific providers worked hard during the pandemic to meet the needs of communities that were not being met by the national response.[39,45] However, the current data cannot assess the separate impact of these activities on non-COVID hospitalisations. While we have described how COVID-related NPIs reduced hospitalisations for respiratory illnesses in children across ethnic groups, we are not suggesting that the *drivers* of health inequities were affected by COVID-19 restrictions. Rather, the wider determinants of health inequities are likely to have been amplified by the pandemic, and their impacts on respiratory hospitalisations reappeared when NPIs were removed.

In summary, our results support the call by Baker and colleagues[46] for a continued mitigation strategy not only for COVID-19 but also for other respiratory illnesses, which builds on learnings from our pandemic response. The central tenets of this approach that integrates COVID-19 control measures with those for seasonal respiratory infections such as influenza and RSV are: i) an enhanced system for delivering vaccinations to ensure high and equitable coverage, ii) the promotion of testing and self-isolation when unwell, supported by paid sick leave, and iii) measures to minimise the transmission of respiratory pathogens in key indoor environments, including schools. In order to be successfully implemented, an evidence-based approach supported by culturally responsive partnerships with both Māori and Pacific primary care providers is necessary. This has the potential to alter the worrying patterns of the re-appearance of inequities we have demonstrated, leading to improvements in respiratory health among children in Aotearoa New Zealand.

COMPETING INTERESTS
Nil.

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Attempt CPR—language matters inside our hospitals

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ABSTRACT

The terms cardiopulmonary resuscitation (CPR) and resuscitation have been used non-specifically and interchangeably. To provide clarity and transparency to clinicians and patients when facilitating conversations about what treatments are warranted and wanted if clinical deterioration occurs in the hospital, CPR must be reframed as its original, official definition in New Zealand: chest compressions and rescue breaths.

Key messages

- CPR has become shorthand for resuscitation, with the terms used interchangeably. Resuscitation measures to preserve life and organ function are far broader than CPR.
- Separation of CPR from other resuscitative measures will result in better clinician–patient conversations and more precise treatment decisions tailored to preventing deterioration and, thus, cardiac arrest.
- In-hospital progressive deterioration leading to natural dying is different from sudden cardiac arrest.

Cardiopulmonary resuscitation (CPR) was initially defined as chest compressions and rescue breaths to manually empty the heart, offering a degree of cerebral perfusion while the cause of cardiac arrest is reversed.[1] In the United Kingdom (UK), this original definition has been replaced. CPR now includes high-voltage electric shocks, ventilation and injection of drugs,[1] and decisions documented in the ReSPECT (Recommended Summary Plan for Emergency Care and Treatment) process.[2] Most other international resuscitation councils, including the New Zealand Resuscitation Council, retain the original definition of chest compressions and rescue breaths (Table 1). Despite this, almost all healthcare practitioners in New Zealand include broader resuscitation measures in their understanding of the term CPR when talking with each other and patients.[3]

This international variance in terminology means that "CPR" and "resuscitation" are used interchangeably and non-specifically.[3] This is particularly significant when considering cardiac arrest in hospitals. CPR is not a definitive treatment. It is part of the broader range of measures that constitute resuscitation, and in a patient with an easily reversible cause of cardiac arrest, bridges a patient to those measures.

In the hospital, most cardiac arrests are not sudden or shockable and follow a period of clinical deterioration. CPR, therefore, has questionable utility, particularly after attempting other resuscitative measures during the peri-arrest state. We will argue that CPR has little value here and withholding it (do-not-attempt-CPR) can cause harm in terms of limiting access to other treatments. Returning to the original definition allows patients access to other resuscitative measures to prevent further deterioration into cardiac arrest while protecting them from harmful interventions at the end of life.

Cardiac arrest is different in hospital

Cardiac arrest in hospitals has poor survival in most locations.[4] Patients are already being treated for medical or surgical conditions, are located in general wards, are mostly unmonitored and have low rates of shockable arrhythmias.[5] Cardiac arrest incidence in hospitals peaks at 48 hours[1] and follows a period of deterioration heralded by a change in patient vital signs in 60% of cases.[6] Such conditions are in marked contrast to cardiac arrest that occurs out-of-hospital, or in-hospital in operating theatres and coronary care units; here cardiac arrest is sudden, and CPR is a vital bridge to defibrillation or other treatment for reversible causes.[4]

It is time to be more explicit about the difference between *sudden* cardiac arrest, when CPR may be an effective first aid intervention, and *subacute* deterioration. For the latter, cessation of cardiac

Table 1: Definition of CPR, language, documentation and decision-making framework from five countries' national cardiac arrest databases compared with New Zealand.

Country	CPR definition	Phraseology	Form	Decision-making framework
US	Chest compressions and rescue breaths as intermediary measures sufficient to maintain cerebral perfusion while definitive treatment is being sought.	Cardiopulmonary resuscitation and resuscitation	Medical Order for Life-Sustaining Treatment (MOLST form)	Patient/family consent required—state-led legislature
UK	Chest compressions, defibrillation, artificial ventilation, drugs	DNACPR	DNACPR forms, advance directives or Recommended Summary Plan for Emergency Care and Treatment (ReSPECT form)	Clinician-led within a shared decision-making framework
Japan	Chest compressions and rescue breaths as intermediary measures sufficient to maintain cerebral perfusion while definitive treatment is being sought.	DNAR	Code confirmation or advance directive	Clinician-led within a shared decision-making framework
Denmark	Chest compressions and rescue breaths	Do-not-resuscitate, do-not-intubate		Clinician-led within a shared decision-making framework
New Zealand	Chest compressions and rescue breaths	DNACPR	Shared goals of care form	Clinician-led within a shared decision-making framework

CPR = cardiopulmonary resuscitation; DNACPR = do-not-attempt cardiopulmonary resuscitation; UK = United Kingdom; US = United States of America.

activity occurs at the point of death despite other attempts at treatment, and often resuscitation.

The latter process is better referred to as natural dying, and in a hospital it can sometimes be a rapid process. Clinicians and patients should appreciate natural dying and its distinction from sudden cardiac arrest. Natural dying occurs when illness or injury exceeds the person's ability to recover, often despite intensive treatments, leading to the secondary cessation of circulation. In the latter situation, where CPR is deployed as the final resuscitation manoeuvre before attempts are halted, CPR serves no medical purpose. It may also be contrary to patient-defined preferences or treatment goals.

Reframing CPR as chest compressions and rescue breaths will provide transparency to clinicians and patients about what treatments are warranted and wanted if clinical deterioration occurs in the hospital. It also affords clinicians clarity in situations where communication and decision-making are complex and emotionally

charged. It offers an individualised plan in the event of deterioration, with nuanced resuscitative measures, like drugs, intravenous fluids, intensive care treatment or defibrillation for monitored arrhythmias. Most importantly, it can incorporate a focus on comfort care without intrusive interventions for dying patients.

CPR benefits only a specific minority of hospitalised patients (mechanism of deterioration)

For out-of-hospital cardiac arrest, the time to initiation of CPR is a key determinant of the outcome, but in hospitals, the relationships are more complex. Favourable outcomes are more strongly linked to the aetiology of cardiac arrest (Table 2) and patient type/location (Figure 1) rather than treatment delay (adjusted odds ratio [OR] for 30-day survival 2.81 for monitored wards [95% CI 2.63–3.01] vs 0.55 for delay in calling [95% CI 0.50–0.61]).[4]

The 1-year survival for in-hospital cardiac arrest for cardiac patients is 39.3% versus 10.7% for non-cardiac patients.[7] Causes of in-hospital cardiac arrest with good outcomes are those that are highly reversible, such as general anaesthesia, intoxication and hypothermia, with survival rates of around 50%.[8]

Conversely, CPR adds little value when cardiac arrest has occurred due to catastrophic diseases such as aortic dissection/rupture or intracerebral haemorrhage (Table 3),[8] or when the cause cannot be treated within the timeframe of cardiac arrest, such as exsanguination or aortic stenosis.[8,9]

Table 2: Cause of cardiac arrest as determinant of outcome.

	Year	N	Study population	Condition	Outcome measure	Outcome
Nolan[1]	2014	23,554	IHCA >16 years	VT/VF	Survival to discharge (%)	49.0%
				PEA		11.4%
				Asystole		8.7%
Tian[10]	2010	49,656	First CPA in ICU	VT/VF	Survival to hospital discharge (%)	30.7/34.2%
				PEA		10.9%
				Asystole		11.1%
Bergum[11]	2015	302	IHCA >18 years of age receiving CPR +/- defibrillation	Cardiac cause	Survival to discharge (%)	30%
				Hypoxic cause		37%
				Thrombosis/PE		27%
				Cardiac tamponade		7%
				PEA		13%
				Asystole		17%
				VF		54%
				VT		53%
Wallmuller[8]	2012	1,041	IHCA in ED	Acute STEMI/NSTEMI	6-month survival + CPC 1–2 (%)	49/46%
				Adverse drug reaction/ intoxication		60%

Table 2 (continued): Cause of cardiac arrest as determinant of outcome.

				Accidental hypothermia		44%
				Metabolic		35%
				Pulmonary		24%
				Exsanguination		13%
				Cerebral		14%
				Sepsis		5%
				Aortic dissection/ rupture		3%
Sulzgruber[9]	2019	51	ICHA with TTE within 2 months prior to event	Aortic stenosis of any severity	Survival/adjusted odds ratio survival to discharge	19%/0.14 (0.04–0.48)

CPA = cardiopulmonary arrest; CPC = cerebral performance category; CPC 1- = good cerebral performance (normal life); CPC 2- = moderate cerebral disability (disabled but independent); CPR = cardiopulmonary resuscitation; DNAR = do-not-attempt-resuscitation; ED = emergency department; ICU = intensive care unit; IHCA = in-hospital cardiac arrest; NSTEMI = non-ST elevation myocardial infarction; PE = pulmonary embolus; PEA = pulseless electrical activity; STEMI = ST-elevation myocardial infarction; TTE = transthoracic echocardiogram; VF = ventricular fibrillation; VT = ventricular tachycardia.

The cost of survival for those who survive

Proponents of the drive towards "catch-all CPR first, think later" algorithmic management of in-hospital cardiac arrest will point to the improvements in survival over the last 20 years for all types of in-hospital cardiac arrest documented in both large United States of America (US)[12] and Swedish registry data[5] (Table 3). However, cardiac arrest survival is highest in countries with the lowest incidence (Table 3). Given the international standardisation of care, it seems likely that patient selection or possibly attitudes towards resuscitation substantively impact survival. Furthermore, adjusted 30-day survival only improved in younger patients, whereas older patients (>85 years) experienced no improvement.[5] It is important to emphasise to proponents of CPR that system improvements such as time to treatment—mainly defibrillation and adrenaline—are also driving survival gains more than chest compressions.[13,14]

For survivors, recovery is complex. Despite 79.5% of US in-hospital cardiac arrest survivors attaining CPC category 1–2,[12] 40% have life-changing disability after discharge[5] and only half

Table 3: Data from the five countries with national in-hospital cardiac arrest databases.

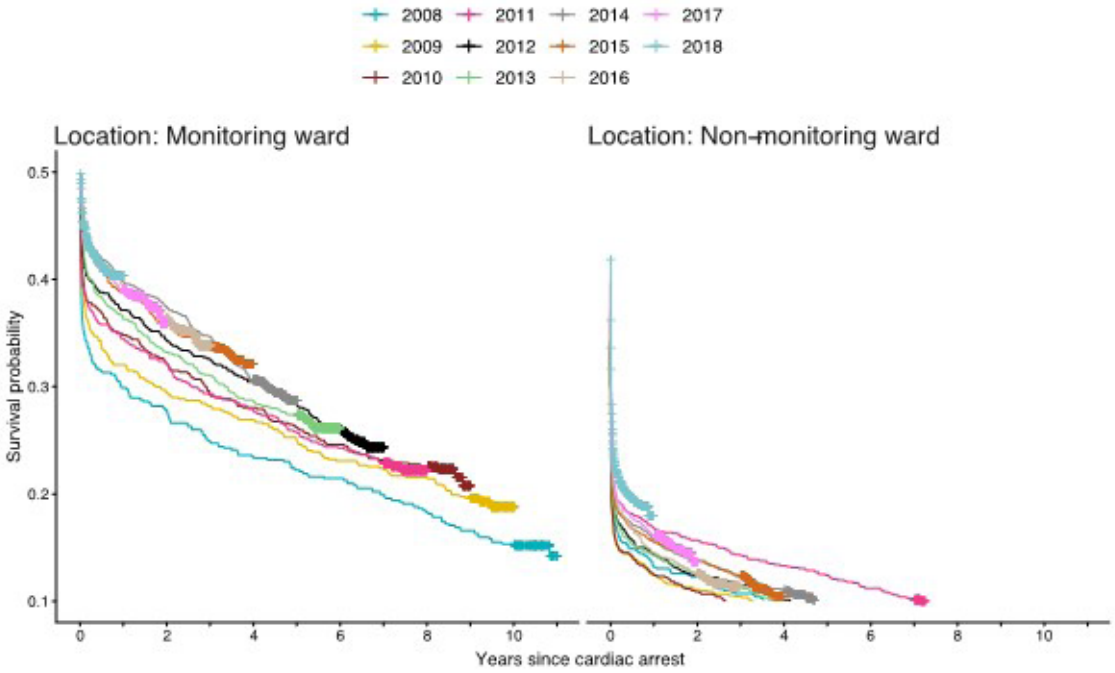
Author Year Country	Incidence	Witnessed	Monitored	Shockable	Condition	RoSC	Survival
Tsao[12] 2022 US (n=33,874)	4.0/1,000 admissions (all cardiac arrest)		56.2%	13.7%	Overall		22.4%* (to discharge)

Table 3 (continued): Data from the five countries with national in-hospital cardiac arrest databases.

Author Year Country	Incidence	Witnessed	Monitored	Shockable	Condition	RoSC	Survival
Peberdy[15] 2003 US (n=14,720)		86%		25%	Overall	44%	17% (to discharge)
					VT/VF	63/58%	35/34%
					Asystole	35%	10%
					PEA	39%	10%
Andersen[16] 2019 Denmark (n=4,069)		77%		18%	Overall	53.8%	27.8% (30 day)
					Shockable	81.7%	57.6%
					Non-shockable	41.8%	16.1%
Nolan[1] 2014 UK (n=22,628)	1.6/1,000 admissions (only cardiac arrest attended by team†)		44%	16.9%	Overall	45%	18.4% (to discharge)
					VT/VF	76%	49%
					Asystole	26.2%	8.7%
					PEA	40.9%	11.4%
Ohbe[17] 2022 Japan (n=274,664)	5.1/1,000 (all cardiac arrest)				Overall		12.7% (to discharge)
					Patients with defibrillation		23.3%
					Patients without defibrillation		10.5%
Hessulf[4] 2018 Sweden (n=18,069)	1.7/1,000 all cardiac arrest	81%	50%	32%			28.5% (30 day)
Adielsson[5] 2020 Sweden (n=23,186)		79.3%		26.3%	Overall	52.2%	30% (30 day)
					Shockable	79.4%	60.6%
					Non-shockable	38.2%	16.9%

RoSC = Return of Spontaneous Circulation; PEA = pulse electrical activity; UK = United Kingdom; US = United States of America; VT = ventricular tachycardia; VF = ventricular fibrillation.
*First decline in in-hospital cardiac arrest survival since records began reflecting the COVID-19 pandemic.
†UK registry data excludes episodes treated by base teams such as those in coronary care or operating theatres.

Figure 1: Kaplan–Meier curves for survival after cardiac arrest, stratified by calendar year at the time of arrest and on the basis of the monitoring level of the ward.



Reproduced with permission.[5]

are discharged home. This harm is not readily available in the statistics.[15] Longer-term survival continues to decline after discharge, particularly for general ward patients compared with those on monitored wards such as coronary care and operating theatres (Figure 1).[5]

Monitored wards include coronary care, intensive care, operating theatres, cardiac catheter laboratories and emergency departments.

CPR can be harmful

Closed chest cardiac massage was the natural evolution from open cardiac massage conducted through an emergency thoracotomy. Although simple to administer, closed chest cardiac massage only produces about 20–40% of the usual cardiac output[18] and causes rib fractures, with older age as a risk factor.[19] It can also cause life-threatening injuries,[20] and this could contribute to the high (60%) incidence of death following the initial return of spontaneous circulation (RoSC).[13,19]

Survival rates for CPR in subacute decline are low

Deciding which patients are likely to benefit and should opt in for "attempt CPR" requires three separate considerations: patient factors, with frailty being more important than age (Table 4), the aetiology of illness and cardiac arrest as outlined above and whether that arrest has occurred despite optimal treatment. Rates of survival after cardiac arrest in sepsis and all patients in intensive care units are low (Table 2).[8,10] In subacute decline, treatment has often already been optimised.

While RoSC occurs in around 50% of in-hospital cardiac arrests, that reprieve is often brief before death ensues.[1] Although injuries related to CPR and resuscitation may contribute, it is more likely that deterioration occurs in a patient not responding to treatment, and cardiac arrest results as the end-point of natural dying.[1] Over 60% of patients who survive their initial cardiac arrest will subsequently have active treatment withdrawn or limited and die naturally during the same hospital admission.[13]

DNACPR should only limit CPR, not halt other forms of resuscitation in hospital

DNACPR decisions must not compromise the quality of care for any patient. Decisions to prevent CPR should not be misinterpreted as an

unofficial stop sign to other appropriate interventions. DNACPR decisions were associated with doubling the risk of death at 30 days for intracranial haemorrhage (OR 2.17 95% CI 1.38–3.41) despite adjustment for disease and age.[21]

Narrowing the definition of CPR to chest compressions and rescue breaths clarifies the practice, enabling clinicians to offer other treatments and resuscitative measures as appropriate.

This is enabled by the New Zealand national Shared Goals of Care form (Appendix), where individual levels of care can be ascribed between four options. Shared Goal of Care A is where the patient is for treatment with curative or restorative intent and includes CPR. Shared Goal of Care B is where the patient is for treatment with curative or restorative intent B but excludes CPR. Option C focusses on improving symptoms with non-burdensome treatments, and D cares for the dying patient. Patients who have been ascribed a Shared Goal of Care B can still access other resuscitative measures in the peri-arrest period aimed at halting their deterioration into cardiac arrest.

Communication with patients and families about CPR in hospital

Despite clear benefits and extensive training, healthcare teams remain hesitant to have comprehensive end-of-life or resuscitation discussions. In a study of patients with advanced cancer recruited to examine the impact of these conversations,

Table 4: Patient factors associated with survival after in-hospital cardiac arrest.

	Study population	Condition	Outcome measure	Outcome
Smith[22] 2019 (n=318)	All IHCA cardiac arrests in tertiary centre	Hospital Frailty Risk score ≥5	% Discharged home (unadjusted OR, 95% CI)	4% (OR 0.13, 0.04–0.41, p<0.001)
		Previous hospital admission		15% (OR 0.54, 0.31–0.95, p=0.03)
		Unplanned admission		16% (OR 0.41, 0.25–0.67, p<0.001)
Hirlekar[23] 2017 (n=11,396)	IHCA >70 Swedish CPR register	70–79 years	% 30-day survival	28%
		80–89 years	% 30-day survival	20%
		>90 years	% 30-day survival	14%
		Prior HF	Unadjusted OR 30-day survival	OR 0.71 (0.65–0.78)
		Prior diabetes		OR 0.87 (0.78–0.96)
		Prior respiratory failure		OR 0.49 (0.43–0.55)
		Prior malignancy		OR 0.7 (0.62–0.79)
		Prior renal dysfunction		OR 0.54 (0.49–0.59)

CPA = cardiopulmonary arrest; CPR = cardiopulmonary resuscitation; HF = heart failure; ICU = intensive care unit; IHCA = in-hospital cardiac arrest.

only 37% of patients reported prior discussions.[24] A review of calls requesting medical emergency advice for hospital inpatients suggests that a third (estimated 30,000 calls per year in New South Wales, Australia) were for end-of-life issues in elderly frail patients who were often unaware that they were dying.[25] Initiatives such as ReSPECT in the UK demonstrate similar low engagement with discussions (6–41% of patients admitted to test sites had a ReSPECT form).[2]

The preferences of patients and their families for cardiac arrest treatment requires clinical support beyond asking a patient if they would like their "heart restarted". This approach undersells the complexity of treatment and does not represent shared decision-making. Patient selections are often confused and paradoxical. Treatment can be complicated and dynamic. For example, respondents to a treatment preference survey indicated that 74% wished to receive chest compressions, whereas only 61% selected defibrillation and 42% ventilation.[26] Over-estimation of surviving CPR is common and imagined to be between 55%.[26] This is perhaps unsurprising due to the misrepresentation of outcomes by clinicians, but also in television and other media.[27]

Initiatives such as ReSPECT and the national Shared Goals of Care programme in New Zealand encourage early discussions. Clinicians ultimately lead the medical decision-making process in these programmes. Although patient engagement has improved, qualitative interviews suggest a culture of *informing* rather than partnering with patients in these discussions, especially for CPR conversations.[28] An example from interview-based analysis, one consultant said:

> *"I went in with quite clear views of what had to be done and as you say the patient's son started to suggest that 'actually he would want to be resuscitated wouldn't you Dad'... and I gently had to steer him away to explain why I didn't think that would be a good idea."*[28]

In the US, stronger tactics with graphic descriptions of resuscitation are common.[29] One doctor's comment in a study of DNAR discussions illustrates how choice of language manipulates patient autonomy:

> *"This is kind of paternalistic, but if I feel strongly that the patient wouldn't benefit from resuscitation, I'll be pretty graphic ... I want you to know we have to press really hard and break ribs."*[29]

The culture of conversations in New Zealand is likely to be similar and may use graphical illustrations to manipulate patient requests or use medical leading of the conversation. Although these practices are not illegal, the opportunity to bring the person and their goals and values into the conversation is completely lost.

Better CPR conversations

The ideal process in hospital is a discussion centred solidly around the patient's goals, and frameworks such as the serious illness conversation guide[30] have been adopted and regionalised for use in New Zealand. Although these frameworks derive broader treatment goals than just CPR, the information gathered from a structured approach will help the clinician better understand what matters to the individual and their whānau. This enables the clinician to make a clinical recommendation incorporating patient-centred goals alongside factors for successful CPR.

For the patient, articulating their goals should be followed with clear explanations of the specific, medically indicated treatments that will support those goals, in the event of deterioration.

Partnering with patients to improve their understanding of CPR as a bridging measure could shift emphasis from graphic illustrations of resuscitation to a more open and honest discussion about what may lie ahead.

Conclusion

The limited scope of CPR (chest compressions and rescue breaths) in hospitalised patients is poorly recognised by the public (and possibly clinicians); a conversation about this is overdue.

We argue that non-specific language around CPR complicates how well it is understood and discussed. Many hospitalised patients at risk of subacute deterioration towards anticipated dying have risk factors for CPR-related injuries and low survival after ROSC. Their treatment should be focussed on preventing cardiac arrest with other measures while preparing to meet their care wishes during dying. Reframing CPR as its original concept and uncoupling it from resuscitation may improve how clinicians discuss treatment options and enable patients to recognise that beneficial treatments are not being withheld.

COMPETING INTERESTS
KG is Chair of the HNZ Canterbury Clinical Ethics Advisory Group.
There are no other competing interests to declare.

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Appendix

New Zealand National Shared Goals of Care form

Shared goals of care plan

Family Name: _____

Given Name: _____ Gender: _____

AFFIX PATIENT LABEL HERE

Date of Birth: _____ NHI#: _____

Discuss the goal of care for this admission with the person, family, whānau or other (as appropriate).
Select the agreed goal of care and document your discussion.

Attempt CPR

A The goal of care is **curative** or **restorative.**

☐ Treatment aims to prolong life.

Attempt CPR: it is clinically recommended and in accordance with the person's known wishes.

Also for referral for ICU level care, 777 calls and all appropriate life sustaining treatments.

Additional comments: _____

Do not attempt CPR

B The goal of care is **curative** or **restorative.**

☐ Treatment aims to prolong life and enhance its quality.

Do not attempt CPR: this is likely to cause more harm than benefit or is not desired by the person.

Referral for ICU level care is appropriate ☐ Yes ☐ No

777 calls are appropriate.

Additional comments (e.g. non-invasive ventilation, dialysis): _____

C The goal of care is primarily **improving quality of life.**

☐ Treatment aims to control symptoms, enhance wellbeing and should be easily tolerated.

Do not attempt CPR: this is likely to cause more harm than benefit.

Referral for ICU level care is unlikely to be appropriate.

777 calls are appropriate ☐ Yes ☐ No

Additional comments (e.g. antibiotics, IV fluids, NG feeding): _____

D The goal of care is **comfort whilst dying.**

☐ Treatment aims to alleviate suffering in the last hours or days of life and allow a natural death.

Consider end of life guidelines such as *Te Ara Whakapiri.*

Do not attempt CPR. Referral for ICU level care and 777 calls are not appropriate.

Additional comments (e.g. pain management, fluids): _____

This plan has been discussed with the person. If not, record reason overleaf.

Name: _____ Date: / / Time: _____

Designation: _____ Signature: _____

☐ SMO informed, name: _____

This plan is not valid unless signed and dated. Clinically review the person if there are concerns or a change in their condition. Any change to the goal of care requires a new plan and the earlier plan crossed out. Include shared goals of care information in the discharge summary.

Side 1 of 2

HQSC SGOC form v18 Sep 2020

SHARED GOALS OF CARE FORM

Appendix (continued): New Zealand National Shared Goals of Care form

Shared goals of care plan

Use this side first to guide the discussion and record key points.

Family Name: _____

Given Name: _____ Gender: _____

AFFIX PATIENT LABEL HERE

Date of Birth: _____ NHI#: _____

Prepare

Consider the person's capacity, their privacy, support people, cultural needs and medical trajectory.

Do they have an:

- Advance Care Plan and/or Advance Directive? ☐ Yes ☐ No ☐ Unknown
- Enduring Power of Attorney (EPA) or legally appointed guardian? ☐ Yes ☐ No ☐ Unknown

If yes, circle either EPA or legal guardian and record their full name:

_____

Seek agreement with the person to have the discussion, with the people they want present.

Full name(s), relationship(s) and role(s) of those present: _____

_____

_____

Discuss

Ask about their understanding of their current condition and what may lie ahead.

Ask how much information they would want to know.

Share your understanding of their current condition and what may lie ahead.

Explore their values and what is important — their priorities, hopes, worries, what helps in tough times and what they would be willing to go through for more time.

_____

_____

_____

_____

_____

_____

_____

Summarise and check for shared understanding.

Recommend and close

Explain your recommendation in plain language, outlining which treatments are more likely to cause benefit than harm.

Reach a decision and document the goal of care overleaf.

Additional comments: _____

_____

_____

_____

_____

☐ Further information in clinical record.

If discussion not held with person, record reason below: _____

_____

_____

_____

_____

Document follow-up plan in the clinical record.

Side 2 of 2

HQSC SGOC form v18 Sep 2020

"Front-load" your co-design—evidence in mental health supports it

Clive Bensemann, Karen O'Keeffe, Arana Pearson, Jacqueline Ryan, Karl Wairama, Wi Keelan

ABSTRACT

Co-design in quality improvement projects is well-established as an effective way of creating more consumer-centred, whānau-centred care, and to shape solutions that work for consumers as well as services. However, in practice, consumers of health services, families and whānau are often consulted after key decisions about project design are made. This can result in tokenism, missed opportunities for improvement and breached obligations to the Māori right to autonomy, self-determination and control of their own destiny as expressed in Article 2 of Te Tiriti o Waitangi.

"Front-loaded" co-design was used in selection of project areas and project design in Te Tāhū Hauora – New Zealand Health Quality & Safety Commission's mental health quality improvement work and has been critical to success. With broad sector consultation, one area mental health consumers agreed was a priority for improvement was elimination of seclusion in mental health services, particularly for Māori who experienced significant health inequity in this area. This aim was considered unachievable by many in the sector at the time. However, the zero seclusion project has successfully contributed to reductions in rates of seclusion of all ethnicities, and continues to do so.

"Front-loaded" co-design with Māori and consumer guidance is critical to this success. Furthermore, true co-design also ensures the mana motuhake and tino rangatiratanga (self-determination and control over one's own destiny) of Māori, and of all peoples who use our health services.

Co-design in quality improvement projects is well-established as an effective way of creating more consumer-centred, whānau-centred care.[1,2] However, co-design in quality improvement often involves consumers of health services, families and whānau *after* key decisions about the project design are made. Such key decisions can include the definition of the problem itself that the project is trying to solve.

Tokenism, missed opportunities and breaching Te Tiriti o Waitangi obligations

"Front-loading" of co-design, or bringing consumer engagement in early into problem and project definition, is, unfortunately, not common. Experienced commentators suggest early consumer engagement is important,[1,3] but does not always occur. Consumer engagement can often be tokenistic, "*more about legitimizing managerial or professional decisions that would have been made anyway*."[4,5] In three major co-design projects (lung cancer, kidney and aneurysm), the authors identify early involvement of consumers as a key feature of effective co-designed quality improvement.[4] The power of the consumer voice lies in it being "*a technology of persuasion*" and means of influencing opinion and debate with clinicians, enhancing project credibility, challenging clinical assumptions and resolving contestation over the appropriateness of proposed changes.[4] As one quality improvement team member concisely articulated:

> *"They're very powerful advocates … They have a moral stature that you can't really question. If a patient tells you that the service feels a certain way, you can't really argue that it doesn't, because that's their experience."*[4]

Starting late with consumers misses major opportunities. Not only can projects fail to properly diagnose and address the problems at hand for those most affected by them, but also in an Aotearoa New Zealand context such an approach actively impinges on the tino rangatiratanga of Māori affected by the problem—Māori right to autonomy, self-determination and control of their own destiny as expressed in Article 2 of Te Tiriti o Waitangi.[6]

Furthermore, leaving consumers out of project definition and design impinges on the self-determination of *all* those directly affected. Early

consumer involvement can both legitimise projects and shape more appropriate responses. Such true co-design is also more creative down the line: a wider range of potential interventions are made available.

What is the problem in mental health (and who decides)?

Extensive evidence and expert consensus recognises that access to, experience, processes and outcomes of healthcare are inequitable for Māori.[7] Specifically, mental illness and how we treat it is also inequitable. The prevalence of mental illness and addiction is one in five for all Aotearoa New Zealanders, but nearly one in three for Māori.[8] In 2017, 41% of adults who experienced potentially harmful seclusion in mental health facilities were Māori, despite Māori representing 17% of the population.[9] To address these inequities and respect the tino rangatiratanga and mana motuhake of those affected, it is critical that Māori affected by improvement projects be engaged early and strongly in co-design. Only this way can improved services be designed that work well for all—and particularly those most affected. Māori want this: a 2024 report from Te Hiringa Mahara—the New Zealand Mental Health and Wellbeing Commission, drawing on the perspectives of "*over 300 people with lived experience of mental distress, substance harm, gambling harm, or addiction and whānau, family, and supporters of people with these experiences*" found conclusively that "*Māori and whānau want to be actively involved in decision-making and the design and delivery of their care*."[10]

Te Tāhū Hauora – New Zealand Health Quality & Safety Commission and mental health and addiction quality improvement

Aotearoa New Zealand's national quality improvement agency, Te Tāhū Hauora – New Zealand Health Quality & Safety Commission, leads work nationally to improve quality and safety across the health and disability system. We have a focus on quality improvement in mental health services, and true co-design was front-loaded into the national mental health and addiction quality improvement programme from the outset. Consumers were engaged and consulted to decide the programme's five priority areas of work. With consumer guidance, these focus areas were established:

- zero seclusion: safety and dignity for all
- connecting care: improving service transitions
- learning from adverse events and consumer, family and whānau experience
- maximising physical health
- improving medication management and prescribing.[11]

Front-loading consumer engagement in problem definition, project design and selection of interventions has borne fruit in the zero seclusion project in particular, which we discuss next.

Evidence from quality improvement in seclusion

Seclusion is defined by Aotearoa New Zealand's *Ngā paerewa Health and Disability services standard* 2021 as "*restraint where a person is placed alone in a room or area, at any time and for any duration, from which they cannot freely exit*."[12] The inequitable use of seclusion in consumers of mental health services, harmful to consumers and to carers alike,[13–15] has been rife in Aotearoa New Zealand[16–18] and Australia.[19–21]

Yet, use of seclusion is not inevitable, nor necessarily bound to happen due to services being under financial and staffing strains. The zero seclusion priority area is an ongoing nationwide quality improvement project designed to minimise such harmful seclusion practices, and recent findings have suggested the efficacy of true co-design in this area, particularly for Māori. Early peer-reviewed findings from the authors of this viewpoint now show this work, including development of a cultural/clinical "kete" (basket) of interventions co-designed in a bi-cultural partnership between consumers and cultural and clinical experts, contributed to a statistically significant 22% reduction in the "equity gap" between Māori and non-Māori/non-Pacific peoples in mean monthly rate of seclusion by September 2022.[22] This reduction in seclusion of Māori was sustained through volatile demand for services and myriad other forms of disruption in the first 2 years of the COVID-19 pandemic to September 2022, the period covered by the study. Data collected internally by the programme suggest these reductions have continued, and will be published in the peer-reviewed literature in due course.

Drawing on Māori governance, leadership, insight and lived expertise in the experience of and approaches to reduction of seclusion was critical to this good result for Māori.

What effective, inclusive co-design can look like—one approach

Across all areas of our mental health and addiction quality improvement programme work, comprehensive, culturally informed co-design processes are emphasised to involve, engage and learn from Māori lived experience from the outset.

Governance

In practice, this means governance of priority areas of work is guided and informed by Māori representation: the small national team includes clinical, cultural and consumer leadership with a senior Māori kaumātua (a respected tribal elder in a Māori community who has been involved with their whānau for many years), quality improvement specialists and data experts. The programme is supported by both a Māori advisory group and a consumer advisory group. A cross-sector leadership group maintains oversight of the programme and advises the programme team.

Design

True co-design should be co-creative, participatory and open, and should directly involve consumers, family and whānau in designing the solutions as well as prioritising the work. Māori and other consumers were engaged in workshops for all five project priority areas, by sharing consumer and whānau stories, in active-participation learning sessions and in project teams in each of the 20 districts in Aotearoa New Zealand's health system (as it was then configured). Māori worldviews and knowledge systems were and continue to be explicitly considered within any co-design process.[23] The consensual approach itself is congruent with the traditional Māori practice of wānanga (open discussion where a group attempts to gain a deeper understanding of an issue). Wānanga brings people together in an open forum explicitly to ensure that many perspectives and solutions are reflected in discussions and solutions. In this way, a bi-cultural (and cultural/clinical) mode of working and partnership was created from the outset of the work and built into the governance of the programme.

Testing of interventions

Our quality improvement approaches align with the Institute for Healthcare Improvement's collaborative breakthrough series methodology.[24] This methodology provides a structure for organisations to collaborate on the selection, testing and implementation of change in specific clinical areas where current practice deviates from best scientific knowledge, improved results would improve quality of care and the possibility of improvement has been demonstrated by at least some sentinel organisations.[24] The methodology has shown powerful improvement overseas[25,26] and in Aotearoa New Zealand.[27,28]

This methodology typically uses improvement science to test evidence-based interventions locally, measure the impact of these changes and—if successful—support other services to implement the changes more widely. However, with much of our work, no pre-existing "bundle" of evidence-based practices was known.

So, a "formative collaborative approach"[29,30] was taken, where harm areas and potential interventions are investigated and established as part of the project. The project teams from across the country were tasked with first applying the co-design knowledge gained from workshops to their own environment. Here, teams are encouraged to understand where opportunities for improvement exist within their systems, to develop and share ideas and test them, contributing to the development of a locally relevant change package informed by Māori lived experience.

Teams then applied quality improvement learning in rapid-cycle tests of change to test, modify and scale-up ideas for change, with a dedicated bespoke measurement framework, including measures of inequity.

Conclusion

The programme uses this partnership between clinical and quality improvement expertise and the expertise in the lived experience of consumers and Māori in both co-design and the formative collaborative. A bicultural partnership of this kind enables consumers and Māori to lead design and delivery of care in their own communities. It requires effective engagement by clinicians and staff with quality improvement expertise with those with lived experience, genuine mutual trust and respect, and the sharing of ideas, values, beliefs and models of wellness.

It is our belief that, through these approaches,

clinical options for improvement are made more acceptable to Māori and can be delivered through Kaupapa Māori health services. This truer form of co-design enables a broader range of options or choices to be tested, developed and scaled and then—ultimately—accepted by the people for whom they are supposed to work.

True co-design is not easy. Early involvement of consumers may well challenge initial assumptions and ultimately shift the direction of the work from what was originally anticipated. However, the rewards are worth it. True co-design ensures projects are credible and legitimate, and ultimately shapes solutions that work for consumers as well as for the services themselves—the true definition of a successful project outcome. Furthermore, true co-design also ensures the mana motuhake and tino rangatiratanga of Māori, and indeed the self-determination that all peoples who use our health services deserve.

COMPETING INTERESTS
There are no competing interests to declare.

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Lead pencil: a case of intractable abdominal pain secondary to lead poisoning

Amy Van der Sluis, Kirsty Sutherland

Ayurvedic medicine has long been practised among Indian and Nepalese cultures dating back to 2500 BC, with China being the first to utilise gold in preparations.[1] It is suggested that up to 80% of the Indian population have used Ayurvedic preparations.[2] Unfortunately, with decreased accessibility to pure Ayurvedic products, secondary to illegality of some base ingredients such as opioid-like substances but also due to scarcity, we are seeing increasing rates of metal toxicity around New Zealand, as substitutions for colloidal gold and other ingredients are being made. Lead toxicity is systemic poisoning by a non-biodegradable metal, primarily inhaled or consumed and digested, leading to symptoms associated with neurocognitive disease, renal impairment and haematological disease.[3–4] Haematologically, lead can interfere with enzyme function, leading to altered heme synthesis and thus anaemia. From a neurological perspective, synaptic pruning is impaired, leading to cognitive and behavioural changes, but in more extreme cases can lead to seizures and coma.[5] Lead competes with uric acid in the proximal tubules, causing increased urate concentrations and alterations in renal function and uric acid excretion.[3,6] The gastrointestinal symptoms of pain and constipation are not well understood.[3]

Case presentation

Mr X, a 30-year-old Indian male, presented to the emergency department with a 5-day history of abdominal pain and constipation. He was reviewed the day prior and discharged with a disimpaction regime before re-presenting with severe abdominal pain and vomiting. Medically, he was previously fit and well, with no surgical history. He had recently relocated from India 8 months prior, was working as a cleaner and had a past history of intravenous heroin use. He had no sick contacts. History and examination were difficult to obtain secondary to pain despite significant opiate administration. Observations remained normal throughout his admission. Hypertension was not a feature of his presentation. His abdomen was soft, but globally tender with no guarding or peritonism. On digital rectal examination there were neither impacted stools nor evidence of blood on the glove.

Biochemical analysis revealed a normocytic anaemia, with normal iron profile and a stable haemoglobin when compared to the day prior. The blood film showed basophilic stippling and giant platelets. He had mildly elevated inflammatory markers, and a lactate of 2. There were no other biochemical anomalies. A computed tomography (CT) scan was performed by emergency department staff, which reported colitis, likely in keeping with Crohn's disease, and commented on hyperdense material in the colon consistent with oral contrast. A surgical referral was made. These findings, however, did not appear to align with the patient's presentation, and the distal colonic oral contrast was not in keeping with the timing of scan and bowel transit time, with no documentation of contrast being administered the day prior.

With the inability to control pain with intravenous opioids, Mr X commenced on a trial of intravenous ketamine under the anaesthetic team. The on-call surgeon was approached for consideration of explorative laparotomy; however, given the absence of an absolute indication for surgery, a referral to medicine was made for abdominal pain with presence of anaemia without evidence of gastrointestinal bleeding i.e., porphyria, haemolytic anaemia, sickle cell anaemia. The trial of ketamine failed to gain adequate pain control, and the patient was escalated to the intensive care unit (ICU).

Repeated questioning led to eventual disclosure of alternative Ayurvedic medication use. Swarna Bhasma, a preparation made by a friend in India, had been consumed over a period of months for improved sexual stimulation. This disclosure led to investigation of heavy metal levels, with the

lead level returning at 5.57umol/L (normal range <0.24umol/L) and other metals within normal ranges. Treatment for lead toxicity was initiated following discussion with the toxicologist at the New Zealand National Poisons Centre. Mr X completed 5 days of IV chelation and was started on bowel decontamination, which was not tolerated well. This involved nasogastric feeding of Glycoprep at a set rate. The patient remained in the ICU for 5 days due to the difficult pain management. He was stepped down to oral chelation after 5 days on the ward and diazepam weaning. Lead levels had returned to normal prior to discharge from hospital; however, there was ongoing heavy metal pooling in the caecum on abdominal X-ray due to incomplete bowel decontamination. Mr X was discharged into the community on day 10 of admission with follow-up bloods and appointment, alongside red flag advice for return to hospital. This is interesting given the half-life of blood lead is approximately 25 days. Five months later, Mr X re-presented with acute psychosis and recent methamphetamine use, but no further self-reported ingestion of lead. Abdominal X-ray showed hyperdense material in the ascending and transverse colon, and gastric antrum and lead levels suggestive of toxicity at 4.12umol/L. He was intubated secondary to encephalopathy and combativity and remained so for the majority of his stay, with multiple failed sedation holds. He underwent endoscopy, bowel irrigation and IV chelation (3g/24hours Edetate calcium disodium infusion) to ensure clearance. He was then switched to Succimer oral chelation under guidance from toxicology.

Discussion

Ayurveda is a traditional alternative medicine practice that is utilised heavily within Indian culture.[7] Therapies are based around herbal and mineral compound preparations, sometimes including metal substances, in order to treat a range of common and chronic issues ranging from constipation and asthma to erectile dysfunction and cancer.[8] The overall Ayurvedic philosophy dates back over 2,000 years and ultimately relates to aligning the living and non-living via the five elements of the universe, with disease occurring when there is an imbalance.[9] The evidence base for Ayurveda is somewhat limited with respect to outcomes; however, studies have assessed the utility of metals in medicine, with Rasashastra, a subdivision of Ayurvedic practice, focussing innately on the collaboration of metals and minerals with herbal therapy.[2,7] Colloidal gold nanoparticles have been studied and are suggested to increase cellular uptake by encapsulation of active drugs.[10–11] In recent times preparations have been found to consist of lead, arsenic and mercury, all toxic substances to humans, with Saper et al. concluding 20% of Ayurvedic medicines found in a Boston store contained potentially toxic lead, mercury or arsenic levels.[2] Previous studies depict significant rates of contaminants of the three aforementioned metals in Ayurvedic medicines, with 35–40% of 6,000 listed Ayurvedic medicines consciously containing a metal component.[2] A Medsafe New Zealand press release in March 2024 noted eight recent cases of lead poisoning from Ayurvedic medicines. There are currently no approved Ayurvedic medicines listed in New Zealand.[12]

Swarna Bhasma, also known as gold Bhasma, is a traditional Ayurvedic medicine often administered orally with honey, ghee or milk and used in the treatment of a variety of disorders including asthma, arthritis and diabetes.[13] It contains nanoparticles of colloidal gold. The therapeutic benefits of gold in medicinal preparations date back as far as 2500 BC in Indian, Arabic and Chinese literature.[1] Uptake of gold particles is via the small intestine. When analysed microscopically, they did not cause complement activation and did not disrupt platelet function. They were capable of absorption via tight junctions to enter the systemic circulation.[3,13]

Kamini and Barshasha are opioid-containing preparations of Ayurveda, often containing opium. These substances were made prescription only and illegal for importation, supply and possession under the *Misuse of Drugs Act 1975*.[14] Lane (2020) describes case studies of 10 men with previous opium and opioid use taking exceedingly high doses of the substances and being unable to reduce due to effects of withdrawal. They were admitted into the Auckland Opioid Treatment Service and started on opioid substitution therapy.[14] Swarna Bhasma, the Ayurvedic medicine in question, also has analgesic properties when assessing its indications. Given Mr X's background of heroin use, the role of Ayurveda in opioid and drug dependency is considered alongside Mr X's selected use for it.

While previously associated with remnant stripping and flakes from residential buildings decorated in lead-based paint, crumbling and settling into dust and soils or occupational

exposure, there have been increased cases of lead being a contaminant or alternative used in metal-based traditional medicines.[3,15–16] The effects of lead poisoning are vast and have an effect on most of the bodily systems. Of note are cognitive impairment, seizures, coma, abdominal pain, infertility and impaired haemoglobin production.[4,5,6,13] Lead binds to red blood cells once absorbed and is distributed to the bone and soft tissues. Prior to the advancements in modern medicines and the introduction of chelating agents, death by lead toxicity was around 65%. This is now less than 5%; however, significant continued morbidity can be associated with the early effects of toxicity such as cardiovascular problems and seizure disorders.[4,17]

Medical treatment of lead toxicity involves removal of exposure source, whether that be ingestion, environmental or occupational, and judicious contamination, chelation and supportive cares.[18] The role of chelation is debated in papers as to its efficacy in long-term reduction in lead levels, with Succimer showing only transient improvement in children.[19,20] Anecdotally, it may reduce mortality in those with encephalopathy; therefore, chelation can be initiated with the discretion of toxicologist input on a case-by-case basis.[18] While symptoms should dissipate post–removal of exposure and reduction in lead levels, neurocognitive symptoms may lag due to delayed excretion from the central nervous system.

Given the rise in cases of lead toxicity due to Ayurvedic medicine use, physicians worldwide need to remain cognisant in and have an underlying suspicion for lead poisoning in cases of unexplained normocytic anaemia. Given low public awareness, and relative difficulty to ascertain ingredients in supplements and preparations, there is a risk of incidental heavy metal exposure. This also highlights the importance of involving public health to exclude alternative causes of lead exposure. Therefore, when amidst a diagnostic conundrum, with symptoms not aligning with investigations, the importance of a multidisciplinary approach and lateral thought processes is imperative to ascertain causality given the implications both medically and surgically.

COMPETING INTERESTS
Nil.

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Clumsy child: what are we missing?

Jeyasakthy Saniasiaya

Dear Editor,

Balance problems are not infrequent in the geriatric population. Nevertheless, awareness of paediatric vestibular and balance conditions remains scarce. Nearly 6–13% of school children have been reported to suffer from balance problems,[1] which have been found to interfere with academic and scholastic performance, as well as cause psychosocial problems. The rise in interest in paediatric vestibular medicine in most parts of the world has increased awareness of balance problems among the younger ones. The prevalence of vestibular dysfunction in children and adolescents is 30.4%,[2] based on a recent meta-analysis.

It is noteworthy that children with balance problems tend to manifest earlier with atypical symptoms, such as being clumsy.[3] Although clumsiness is common among toddlers, appearing clumsy beyond 3 years of age should raise a red flag of a possible underlying vestibular impairment. A clumsy child is typically referred for neurodevelopmental assessment to exclude various sensory processing and integration disorders such as autism spectrum disorder (ASD) and attention-deficit hyperactive disorder (ADHD). However, concomitant presentation such as hearing loss should raise suspicion of a possible vestibular impairment.

A child is typically termed as "clumsy" in a child with normal intelligence who frequently falls with no apparent cause, bumps into cupboards and doors, finds it difficult to climb or descend stairs and may struggle to perform age-appropriate self-care activities.

Left untreated, research has shown that children with clumsiness secondary to vestibular dysfunction tend to struggle with reading and learning,[4] which typically requires an intact gaze stabilising function, and this, in the long term, may result in poor scholastic performance, psychosocial issues and poor overall quality of life.[4]

Sadly, due to a lack of awareness, physicians and general practitioners may disregard a "clumsy child" due to the belief that the child will eventually catch up. Parents and physicians generally are not aware that clumsiness could be due to an underlying vestibular impairment that remains unnoticed and tends to manifest at a later age or following an acute decompensation event such as stress, psychological issues, trauma or infection.[2] Besides that, the robust neuroplasticity among children with compensation from the vision and proprioception is another factor that may lead to the delay in the diagnosis of vestibular dysfunction.[2]

Currently, assessment of a clumsy child focusses on conditions like ADHD[1] and ASD,[1] and neuromuscular or neurological conditions, as many physicians are unaware that vestibular dysfunction could be the culprit. The significant contribution of the vestibular system to our balance system cannot be denied. Yet, peripheral vestibular assessment is not incorporated as a main assessment criterion when assessing a child with clumsiness assessment. We would like to highlight that vestibular and balance assessment is performed as a routine practice so that vestibular dysfunction in children can be identified earlier and referred for further assessments. A thorough vestibular investigation and quantification can be carried out, as well as early commencement of vestibular rehabilitation therapy, which will ensure the child is able to carry out and perform age-appropriate activities and learning.

Early vestibular rehabilitation therapy improves gaze stability, perception of verticality, balance and motor development and alleviates symptoms of motion sickness and dizziness.[5] In addition, early rehabilitation in an otherwise "normal" child with vestibular dysfunction will enable them to catch up with their age- and gender-matched peers. Moreover, timely treatment of balance function in children has satisfying and rewarding outcomes, improving cognitive and psychological wellbeing.

COMPETING INTERESTS
None.

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Lesions of the Cauda Equina with Clinical Notes of a Case.

NZMJ, 1925

By F. V. BEVAN BROWN, M.D., M.R.C.P., *and* P.S. FOSTER, F.R.C.S.

Tumours of the cauda equina are sufficiently rare to justify the description of a case when one occurs, especially when, as in the present instance, the lesion is successfully located and dealt with by operation.

The tumours that may occur are the same as those found elsewhere in connection with the spinal cord, neurofibromata probably being the most common. Gunshot wounds and fractures involving the lumbar and sacral vertebræ may also produce the symptoms that are typical of lesions in this part of the body. Such symptoms are:—

(1) Subjective, comprising chronic intermittent pains round about the pelvic girdle, in the hips, or down the legs following the course and distribution of one or more of the nerve trunks from the lumbar or sacral plexus. Sciatica is simulated, though the pain is more frequently bilateral. These pains are usually the first symptom of trouble and the only one for many months; careful investigation at this stage may enable a diagnosis to be made. The later symptoms are:—

(2) Incontinence of bladder followed by paralytic distension with overflow; loss of sexual power and loss of control of rectum.

(3) Segmental anæsthesias and paræsthesias corresponding exactly to spinal segments and the nerve roots issuing therefrom. For example: a saddle-shaped area across the buttocks (S3, S4, S5) is an important diagnostic finding.

(4) Flaccid paralysis of lower neuron type which may involve all the muscles supplied by the lumbo-sacral nerves on both sides, but which is more frequently segmental in character, one muscle group being spared and another being involved. The segmental and unsymmetrical character of the anæsthesia and paralysis distinguishes tumours of the cauda equina from tumours involving the lumbar enlargement, for in the latter case there is sooner or later complete motor and sensory paraplegia. The diagnosis between the two conditions may, however, be exceedingly difficult, especially since the tumour may be extensive enough to affect both situations. Such was actually the condition in the case shortly to be described.

(5) Trophic changes, especially bed sores, occur.

The level at which the tumour lies determines the symptoms in each particular case. For example, with a tumour situated at the level of the first and second sacral vertebræ the quadriceps and adductor muscles would remain unaffected, and the buttocks, hamstrings and muscles below the knees would be involved. The sensory changes would be similarly determined.

Other conditions from which a lesion of the cauda equina requires to be distinguished are:—(1) Sciatica; (2) pelvic tumour; (3) tabes dorsalis; (4) peripheral neutritis; (5) progressive muscular atrophy; (6) anterior poliomyelitis; (7) syringo-myelia.

Mrs. A. B., aged 51, was admitted into the Christchurch Hospital in October, 1923. She complained of chronic pain in the right hip and knee which had been present on and off for one year, and was growing worse. It was noted that her husband gave a double plus Wassermann reaction. The only abnormal physical signs observed at this time were:—Sluggist pupils and an absent knee jerk on the right side. A diagnosis of sciatica was made, septic teeth were extracted and she was discharged. She was re-admitted in March, 1924, complaining of the same pain, which was becoming more severe, and by this time weakness of the right leg had developed, causing difficulty in walking. It was noted that both knee and ankle jerks were present but were sluggish. By 19th April, paralysis of the bladder with overflow had developed, necessitating the regular use of a catheter. The Wassermann reaction of the blood was negative. No abnormal signs were discovered in the central nervous system except those already mentioned. Examination of the cerebro-spinal fluid showed a normal finding and its Wassermann reaction was negative. Two further examinations of the fluid again showed it to be normal.

By 1st July there was extreme loss of power in the right leg and to a less extent in the left. Wasting of the quadriceps and of all the muscles below the knee on both sides had developed by this time, but the reflexes at the knee and ankle were present, though very difficult to elicit. There was severe intermittent pain in the right hip and down both legs, especially down the back of the right leg. The planter reflexes were flexor and the sensations in the legs were normal except that discrimination between heat and cold was imperfect. There were no other abnormal physical signs in connection with the C.N.S. at this stage. X-ray examination of the dorsal, lumbar and sacral vertebræ was negative.

By 14th August, there was complete flaccid paralysis of the lower limbs, including the buttocks, but not including the abdominal muscles. The knee and ankle jerks were now absent. Bed sores had developed, and the bladder required regular catheterization. No segmental anæsthesia could be definitely found except over the buttocks, where the characteristic saddle-shaped area was mapped out, which showed absence of sensation to touch and pin prick. Below the knees there was complete anæsthesia; above the knees the anæsthesia was partial and indefinite.

The light reflex all along had been difficult to elicit and this fact, combined with the other features of the case, had made the diagnosis of tabes dorsalis a probable one, until the marked muscular wasting and paralysis had developed. A lesion either of the lumbar enlargement or of the cauda equina was suspected and finally diagnosed, and an operation was decided upon with this diagnosis in view.

Operation.—On 7th October, 1924, an operation was performed. With the patient in the prone position an incision was made in the midline from the twelfth dorsal to the third lumbar spine. Laminectomy of the first and second lumbar vertebræ was done. On opening the dura mater a free escape of cerebro-spinal fluid occurred. The cauda equina was found to have a tumour lying dorsally upon its commencement, and extending upwards on the lumbar enlargement. The lamina of the last dorsal vertebræ was removed and the whole tumour exposed. It was an elongated solid tumour about two inches in length. It was held by flimsy attachments of arachnoid matter, and was removed very easily, and without bleeding of any consequence. The dura was sutured and the spinal muscles drawn together with chromic gut sutures. The wound was closed with silkworm gut sutures. The operation occupied less than an hour and was very well borne. The patient was kept in the head-low position to prevent leakage of cerebro-spinal fluid from the wound, which healed by first intention.

The tumour was reported by Dr. Pearson to be a vascular perithelioma.

There was very little shock after the operation, which was quickly recovered from, and the skin healed aseptically. The patient noticed at once that the severe pain in the hip and down the right leg had disappeared. At the end of a fortnight bladder sensation had returned, and the paralytic distension was replaced by frequency without control. Massage, passive movements and faradism were carried out daily on both legs, and, as improvement took place, active movements were encouraged and were performed in a limited manner.

At the present time, 30th December, two and a-half months after the operation, the condition of patient is as follows:— Her general health is much improved, mainly because her sleep is undisturbed by pain. The bed sores have healed; sensation has returned in both legs and is practically normal, though touch sensation below the knees is still defective. The patient complains of an aching pain in both legs, especially at night, dull in character, different from her previous pain and not severe enough to prevent her sleeping. Limited voluntary movements have returned in all muscle groups, and the muscles themselves are increasing in size. The legs are still very weak, especially the right leg; the muscle groups that show least improvement are the hamstrings and the anterior tibial muscles of the right leg. There is faradic response present in all muscle groups. The knee and ankle jerks are present on the left side, but absent on the right side. In the last few days bladder control has been present.

In view of the improvement that has already taken place, it is reasonable to expect that ultimately the patient will be able to walk, and that recovery, more or less complete, will take place.

Erratum

URL: https://nzmj.org.nz/journal/vol-138-no-1608/support-for-and-likely-impacts-of-endgame-measures-in-the-smokefree-aotearoa-action-plan-findings-from-the-2020-2021-internation

Support for and likely impacts of endgame measures in the Smokefree Aotearoa Action Plan: findings from the 2020–2021 International Tobacco Control New Zealand (EASE) surveys

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On 28 February 2025, two corrections were applied to this manuscript to ensure the description of study participants is accurate:

1. In the methods section on page 41, the description originally read: "…study that surveys people who currently smoke or quit smoking within the last 2 years.[8] Survey waves are conducted every 12–18 months, and participants lost to follow-up are replenished by new participants.
   Participants are eligible to take part if aged ≥18, living in Aotearoa New Zealand, and:

   - currently smoke cigarettes or tobacco at least monthly, and have smoked at least 100 cigarettes in their lifetime, or
   - previously smoked at least monthly, have smoked at least 100 cigarettes in their lifetime and quit smoking within the past 24 months."

   The text was incorrect regarding requirements to have smoked 100 cigarettes (for those who currently smoke) and to have been quit for less than 2 years (for those who have quit). We have corrected this to read: "… study that surveys people who currently smoke or quit smoking within the last 2 years **at entry into the study at Wave 3; re-contacted participants who had quit smoking could stay in the study until they had been quit for 5 years**.[8] Survey waves are conducted every 12–18 months, and participants lost to follow-up are replenished by new participants. **New participants at Wave 3 are eligible** to take part if aged ≥18, living in Aotearoa New Zealand, and:

   - currently smoke cigarettes or tobacco at least monthly, **or**
   - **previously smoked at least monthly, have smoked at least 100 cigarettes in their lifetime and quit smoking within the past 24 months."**

2. In the abstract on page 40, the description originally read: "… people who smoke or who recently (≤2 years) quit smoking."

   We have corrected this to read: "… people who smoke or who **recently quit smoking."**