The
New Zealand
Medical Journal
Te ara tika o te hauora hapori

Journal of the Pasifika Medical Association Group

Vol 135 | No 1558 | 2022 Jul 15

A new opportunity for a fairer, more equitable approach to alcohol supply—minus the marketing

Acute alcohol use and suicide deaths: an analysis of New Zealand coronial data from 2007–2020

District health board engagement with the living wage movement: evidence from official information requests

The New Zealand **Medical Journal**
Te ara tika o te hauora hapori

Publication information

published by the Pasifika Medical Association Group

NZMJ Editor
Professor Frank Frizelle

NZMJ Production Editor
Brooke Soulsby

Other enquiries to:

PMA Group
2/69 The Terrace
Wellington 6140

To contribute to the *NZMJ*, first read:
www.nzma.org.nz/journal/contribute

To subscribe to the *NZMJ*, email

nzmj@pmagroup.co.nz

Subscription to the *New Zealand Medical Journal* is free and automatic to those who were NZMA members prior to June 2022, and will be free and automatic until the end of October 2022.

Private subscription is available to institutions, to people who are not medical practitioners, and to medical practitioners who live outside New Zealand. Subscription rates are below.

All access to the *NZMJ* is by login and password, but IP access is available to some subscribers.

Read our Conditions of access for subscribers for further information
www.nzma.org.nz/journal/subscribe/conditions-of-access

If you are a member or a subscriber and have not yet received your login and password, or wish to receive email alerts, please email: nzmj@pmagroup.co.nz

Subscription rates for 2022

New Zealand subscription rates		Overseas subscription rates	
Individuals*	$360	Individual	$503
Institutions	$680	Institutions	$700
Individual article	$45	Individual article	$45

*NZ individual subscribers must not be doctors (access is via NZMA Membership)

New Zealand rates include GST. No GST is included in international rates.

Note, subscription for part of a year is available at pro rata rates.

Individual articles are available for purchase by emailing nzmj@nzma.org.nz.

Contents

Editorial

Articles

Viewpoints

Clinical correspondence

100 years ago

Summaries

Vasovagal syncope triggered by recent moderate weight loss?

Brent Cumming, Christopher Frampton and David Jardine

Vasovagal syncope [or fainting] is a common condition which often starts in adulthood for no particular reason. Causes previously recognised include blood pressure medication, phobia, anaemia, fever and extreme fitness. Recent weight loss [of about 10Kg] has not been reported therefore this is a new observation which may be useful for doctors dealing with blackouts that are not clearly cardiac in mechanism.

New Echocardiography Reference Ranges for Aotearoa (NewERA) Study: the application of international echocardiographic reference values to linear measurements of the hearts of healthy, young Māori and Pacific adults may not detect cardiac enlargement

Gillian A Whalley, Allanah Harrington, Jonathan Christiansen, Bettina Ikenasio, Arun Deo, Greg D Gamble, Sue Crengle

Heart ultrasound is often used to identify abnormalities, including enlargement but comparing the measurements to normal ranges. These normal ranges were developed in white Americans and are used all around the world. But this research shows that if these numbers are applied to Māori and Pacific peoples this may result in incorrect diagnosis and potentially delay treatment.

District health board engagement with the living wage movement: evidence from official information requests

Julie Douglas, Heather Came, Leah Bain and Grant Berghan

The DHBs in New Zealand have an employment goal of reducing social inequalities, yet most current DHBs continue to pay wages for some workers at or marginally above the minimum wage. It is clearly demonstrated that this level of income is inadequate and low household incomes lead to poor health, educational and other social outcomes. We argue that New Zealand's public health organisations, as large employers, need to model good employment relations and pay at a minimum a living wage to all employees and contractors. For many Māori and Pasifika families household income needs to be lifted to ensure more equitable social outcomes. This ultimately benefits all of society.

Diabetes mellitus prevalence in Northland New Zealand schizophrenia patients on clozapine

Nicole M McGrath, Verity Humberstone, Ashley C Abraham

Clozapine is the only treatment with a specific indication for treatment resistant schizophrenia and it can increase the chance of developing diabetes. In Northland, 41% of patients on clozapine have either diabetes or pre-diabetes. The majority of patients on clozapine with diabetes are Maori and blood sugar control is higher than recommended. Improving the physical health of people with schizophrenia is required using culturally appropriate and easily accessible services.

Can physical activity be simplified for health benefit?

Chey G Dearing, Carl D Paton

We designed a NZ specific simple physical activity questionnaire and tested if it could predict health in NZ because current guidelines are controversial. We found that we could predict the gold standard laboratory measure of general health and fitness (VO2Peak) and also psychological stress status from activity type and frequency. Our research suggests that there may be no need to measure for how long an individual performs physical activity. Simply performing two vigorous type (e.g. running) physical activities per week may be recommended to decrease risk of psychological stress and to improve health.

Revised Guidelines for smoking cessation in New Zealand, 2021

Jessica McCormack, Natalie Walker, Hayden McRobbie, Karen Wright, Vili Nosa, Basil Fernandes, Chris Bullen

The paper summarises current scientific evidence on the best ways New Zealand health workers can help people to stop smoking. Healthcare workers should ask and briefly advise all people who smoke to stop smoking, regardless of whether they say they are ready to stop smoking or not. They should offer smoking cessation support – both advice and tips for how to stop and medicines that help make withdrawal from smoking easier. The paper includes advice around the use of vaping as a tool for stopping smoking, and how to support Māori, Pacific, pregnant women, and people with mental illness and other addictions to stop smoking.

Acute alcohol use and suicide deaths: an analysis of New Zealand coronial data from 2007–2020

Rose Crossin, Lana Cleland, Annette Beautrais, Katrina Witt, Joseph M Boden

We found that over one quarter of all suicide deaths from 2007 to 2020 in Aotearoa New Zealand happened when the person had consumed alcohol. This was especially true for younger people, and for Māori and Pasifika. Reducing the overall level of alcohol consumption in Aotearoa New Zealand could reduce the incidence of suicide, particularly for the most affected groups.

A new opportunity for a fairer, more equitable approach to alcohol supply —minus the marketing

Sally Casswell

It is good news our Government has now committed to a review of our alcohol legislation. Advocates, including the Health Coalition Aotearoa, have produced recommendations for the scope of the review, including giving effect to Te Tiriti o Waitangi in the legislation, stricter legal restrictions on availability and reform of the licensing process to give communities the voice they were intended to have.[1] A key issue the review must traverse is how can we ensure safe and responsible supply of alcohol while reducing the inequities in wellbeing and health to which alcohol significantly contributes.

One aspect not yet clear is whether the scope of the review will include adequate consideration of alcohol marketing. Alcohol marketing is mentioned in the current Sale and Supply of Alcohol Act but remains ignored and unenforced. Instead, Aotearoa New Zealand suffers, along with many similar countries, from an acceptance of pervasive alcohol marketing and the façade of an industry run voluntary code, providing no real protection from exposure to powerful and persuasive encouragement to drink and drink more.

The evidence supporting a need for regulation of marketing is clear. There is a causal effect of alcohol marketing on younger people where most of the research has been focused.[2] Exposure to alcohol marketing leads to young people drinking at a younger age and drinking more. In Aotearoa, tamariki Māori are exposed to five times as much alcohol marketing compared with others,[3] and this is likely to contribute to consumption of larger amounts of alcohol products by Māori rangitahi.[4] In turn, this contributes to the striking inequity in premature mortality, with Māori more than twice as likely to die from alcohol attributable causes.[5]

One of the benefits of alcohol marketing for the global producers is to recruit new consumers and, especially important for them, an ongoing supply of heavy consumers, described in industry sources as "the heavy drinking loyalists of tomorrow".[6] Everywhere commercial alcohol producers rely on heavy consumption for significant proportions of their sales and profits, approximately 50% in Aotearoa.[7]

Marketing's effects are broad and therefore the urgently needed policy response must go beyond a focus on protecting young people. Research has also indicated impacts of marketing among adult drinkers, especially among heavier drinkers and those who are attempting to reduce their consumption. Heavy drinkers find alcohol advertising more appealing, and marketing is more likely to lead to consumption; problem drinkers are both more exposed to and more interested in alcohol marketing. They report distress and threats to their sobriety from repeated exposure.[8]

Alcohol is one of the most heavily advertised products globally. The big global corporations, such as the Asahi Corporation, owner of the heavily promoted Ready To Drink (RTD), Long White, have ample resources to market their products. Integrated marketing campaigns use sophisticated creative material, branded events and take advantage of the unprecedented targeting the use of digital data now allows. The ubiquity of the marketing creates a one-sided picture of alcohol products as if they are ordinary commodities. The cumulative effect over time is a normalisation of alcohol products that may constrain the policy options believed to be appropriate, such as the need to regulate affordability and accessibility to prevent increases in alcohol harm.[9]

There is growing recognition that this marketing endeavour is unfair to all but the transnational alcohol corporations that produce, and market, the bulk of the global and New Zealand alcohol market, and their marketing partners such as the owners of the global branded sports and music events. Concern has been fuelled by the rapid and dynamic expansion of alcohol marketing in the digital media.[10] The data we shed in our daily lives are being sold to enable targeting of individuals, look alike audiences, and to increase the power of marketing in the digital ecology in which

people now spend much of their lives; 94% of New Zealanders were active internet users in 2021.

This expansion of alcohol marketing into the digital ecology is transformational and the ease with which it crosses national boundaries has stimulated considerable international concern.[11] Digital marketing takes advantage of data about interests, emotional states, location, brand preferences and response to marketing and creates a seamless environment in which marketing can transform into purchase at the touch of a button. There has been a marked increase in online purchase in Aotearoa during the COVID-19 pandemic.[12] Digital marketing ensures a very effective use of the advertising dollar; for example, for as little as US$2 an advertising campaign based in Australia could reach one thousand young people profiled as interested in alcohol.[13] Engagement with alcohol marketing in the digital media is also more powerful than with traditional modes. [14]

Despite increasing concerns over privacy and the commodification of digital data, effective regulation of digital platforms has not yet been achieved. However, the example of tobacco shows that where governments put in place comprehensive bans on marketing, this reduces exposure to marketing in all modes. Within the World Health Organization, discussions are currently taking place towards an international code to regulate alcohol marketing, both to support the uptake of national bans on alcohol marketing and to respond to cross-border marketing.

The forthcoming review of alcohol legislation in Aotearoa provides an opportunity to re-evaluate our regulation in the context of the changed alcohol environment. This will include filling gaps in current law, such as failure to regulate alcohol marketing, and including online delivery and giving effect to Te Tiriti, while also reforming regulatory processes such as when the licencing process has not provided adequate opportunity for local government and communities to have their say. Above all, this reform could support te oranga (full participation in society) and te mana whakahaere (autonomy), which are in themselves important elements of Māori health.[15] The reform could also provide an opportunity to protect those most vulnerable to alcohol harm, and contribute to fairer and more equitable outcomes.

Supplementary URL: https://shoreandwhariki.ac.nz/

COMPETING INTERESTS
Nil.

CORRESPONDING AUTHOR INFORMATION
Professor Sally Casswell, FRSNZ, ONZM: Professor of Public Health and Social Research; Health Coalition Aotearoa Board Member; Director, Social and Health Outcomes Research and Evaluation (SHORE), SHORE & Whariki Research Centre, College of Health, Massey University, New Zealand. S.Casswell@massey.ac.nz

URL
www.nzma.org.nz/journal-articles/a-new-opportunity-for-a-fairer-more-equitable-approach-to-alcohol-supply-minus-the-marketing

REFERENCES

1. Health Coalition Aotearoa. Priorities for amendments to the Sale and Supply of Alcohol Act. Appendix 1 Roopu Apaarangi Waipiro. 2021, August 25. Available from: https://www.healthcoalition.org.nz/wp-content/uploads/2022/05/Appendix-priorities-of-Health-Coalition-Aotearoa-re-SASAA-reform-26.08.21-002.pdf.
2. Sargent JD, Babor TF. The Relationship Between Exposure to Alcohol Marketing and Underage Drinking Is Causal. J Stud Alcohol Drug. 2020;Supplement 19:113-24. doi: 10.15288/jsads.2020.s19.113.
3. Chambers T, Stanley J, Signal L, Pearson AL, Smith M, Barr M, et al. Quantifying the nature and extent of children's real-time exposure to alcohol marketing in their everyday lives using wearable cameras: Children's exposure via a range of media in a range of key places. Alcohol Alcohol. 2018;53:626-33.
4. Fleming T, Ball J, Peiris-John R, Crengle S, Bavin L, Tiatia-Seath J, et al. Youth19 Rangatahi Smart Survey, Initial Findings: Substance Use. Youth19 Research Group, The University of Auckland and Victoria University of Wellington; 2020. Available from: https://communityresearch.org.nz/wp-content/uploads/2021/12/Youth19SubstanceUseReport.pdf.
5. Connor J, Kydd R, Shield K, Rehm J. The burden of disease and injury attributable to alcohol in New Zealanders under 80 years of age: marked disparities by ethnicity and sex. N Z Med J. 2015;128:15-28.
6. Hessari NM, Bertscher A, Critchlow N, Fitzgerald N, Knai C, Stead M, et al. Recruiting the "heavy-using loyalists of tomorrow": An analysis of the aims, effects and mechanisms of alcohol advertising, based on advertising industry evaluations. Int J Environ Res Public Health. 2019;16:4092. doi: 10.3390/ijerph16214092.
7. Cuong PV, Casswell S, Parker K, Callinan S, Chaiyasong S, Kazantseva E, et al. Cross-country comparison of proportion of alcohol consumed in harmful drinking occasions using the International Alcohol Control (IAC) study. Drug Alcohol Rev. 2018;37:S45-S52.
8. Alcohol Focus Scotland. Realising our rights: How to protect people from alcohol marketing. A Report by the Alcohol Marketing Expert Network. 2022. Available from: https://www.alcohol-focus-scotland.org.uk/media/440173/realising-our-rights-alcohol-marketing-report-summary.pdf.
9. Babor T, Caetano R, Casswell S, Edwards G, Giesbrecht N, Graham K, et al. Alcohol: No Ordinary Commodity Research and Public Policy. 2nd ed. Oxford: Oxford University Press; 2010.
10. Carah N, Brodmerkel S. Alcohol marketing in the era of digital media platforms. J Stud Alcohol Drug. 2021;82:18-27.
11. World Health Organization. Reducing the harm from alcohol – by regulating cross-border alcohol marketing, advertising and promotion: A technical report. 2022. Available from: https://apps.who.int/iris/rest/bitstreams/1422772/retrieve.
12. Huckle T, Parker K, Romeo J, Casswell S. Online alcohol delivery is associated with heavier drinking during the first New Zealand COVID-19 pandemic restrictions. Drug Alcohol Rev. 2020;published online Nov 30. doi 10.1111/dar.13222.
13. Casswell S. Alcohol marketing has crossed borders and entered the metaverse – how do we regulate the new digital risk? The Conversation; 2022, May 23 [cited 2022]. Available from: https://theconversation.com/alcohol-marketing-has-crossed-borders-and-entered-the-metaverse-how-do-we-regulate-the-new-digital-risk-183334.
14. Noel J, Sammartino C, Rosenthal S. Exposure to Digital Alcohol Marketing and Alcohol Use: A Systematic Review. J Stud Alcohol Drug. 2020;Supplement(s19):57-67.
15. Durie M. Te Pae Mahutonga: a model for Maori health promotion. Health Promotion Forum Conference, Napier; 1999.

Vasovagal syncope triggered by recent moderate weight loss?

Brent Cumming, Christopher Frampton and David Jardine

ABSTRACT

AIM: In adults, the onset of vasovagal syncope is often unexplained. We wished to explore if moderate weight loss triggers the onset of vasovagal syncope (VVS).

METHODS: A retrospective case-control study comparing demographic characteristic, syncope symptoms, and tilt-table results of patients who had recently lost weight (n=57), with randomly selected weight-stable patients (n=73), and controls, patients without syncope (n=24).

RESULTS: VVS was diagnosed in 480 out of 1,209 clinic patients of whom 57 (11.9%) reported moderate weight loss. The mean (SD) reported weight loss was 11.5 (7) kg over 18.7 (13) months. Age and gender did not differ between groups: in the weight loss, weight stable, and control groups the mean age was 44.8, 45.2, and 44 years respectively; and proportion female 60%, 64%, and 54%. Body weight, mass index and calculated blood volume at presentation were also similar in the different groups. Weight loss preceded or coincided the onset of syncope in 80% of patients; the length of time over which weight loss occurred was associated with the length of time of syncope symptoms, product moment correlation coefficient 0.45, p=0.001. Syncope in childhood and teenage years was less frequent in the weight loss group compared to the weight stable group: 37% vs 53%. After 10 minutes of head-up tilt, stroke volume was preserved in both syncope groups compared to controls; percentage of baseline mean (SD) in the weight loss, weight stable, and control groups: 71(18), 69(10), and 61 (11) respectively; despite lower blood pressure in the weight loss groups with mean (SD) 90 (14) mmHg, 93 (13) and 103 (14) respectively.

CONCLUSIONS: Some patients have onset of VVS within a few months of weight loss resulting in earlier presentation to clinic. The physiological mechanism for this is uncertain.

Postural symptoms and vasovagal syncope (VVS) syncope are recognised chronic complications of severe weight loss, greater than 40kg; following bariatric surgery.[1,2] The relationship of syncope symptoms within months of moderate weight loss, between 5kg and 40kg, has not been reported. Additionally, moderate weight loss is usually achieved by lifestyle changes, for example dieting and exercise, rather than bariatric surgery. At our syncope clinic we had noted an apparent increase in the number of patients presenting for assessment with recent VVS apparently triggered by moderate weight loss.

The benefits of weight loss include decreased blood pressure and blood volume, both of which are probably secondary to a fall in sympathetic activity.[3] This activity is controlled by diverse mechanisms including the renin-angiotensin system, insulin levels, leptin, and the baroreflexes.[3,4] We postulated that weight loss and decreased central blood volume may predispose some patients to posture-triggered vasovagal syncope. With 10kg of weight loss, total blood volume falls by about 500ml, representing 10% of circulating volume, and approximately half of this is central blood volume.[5,6] Central blood volume is the major determinant of stroke volume and both are observed to fall immediately when the human body is tilted head-up.[7,8] If tilt is continued, a progressive fall in stroke volume is the key mechanism leading to syncope.[9] Despite the importance of central blood volume to maintenance of mean arterial pressure in the upright position, weight loss is not listed as a risk factor for posture-triggered VVS in review articles and guidelines.[10–13] Based on the complex mechanisms controlling sympathetic nerve activity, the relationship between weight loss and the onset of vasovagal syncope is unlikely to be simple. For example, the sigmoid nature of baroreflex responses might prevent BP from falling until blood volume falls below a certain threshold. To clarify, the association between weight loss and the onset of VVS in our clinic population, we examined the association between weight loss and other possible confounding demographic characteristics, or medical conditions, which can also cause syncope. Secondly, we wanted to explore the temporal relationship between recent weight loss and the onset of syncope symptoms. If weight loss is an important predisposing factor to VVS then: (a) it should precede the onset of fainting; (b) it might dictate a relatively short fainting

history; (c) there might be an association between the duration of fainting symptoms and the length of time over which weight loss occurs; and (d) it might trigger VVS in patients who have never fainted before. Finally, we explored non-invasive haemodynamic data from head-up tilt to see if weight loss was associated with an exaggerated fall in stroke volume, which may be a possible mechanism for VVS in these patients.

Methods

This was a retrospective case-control study comparing demographic and other characteristics, in relation to syncope histories of VVS patients, with and without weight loss. Head-up tilt responses were also compared for two weight loss groups, with those of a control group without syncope symptoms. All patients were selected from our syncope clinic and the majority were referred by general practitioners. All patients in this study were assessed in syncope clinic by the same doctor (DLJ) over a six-year study period between January 2014 and December 2019.

Clinic procedures

A week before attending clinic, patients were sent a syncope questionnaire (see Appendix) which detailed the onset, severity and duration of syncope symptoms, as well as predisposing factors, for example drug treatment, background medical conditions and syncope in childhood. There was a specific question about syncope in childhood, as life-long susceptibility might be less prevalent in patients fainting in response to recent physiological changes such as pregnancy, anaemia, or weight loss. The questionnaire was reviewed with the doctor during the first part of the clinic assessment. In clinic patients were specifically asked about weight loss, including magnitude, duration and possible aetiology. The duration of weight loss was then collated with the syncope history so that patients could confirm or refute a temporal association. The practice of a pre-clinic questionnaire was to allow patients sufficient time to remember and document syncope symptoms before being asked about weight loss. If patients were uncertain about current weight and height, these measurements were made in clinic and additionally past measurements from the electronic record were reviewed. Therefore, although quantification of recent weight loss was by self-report, these estimates were validated against other clinical records. Posture-triggered VVS was diagnosed on the basis of an expert history, a normal ECG, and the exclusion of other possibilities using an abbreviated tilt test.[14,15] A positive 40 minute tilt test is not sensitive for VVS and, although clinically useful in some patients, is generally not be used as an inclusion criterion for studies of this nature.[10,16] On the other hand, a limited tilt test is useful to exclude diagnoses such as postural tachycardia syndrome (POTS), drug-related postural hypotension (DRPH), and neurogenic orthostatic hypotension.[15] The clinic review included a focussed cardiovascular examination and a 12-lead ECG, followed by an abbreviated head-up tilt test, (supervised by David L Jardine). All these occurred during the same clinic session. For the tilt test patients initially rested in the horizontal position on a hydraulic tilt table and a cuff was placed around the right index finger for continuous plethysmographic blood pressure recordings (FINAPRES, The Netherlands).[17] When blood pressure and heart rate were stable, usually after 10 minutes, patients were tilted to the head-up 70-degree position with foot support. No provocative manoeuvres were used.[15] The time taken to get from horizontal to tilt angle was 20s. All patients were tilted for a maximum of ten minutes if symptoms permitted, and then returned to the horizontal position for a further five minutes. A diagnosis of VVS required all of the following:

1. a typical history, based on the questionnaire and expert review in clinic, consisting recurrent episodes of transient loss of consciousness occurring when upright in certain situations and following the usual stimuli e.g., prolonged standing, standing up too quickly, blood phobia,[10-14]
2. no features in the history to suggest other conditions e.g., cardiac syncope, epilepsy, orthostatic hypotension, DRPH or POTS,[15]
3. a normal or vasovagal response to abbreviated tilt.

Patient groups

Data on all patients attending the syncope clinic during the study period were reviewed.

Patients were not used in the study if there was: a history of bariatric surgery; weight loss exceeding 40kg; or weight loss starting more than five years before assessment in clinic.

The weight loss group (WL) were selected based on: a clinical diagnosis of VVS; and moderate, and sustained weight loss of between 5kg and 40kg within five years of the syncope clinic assessment. Weight-stable group (WS) were randomly selected from clinic patients based on: a clinical

diagnosis of VVS without moderate weight loss as defined above. Control group (C) were randomly from clinic patients during the study period did not have syncope or weight loss.

Calculated blood volume was estimated using the Nadler equations.[18]

Men: Total blood volume = 0.3669 (Height) 3 + 0.03219 (Weight) + 0.604

Women: Total blood volume = 0.3561 (Height) 3 + 0.03308 (Weight) + 0.1833

The accuracy of the Nadler equation for estimating blood volume may vary, depending on the magnitude and the aetiology of the weight loss.[19]

Hemodynamic measurements included blood pressure as the mean arterial pressure (MAP), heart rate (HR), and stroke volume (SV)—all averaged over one-minute periods. Stroke volume was derived from the blood pressure waveform using the MODELFLOW algorithm and expressed as % baseline.[17] Baseline values were measured in the horizontal position, in the last minute before head-up tilt; early tilt included the third minute of tilt; end of tilt included the tenth minute of tilt, and this was immediately before tilt-back to the horizontal position.

Statistical methods

The three groups were compared using one-way ANOVA, for scale variables, and Chi-squared tests, for categorical variables; and as appropriate and t-tests were used to clarify differences between the groups. Linear regression and product moment correlation coefficients were used to assess associations between continuous variables.

SPPS statistics software version 26 (IBM Corp, Armonk, NY, USA) was used.

After consultation, we were advised by our local ethics committee that formal approval was not required. This study was therefore undertaken under the auspices of the Research Office (University of Otago) and our hospital Quality Control committee.

Results

Over the six-year study period, 480/1,209 (40%) of patients seen in the syncope clinic had VVS. Of these patients 57/480 (11.9%) reported a history of moderate weight loss, between 5kg and 40 kg within five years of the clinic assessment: designated the weight loss (WL) group (Figure 1). From the remaining VVS patients, n=423, a random selection was made of unmatched patients without weight loss, designated the weight stable (WS) group, n=73. Additionally, a control (C) group was selected of patients with neither of weight loss nor syncope, n=24.

The demographic and other clinical characteristics of the patients are summarised in Table 1. There was no evidence of a difference between groups in weight, gender, body mass index, or calculated blood volume. Mechanisms for weight loss in the WL group included lifestyle (n=25), unknown (n=17), anxiety or depression (n=9) and medical conditions (n=6). Medical conditions contributing to weight loss included Crohn's disease, hyperthyroidism, and dysphagia. Both syncope groups had other treated medical conditions not thought to be related to weight loss. The most frequent medications used were serotonin-specific reuptake inhibitors, proton pump inhibitors, thyroxine, and statins. Very few patients in the VVS groups were using blood pressure lowering medication; one in the WS group and two in the WL group. This was, however, likely an artefact of the clinical assessment, because patients with syncope onset coinciding with starting of medications usually had an abnormal early response to tilt and were classified as having DRPH rather than VVS.

In the WL group, mean (SD) weight loss and calculated change in blood volume were 11.5 (7) kg and 0.4 (0.2) L respectively, occurring over 18.7 (13) months. The distribution of weight loss is shown in Figure 1. Weight loss preceded the onset of syncope in 80% of patients. The duration of syncope symptoms was shorter in the WL group compared to the WS group: mean (SD) 13.5 (15) versus 32.9 (44) months, p=0.002. The distribution of syncope symptoms over time was skewed with a long right tail. Although, in the majority of both groups symptoms started within 24 months of presentation, the distribution was more skewed in the WS group: 22/75 (29%) of the WS group had prolonged symptoms versus only 8/57 (14%) in the WL group. In the WL group there was evidence of an association between the duration of symptoms and time over which weight loss occurred, product moment correlation coefficient 0.45, p=0.001; with a slope (95% CI) of 0.48 (0.22 to 0.75) (see Figure 2). There was no evidence of an association between symptom duration and the magnitude of weight loss; product moment correlation coefficient -0.03, p=0.85. The proportion of patients with a history of syncope in childhood and teenage years was lower in the WL group, 23/57 (37%) compared to the WS group, 39/73 (53%).

No patients had syncope during the tilt-test. Haemodynamic variables before tilt (baseline) and at the two measurement times are summarised in Table 2. The baseline values of the haemodynamic variables were similar in all groups. There was strong evidence of a difference in mean arterial blood pressure in the two VVS groups compared

Table 1: Demography, medical conditions and medications of control, weight stable and weight loss groups.

	Clinical group mean (SD)			
	Control N=24n=24	**Weight stable N=73 n=73**	**Weight loss N=57 n=57**	**P**
Age (years)	44 (16)	45.2 (20)	44.8 (18)	0.97
Weight (kg)	75.5 (18)	72.5 (16)	73.4 (16)	0.75
Height (cm)	168.9 (7)	168.6 (9)	168.4 (9)	0.92
BMI	26.5 (6)	25.4 (5)	26.0 (5)	0.66
Blood volume (L)	4.6 (0.8)	4.5 (0.8)	4.5 (0.8)	0.77
Change in weight (kg)			11.5 (7)	
Change in blood volume (L)			0.4 (0.2)	
Weight loss time (months)			18.7 (13)	
Duration of symptoms (months)		32.9 (44)	13.5 (15)	0.002
	n (%)	n (%)	n (%)	
Childhood syncope		39 (53)	23 (37)	0.06
Female	13 (54)	47 (64)	34 (60)	0.65
Medical conditions				
Anxiety/depression		8 (11)	7 (12)	0.82
Phobia		9 (12)	4 (7)	0.32
Migraine		3 (4)	0 (0)	0.26
Others		18 (25)	16 (28)	0.66
Medications				
Serotonin specific reuptake inhibitor		7 (10)	9 (16)	0.29
Proton pump inhibitor		7 (10)	5 (9)	0.87
Statin		3 (4)	4 (7)	0.70
Anti-hypertensive medication use		0 (0	2 (4)	0.20
Weight loss mechanism				
Life style			25 (44)	
Unknown			17 (30)	
Anxiety/depression			9 (16)	
Medical condition			6 (10)	

Table 2: Early tilt haemodynamic data: controls versus syncope patients with and without weight loss. Values represent means ± sd.

	Clinical group mean (SD)			
	Control (n=24)	**Weight stable (n=73)**	**Weight loss (n=57)**	**P**
Mean arterial blood pressure (mmHg)				
Baseline	87 (12)	82 (12)	83 (12)	0.22
3 min tilt	102 (12)	90 (3)	92 (13)	0.001
10 min tilt	103 (14)	93 (13)	90 (14)	0.001
Heart rate (beats per minute)				
Baseline	73 (12)	71 (11)	70 (10)	0.34
3 min tilt	83 (13)	79 (11)	80 (14)	0.32
10 min tilt	87(14)	84(14)	84(16)	0.71
Stroke volume (percentage of baseline)				
3 min tilt	65 (12)	70 (11)	67 (12)	0.34
10 min tilt	61 (11)	69 (10)	71 (18)	0.01

Figure 1

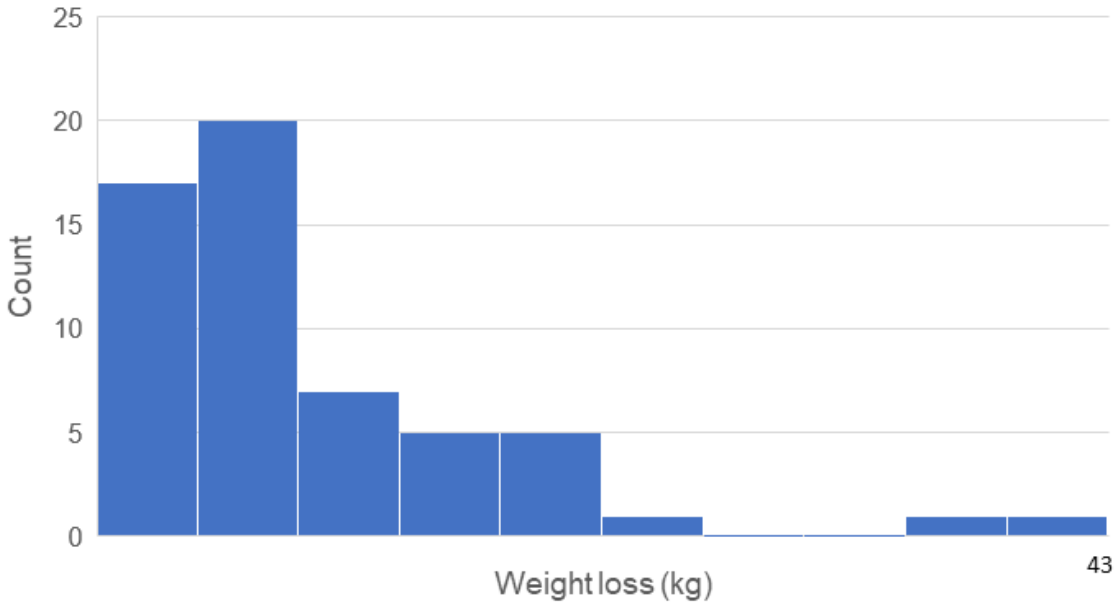
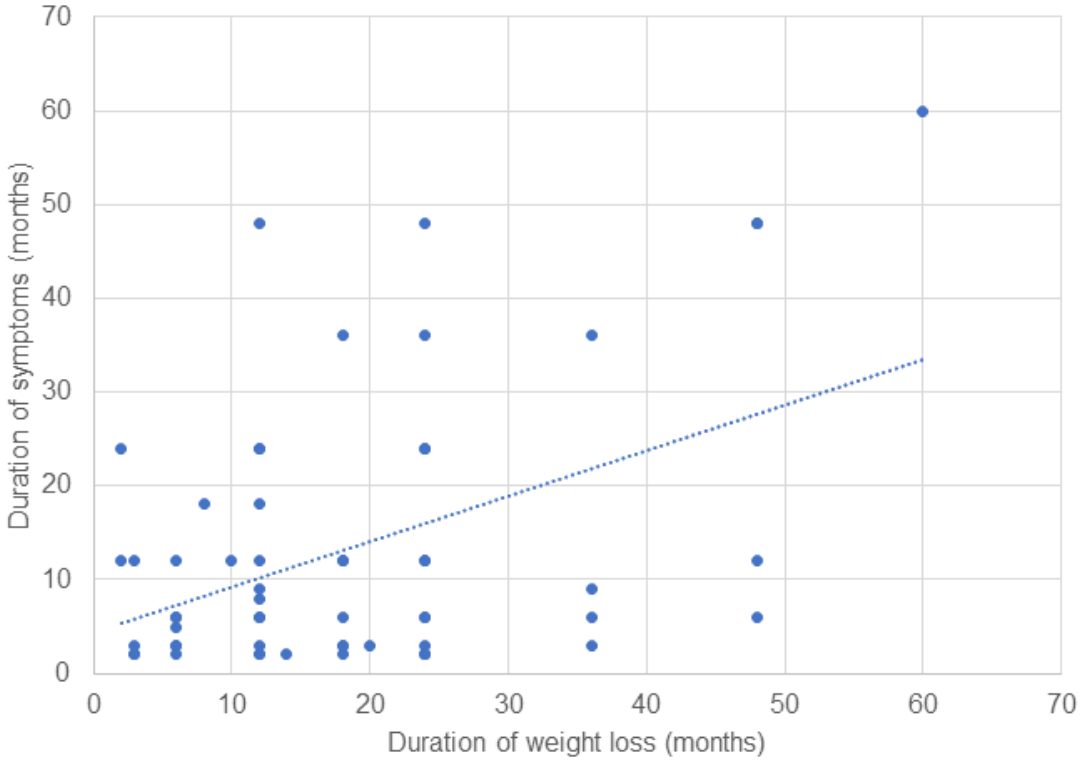


Figure 2



to control, there was no evidence of a difference in heart rate, and although there was no evidence of a difference in stroke volume after three minutes; the control group had a lower stroke volume after 10 minutes of tilt.

Discussion

We found that recent moderate weight loss was rather common in patients presenting to our clinic with vasovagal syncope. Weight loss in most patients was intentional, through dieting and exercise; however, many patients were uncertain as to the cause. Apart from weight loss, the demographic characteristics, background medical histories and medications of this group were no different to other VVS patients. VVS onset usually followed or coincided with the onset of weight loss resulting in a shorter duration of syncope symptoms before clinic assessment. The duration of VVS symptoms was associated with the time interval over which weight loss occurred. Furthermore, fewer patients with weight loss reported syncope in earlier life, suggesting that onset of syncope was secondary to a physiological change, not a life-long predisposition. In the absence of other possible confounders it seems likely that weight loss, and the associated fall in blood volume, were the most likely physiological explanations for the synchrony between the onset of weight loss and postural VVS. We further hypothesised that patients with weight loss and decreased central blood volume might have an exaggerated fall in stroke volume during head-up tilt. However, we found that even though blood pressure was lower in both syncope groups during early tilt, stroke volume changes were less than in controls. Although adipose tissue is relatively low in blood volume, studies in dieting patients report reductions of both total and central blood volume within months.[6,20] We calculated that moderate weight loss, on average 12kg, would include 0.4L of blood volume, half of which is centrally distributed and the main determinant of stroke volume.[18] During tilt SV fell by approximately 30% in all of our patients. This occurred mainly in the first three minutes, consistent with previous studies on VVS.[9] We did not study tilt responses beyond ten minutes and so cannot comment on how weight loss might have affected the later changes preceding syncope. Crucially, our methods did not allow direct measurements of central blood volume or absolute SV levels immediately before tilt. Instead, we compared only changes in SV after tilt which has an uncertain relationship with absolute baseline levels. Furthermore, because of the retrospective nature of this study, we cannot determine how

stroke volume and blood pressure may have fallen during the months over which weight loss occurred. Presumably the blood pressure level was similar in the two syncope groups because in the WL group it had fallen from higher levels. Therefore, most of the important changes in MAP and SV probably occurred during the months before clinic assessment and it is not surprising that our tilt data was not helpful. This in no way refutes our important finding of the association between weight loss and VVS.

It is possible that the fall in blood pressure, consistently observed after weight loss predisposes some patients to recurrent vasovagal syncope.[1,5] New-onset syncope has been observed in other situations when blood pressure is lowered, e.g., following the introduction of antihypertensive medication and during pregnancy.[10] Normally, arterial baroreflexes buffer acute falls in stroke volume and blood pressure in response to postural changes. After weight loss, although the baroreflexes become more sensitive, they reset and modulate heart rate and sympathetic nerve activity at lower MAP levels.[3,21] However, the absolute MAP at which syncope occurs remains the same (approximately 60mmHg), therefore the lower the MAP levels at which the baroreflex curve operates, the more likely the patient is to develop syncope.[22] Other studies have used head-down bed rest (over three weeks) to lower blood volume and reported no changes in arterial baroreflex function despite clear demonstration of orthostatic intolerance.[23] We emphasise that in our study (and other weight loss studies) the weight change was greater and over a much longer time interval, therefore a major "left" shift of the baroreflex curves towards lower MAP levels is likely.[3,21] Re-setting is complicated and involves not only arterial but also cardiopulmonary baroreflexes which control renin, vasopressin and endothelin secretion.[24,27] Furthermore, cardiopulmonary baroreflexes also modulate sympathetic activity and augment arterial baroreflex function when central blood volume is decreased.[28,29] In view of these interactions and the nature of baroreflex responses, it is not surprising that we were unable to demonstrate a strong linear correlation between the recent duration of weight loss and syncope symptoms.

Limitations

In this study, the estimation of duration of syncope symptoms and weight loss depended on patient recall. Onset of syncope after weight loss may have biased how some patients remembered their symptoms. We think this was partly mitigated by sending the patients a written questionnaire and checking their reported weight data with the electronic record as described in the methods. We were unable to directly measure central blood volume or compare absolute stroke volume levels at baseline. Sample size and statistical power were limited by the numbers of controls and patients presenting with weight loss. Multiple comparisons between these groups may have increased the risk of a type I error. An ideal future study would prospectively measure weight loss, tilt responses, and symptoms before and after dietary intervention.

Conclusion

In the majority of patients presenting to our clinic with recurrent blackouts occurring in a standing or sitting position, the diagnosis is vasovagal syncope.[15] It is usually made by taking a careful history.[10,12,14] When the history is unclear, other less common causes can be excluded by the appropriate investigations, for example long-term cardiac monitoring for arrhythmia or tilt testing for postural hypotension.[10,12] If these results are normal, patients can be reassured that the diagnosis is still most likely to be VVS because it is so prevalent in all age groups. In some, the diagnosis is supported by a satisfactory response to treating predisposing factors e.g., anaemia, dehydration, prolonged bedrest, drugs, pregnancy, or fever; but in others there are no associated changes other than weight loss. The results of this study are consistent with that in a subset of patients with recent onset VVS, there may be an association with simultaneous moderate weight loss. This association is generally not recognised by patients and has not previously been reported. This may be because the temporal association between duration of weight loss and onset of syncope is not simple. We suspect that when weight stabilises at a lower level and the baroreflex mechanisms re-set, the time interval during which the patient remains symptomatic is variable. We plan a follow-up study to examine the length of this time interval and what baroreflex changes occur. In the meantime, we reassure our patients that the symptoms will improve (without any form of medication), and they are discouraged from putting the weight back on.

COMPETING INTERESTS
Nil.

AUTHOR INFORMATION
Brent Cumming MB ChB: Department of General Medicine, Christchurch Hospital, Riccarton Rd, Christchurch 8410 New Zealand.
Christopher Frampton PhD: Department of Medicine, Christchurch school of Medicine, University of Otago, Christchurch 8410 New Zealand,
David Jardine FRACP, MD: Department of General Medicine, Christchurch Hospital, Riccarton Rd, Christchurch 8410; Department of Medicine, Christchurch school of Medicine, University of Otago, Christchurch 8410, New Zealand.

CORRESPONDING AUTHOR
David L Jardine: Dept Gen Medicine, ORCHID 0000-0002-5925-7623. Ph: 00643 3641021. david.jardine@cdhb.govt.nz

URL
www.nzma.org.nz/journal-articles/vasovagal-syncope-triggered-by-recent-moderate-weight-loss

REFERENCES
1. Billakanty SR, Kigman MD, Kanjwal YM et al. New onset orthostatic intolerance following bariatric surgery. Pacing Clin Electrophysiol 2008;31:884-888.
2. Ponnusamy V, Owens AP, Purkayastha S, et al. Orthostatic intolerance and autonomic dysfunction following bariatric surgery: a retrospective study and review of the literature. Autonom Neurosci 2016;198:1-7.
3. Grassi G, Seravalle G, Columbo M et al. Weight reduction, sympathetic nerve traffic and arterial baroreflex in obese normotensive humans. Circulation. 1998;97:2037-2042.
4. Lambert E, Esler MD, Schlaich MP et al. Obesity-Associated Organ Damage and Sympathetic Nervous Activity. Hypertension 2019;73:1150-1159.
5. Messerli FH, Christie B, DeCarvalho JG et al. Obesity and essential hypertension: hemodynamics, intravascular volume, sodium excretion and plasma renin activity. Arch Intern Med. 1981;141:81-85.
6. Reisin E, Frohlich ED, Messerli FH et al. Cardiovascular changes after weight reduction surgery. Ann Intern Med. 1983;98:315-319.
7. Stewart JM, McLeod KJ, Sanyal S et al. Relation of postural vasovagal syncope to splanchnic hypervolemia in adolescents. Circulation. 2004; 110:2575-2581.
8. van Lieshout JJ, Harms MP, Pott F et al. Stroke volume of the heart and thoracic fluid volume during head-up and head-down tilt in humans. Acta Anaesthesiol Scand. 2005;49:1287-1292.
9. Verheyden B, Liu J, van Dijk N et al.. Steep fall in cardiac output is the main determinant of hypotension in drug-free and nitroglycerin-induced orthostatic vasovagal syncope. Heart Rhythm. 2008;5:1695-1701.
10. Brignole M, Moya A, de Lange FJ et al. Guidelines for the diagnosis and management of vasovagal syncope. Eur Heart J 2018; 39:1883-1948.
11. Colman N, Nahm K, Ganzeboom KS et al. Epidemiology of reflex syncope. Clin Autonom Res 2004; 14 Suppl 1:9-17.
12. Shen WK, Sheldon RS. ACC/AHA/HRS guidelines for the evaluation and management of patients with syncope. J Am Coll Cardiol 2017;70:e41-e109.
13. van Dijk GG, Thijs RD, Benditt DG and Wouter Wieling. A guide to disorders causing transient loss of consciousness: focus on syncope. Nat Rev Neurol 2009;5:438-448.
14. Wieling W, Kaufmann H. What is the best method to diagnose vasovagal syncope? Clin Autonom Res 2021;3:335-337.
15. Al-Busaidi IS, Jardine DL. Different types of syncope presenting to clinic: do we miss cardiac syncope? Heart Lung Circ. 2019:S1443-9506(19)31454-4. doi: 10.1016/j.hlc.2019.09.008.
16. Moya A. Tilt testing and neurally-mediated syncope: too many protocols for one condition or specific protocols for different situations? Eur Heart J 2009;30:2174-2176.
17. Bogert LW, van Lieshout JJ. Non-invasive pulsatile arterial pressure and stroke volume changes from the human finger. Exp Physiol. 2005;90:437-446.
18. Nadler SB, Hidalgo JH, Bloch T. Prediction of blood volume in normal human adults. Surgery. 1962;51:224-232.
19. Funkhouser RK, Pritchard WH, Little AS. Change in relationship of blood volume to weight in congestive heart failure. Circulation 1957;16:548-557.
20. Alexander JK, Peterson KL. Cardiovascular effects of weight reduction. Circulation 1972;45:310-318.
21. Alvarez GE, Davy BM, Ballard TP et al. Weight loss increases cardiovagal baroreflex function in obese young and older men. Am J Physiol Endocrinol Metab. 2005;289:E665-E669.
22. Wieling W, Thijs RD, van Dijk N et al. Symptoms and signs of syncope: a review of the link between physiology and clinical clues. Brain 2009; 132: 2630-2642.
23. Kamiya A, Michikami D, Fu Q et al. Pathophysiology of orthostatic hypotension after bedrest: paradoxical sympathetic withdrawal. Am J Physiol

Heart Circ Physiol 2003;285:H1158-H1167.
24. Grassi G, Giannattasio C, Cuspidi C et al. Cardiopulmonary receptor regulation of renin release. Am J Med. 1988;84 (Suppl 3A):97-104.
25. Hainsworth R. Cardiovascular control from cardiac and pulmonary vascular receptors. Exp Physiol 2014;99:312-319.
26. Jacobsen T, Morgan B, Scherrer U et al. Relative contributions of cardiopulmonary and sinoaortic baroreflexes in causing sympathetic activation in human skeletal muscle circulation during orthostatic stress. Circ Res. 1993;73:367-378.
27. Vissing SF, Scherrer U, Victor RG. Relation Between Sympathetic Outflow and Vascular Resistance in the Calf During Perturbations in Central Venous Pressure. Evidence for Cardiopulmonary Afferent Regulation of Calf Vascular Resistance in Humans. Circ Res 1989;65:1710-1717.
28. Ichinose M, Saito M, Kitano A et al. Modulation of arterial baroreflex dynamic response during mild orthostastic stress in humans. J Physiol 2004;557:321-330.
29. Ogoh S, Brothers RM, Barnes Q et al. Effects of changes in central blood volume on carotid-vasomotor baroreflex sensitivity at rest and during exercise. J Appl Physiol 2006;101:68-75.

New Echocardiography Reference Ranges for Aotearoa (NewERA) Study: the application of international echocardiographic reference values to linear measurements of the hearts of healthy, young Māori and Pacific adults may not detect cardiac enlargement

Gillian A Whalley, Allanah Harrington, Jonathan Christiansen, Bettina Ikenasio, Arun Deo, Greg D Gamble, Sue Crengle

ABSTRACT

AIMS: To develop ethnic-specific echocardiography reference ranges for Aotearoa, and to investigate the impact of indexation to body surface area (BSA). Current reference international ranges are derived from people of mostly NZ European ethnicity and may not be appropriate for Māori and New Zealanders of Pacific ethnicity, who both experience high rates of cardiovascular disease.

METHODS: Echocardiography was performed in a cross-sectional study of 263 healthy adults (18–50 years): Māori (N=71, 43 female), Pacific (N=53, 28 female), European (N=139, 74 female). Linear measurements of the left heart are reported and indexed to BSA. The upper/lower limit of normal (ULN/LLN) by ethnicity and sex were derived (quantile regression). Ethnic- and sex-specific differences were examined using ANOVA.

RESULTS: The ULN was higher for all un-indexed dimensions in men compared to women, and for most indices the ULN was smallest in NZ Europeans and largest in Māori and Pacific peoples. Indexation reversed these relationships: NZ Europeans had higher ULN for many measurements.

CONCLUSIONS: Indexing to BSA introduced bias that preferences the NZ European ethnicity by creating an upper limit reference threshold that far exceeds this sample's upper range. As a result, this may lead to under-recognition of cardiac enlargement in Māori and Pacific patients, and in particular for women. Unique reference ranges for all ethnic groups and sexes are required to optimally detect and manage cardiovascular diseases (CVD) in Aotearoa.

Echocardiography is used to detect and monitor structural and functional cardiovascular diseases (CVD) by comparing quantitative measurements (such as heart wall thickness and chamber size) to population reference values.[1] Recently, the impact of ethnicity upon echo measurements has been raised. The Echocardiographic Normal Ranges Meta-Analysis of the Left heart (EchoNoRMAL),[2] an individual person meta-analysis with >20,000 participants, demonstrated important sex and ethnic differences in the normal echocardiographic reference ranges between NZ European, Asian and South Asian cohorts. Overall, the Asian cohorts had smaller hearts compared to the NZ European cohorts; and women had smaller hearts across all ethnic groups.[2]

Heart size is closely linked with body size, and guidelines recommend echocardiography measurements are indexed (divided by) by body surface area (BSA)[1] to allow comparison between individuals of differing sizes. But BSA is an imperfect indexation variable, and previous research suggests that body composition and fat free mass (FFM) is a better independent predictor of heart size than BSA.[3,4] Body composition is also linked

to both sex and ethnicity: women have lower FFM than men for the same BMI; and Asian and Indian individuals have lower FFM than Caucasians of similar height and weight, who in turn have less FFM than African American individuals.[5] These differences may explain the sex and ethnic differences observed in heart size.

In New Zealand, CVD is a leading cause of mortality, and mortality rates are highest within the indigenous Māori[6] and Pacific populations.[7] Māori and Pacific individuals also have higher FFM compared with NZ Europeans;[8] therefore it is conceivable, indeed likely, that normal heart size is larger in Māori and NZ Pacific peoples. In the Hauora Manawa Heart Study,[9] echocardiography revealed that Māori had larger left ventricular (LV) and aortic dimensions, thicker LV walls and higher prevalence of LV hypertrophy (LVH) compared with non-Māori. Whilst this may reflect higher disease burden, it is probable that the true incidence of dilatation and LVH was overestimated by using the international reference values, as they were derived mostly from NZ European individuals.[1] At the time there were, and remain, no appropriate reference ranges for clinical application in Māori, nor indeed Pacific peoples.

Our objective was to establish normal reference ranges for echocardiography applicable to both New Zealand and Pacific Islands populations. Our hypothesis was that heart size would be larger in Māori and NZ Pacific peoples and that reference values that include indexation to BSA, which does not account for body composition, may be inappropriate in a cohort of mixed ethnicity. As a result, the echocardiography measurements may not be optimised in these groups, who are also at the higher risk of CVD.

Methods

Study population

This targeted cross-sectional study recruited three age-matched healthy cohorts: Māori, NZ Pacific, NZ European. Between July 2015 and September 2017, participants were recruited through convenience sampling (word of mouth, newspaper articles, primary care practices, workplaces, and recreational sporting groups). Consenting participants attended a single visit at our research facility Awhina Health Campus or at community clinics in various locations (including primary healthcare facilities and workplaces) where demographic data, and clinical and family history were collected, and clinical measurements were taken: height, weight, body composition (Tanita Body Composition Analyzer SC-330), automated blood pressure (BP), point of care total cholesterol and blood glucose (CardioChek PA); and where echocardiography was performed. Body mass index (BMI) was calculated (weight/height^2) and BSA calculated by the DuBois formula.[10] Body composition was assessed using sex-specific non-athlete settings, and fat free mass (FFM) was calculated as total weight less fat mass, and included bone mass.

Participants were invited to begin their individual visit with the research team with a karakia, and also offered the remnant of their blood sample to take home. All remaining blood samples were collated in a single medical waste container (separate from general waste) for a cremation ceremony at the study completion. Participants were given a $20 fuel voucher as a koha, as well as pamphlets about reducing the risk of stroke, diabetes and heart disease. These were available in English, te reo Māori, Samoan and Tongan languages. All participants provided signed written consent. The study was conducted in accordance with the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) statement11 and was approved by the Southern Health and Disability Ethics Committee (approval number 15/STH/96).

Inclusion and exclusion criteria

Participants aged 18–50 years who self-identified as Māori, NZ European, or Pacific Island ethnicity, with good health, were invited. NZ Pacific peoples included participants who identified as either Cook Island Māori, Fijian, Niuean, Samoan, Tahitian or Tongan. Participants who identified as Fijian Indian Pacific were excluded. Other patient exclusion included: random (non-fasting) total cholesterol of >7·0mmol/L or glucose of >10mmol/L; BMI >40; currently or recently (<3 months) pregnant; hypertension (greater than 145/90 on two different automated BP measurements); history of CVD, diabetes, renal failure or other serious conditions (including lung disease or asthma on regular medication (N=2)); taking any cardiovascular medications (except statins); and significant incidental echo findings.

Ethnicity determination

Ethnicity was self-identified, and participants were able to select more than one group, in which case, group allocation was ascribed according to the prioritisation method in the New Zealand Ministry of Health's ethnicity data protocol:

1) Māori, 2) Pacific, 3) Asian, 4) European.[12] This ensured that participants were only counted in one group. For example, if a participant reported both Māori and European ethnicity, they were allocated to the Māori group. If a participant selected Māori and Pacific, they were also allocated to the Māori group.

Echocardiography

Echocardiography was performed by experienced sonographers or cardiology fellows according to a standard research protocol adherent to the ASE Guidelines (Philips CX50 or Siemens SC2000prime). Full echo data are available, but this publication includes linear 2D measurements of the left heart: left ventricular internal end-diastolic dimension (LVIDd); left ventricular internal end-systolic dimension (LVIDs); left ventricular outflow tract (LVOT); and aortic root and proximal ascending aorta. These measurements were made (average of three beats) off-line (Philips Q Station), and by a single reader (GAW) at the conclusion of the study in random order blinded to ethnicity, sex or other clinical information. All measurements were obtained according to recommendations of the American Society of Echocardiography Chamber Quantification Guidelines.[1]

Statistical analysis

Exploratory data analysis revealed that all of the variables were normally distributed. Quantile regression was used to determine the 95th and 5th centiles to determine upper limits of normal (ULN) and lower limits of normal (LLN) for each echo measurement. ANOVA was used to determine difference between the three ethnic groups, sex and the interaction of sex and ethnicity. *Post hoc* analysis was performed using Tukey method.

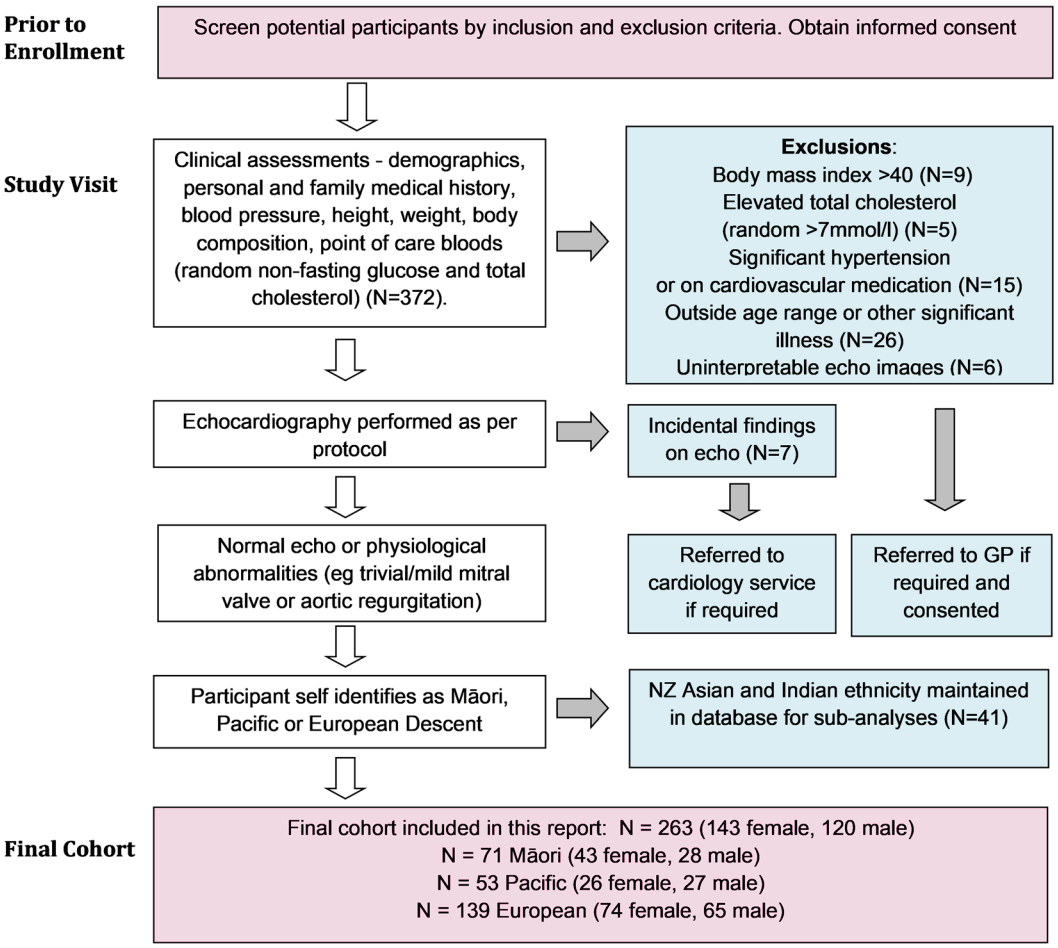
Results

Study population

After initial screening, 372 participants attended the first visit and 109 were excluded, leaving a final cohort of 263: 71 Māori (43 female, 28 male); 53 NZ Pacific (26 female, 27 male); and 139 NZ European (74 female, 65 male) participants (Figure 1).

The groups were well-matched in terms of age,

Figure 1: Recruitment flow chart.



height, blood pressure and heart rate (Table 1). Significant differences were observed in weight and body composition, with Māori having higher weight, fat mass (FM), fat free mass (FFM) and bone mass than NZ Europeans in both males and females, and with Pacific peoples having the highest. The same pattern was observed in each sex and for calculated BMI and BSA: the NZ European cohort had the lowest, and Pacific the highest, with Māori in between. No significant differences were observed between self-reported physical activity status.

Linear measurements of the left ventricle

For linear LV measurements, the ULN and LLN were higher in men compared to women and varied significantly by ethnicity: the NZ European cohort had the smallest chambers compared to both the Pacific and Māori cohorts (Table 2). Indexation to BSA did not remove the sex differences but did change the order of the ethnic group differences, in such that now the NZ European group had the largest hearts. The only interaction between ethnicity and sex noted was for LVIDs and LVIDs/BSA, which are measures of both size and function.

Post hoc analyses within these sex groups revealed trends towards the differences noted above, but the only significant difference in unindexed measurements was for LVIDs, where NZ Pacific men had larger LVIDs compared to both NZ European and Māori men (Figure 2). But, when indexed to BSA, these differences in men were eliminated; however, significant differences between ethnicities emerged in women. NZ Pacific women had smaller hearts compared to both the Māori and NZ European women (Figure 2).

Raw unindexed measures of the after larger and before LV

Men had larger LV outflow tract (LVOT), aortic root (AoR) and ascending aortic (AscAo) dimensions than women (Table 2), and significant differences were seen across ethnicities. The relationship was similar to that observed for LV measurements; the European cohort had the smallest compared to both the Pacific and Māori groups. Indexation removed the sex differences for both LVOT and AoR (Table 2) and introduced a significant interaction between ethnicity and sex for LVOT/BSA, and the relationship across the ethnic groups altered such that the European cohort no longer had the smallest measurements: NZ European women now had the largest LVOT/BSA measurements (Figure 3).

Comparison with other reference values

There was general agreement between the ULN seen in this NZ European cohort when compared to both ASE/EACVI and EchoNoRMAL indexed variables[1,2] for both men and women (Table 3) and where differences are seen, these are of marginal clinical relevance. However, comparing the distribution of the data for LVIDd with the ASE/EASCVI reference values, a substantial proportion (19% of European men, 26% of European women; 29% of Māori men, 42% of Māori women; and 15% of Pacific men, 27% of Pacific women) fell outside of the reference ranges for raw measurements of LVIDd (Figure 4). In both sexes, the data for Māori and Pacific peoples was shifted to the right for un-indexed LVIDd resulting in higher levels of "abnormal" measurements in Māori men (28.5%) and women (42.3%), but not Pacific participants. Indexation to BSA shifted the distributions to the left and eliminated all abnormal measurements in the Pacific group and a substantial proportion in the Māori groups. In the European group, indexation reduced this from 19–5% in men and 26–6% in women. In both the Māori and Pacific groups, the reduction was even greater: 29–7% in Māori men and 42–3% in Māori women; 15–0% in Pacific men and 27–0% in Pacific women.

Discussion

This study has shown, important differences in echocardiographic reference ranges between New Zealanders of European, Māori and Pacific ethnic groups. The results are consistent with previous research showing that echocardiographic heart size, is dependent on sex and ethnicity,[13,14] and suggests that current international Caucasian reference values are not applicable in Aotearoa, and worse, will contribute to poorer health outcomes due to misdiagnosis when used in Māori and Pacific peoples. Specifically, we found that heart size is different among these ethnic groups, and that application of the current international guidelines, specifically indexation to BSA, is an imperfect adjustment that may mask the presence of pathological abnormalities.

Indexation to BSA is intended to allow fair comparison of heart size amongst people of different body habitus. But from this data, it is apparent that unintentional preference may be introduced in healthcare delivery, in a way that preferences NZ European ethnicity: for example, among Māori and NZ Pacific peoples using a reference range, derived from a Caucasian population, may result

Table 1: Baseline demographics and clinical measurements.

A – Male participants	NZ European N=65	Māori N=28	Pacific N=27	ANOVA p	*Post Hoc* Tukey		
					M v P	M v E	E v P
Age, years	34.9 ± 9.4	32.6 ± 9.5	33.9 ± 10.0	0.570	0.88	0.547	0.886
Height, cm	180.2 ± 7.6	179.8 ± 6.3	178.8 ± 7.1	0.726	0.889	0.963	0.703
Weight, kg	84.8 ± 13.3	92.8 ± 13.9	101.6 ± 14.7	<0.001	0.051	0.028	<0.0001
Systolic BP, mmHg	133.9 ± 12.7	135.9 ± 17.6	136.9 ± 10.5	0.579	0.954	0.795	0.591
Diastolic BP, mmHg	81.9 ± 9.1	81.8 ± 10.0	87.2 ± 7.9	0.037	0.116	0.982	0.033
Heart rate, bpm	66.1 ± 10.2	69.3 ± 12.2	65.9 ± 8.6	0.351	0.45	0.364	0.996
Glucose, mmol/l	5.0 ± 1.19	5.1 ± 1.13	4.9 ± 0.82	0.725	0.704	0.857	0.908
Total cholesterol, mmol/l	4.4± 1.19	4.3 ± 1.03	3.9 ± 0.70	0.108	0.331	0.895	0.09
BSA, m^2	2.04 ± 0.17	2.16 ± 0.20	2.20 ± 0.18	0.001	0.235	0.121	<0.0001
BMI, kg/m^2	26.1 ± 3.8	30.3 ± 5.8	31.7 ± 3.6	<0.001	0.011	0.007	<0.0001
Fat free mass, kg	66.6 ± 7.5	70.2 ± 7.0	75.1 ± 9.1	<0.001	0.061	0.102	<0.0001
Fat mass, kg	18.2 ± 8.6	22.6 ± 9.1	26.6 ± 8.2	<0.001	0.207	0.061	<0.0001
Muscle mass, kg	63.3 ± 7.2	66.8 ± 6.6	71.4 ± 8.7	<0.001	0.061	0.102	<0.0001
Bone mass, kg	3.30 ± 0.35	3.47 ± 0.31	3.69 ± 0.42	0.002	0.056	0.104	<0.0001

Table 1 (continued): Baseline demographics and clinical measurements.

B – Female participants	NZ European N=74	Māori N=43	Pacific N=26	ANOVA p	*Post Hoc* Tukey		
					M v P	M v E	E v P
Age, years	36.9 ± 10.7	34.1± 10.1	37.1 ± 9.4	0.311	0.475	0.324	0.998
Height, cm	166.4 ± 6.3	166.4 ± 6.4	167.3 ± 5.7	0.242	0.818	1.0	0.786
Weight, kg	66.9 ± 14.5	78.6 ± 15.2	84.2 ± 15.8	<0.001	0.287	<0.0001	<0.0001
Systolic BP, mmHg	121.5 ± 9.9	127.0 ± 14.1	129.1 ± 13.0	0.006	0.758	0.042	0.016
Diastolic BP, mmHg	77.3 ± 8.2	81.6 ± 8.9	82.6 ± 7.4	0.006	0.708	0.05	0.015
Heart rate, bpm	69.4 ± 10.3	71.9 ± 14.1	68.7 ± 10.5	0.431	0.50	0.503	0.956
Glucose, mmol/l	4.9 ± 1.46	5.3 ± 1.16	5.0 ± 1.39	0.232	0676	0.202	0.676
Total cholesterol, mmol/l	4.5 ± 1.17	4.4 ± 0.96	4.3 ± 1.03	0.597	0.905	0.821	0.0599
BSA, m^2	1.74 ± 0.18	1.86 ± 0.18	1.93 ± 0.18	<0.001	0.325	0.001	<0.0001
BMI, kg/m^2	24.1 ± 4.9	28.4 ± 5.1	30.1 ± 5.4	<0.001	0.369	<0.0001	<0.0001
Fat free mass, kg	45.8 ± 4.7	48.7 ± 5.6	51.6 ± 6.5	<0.001	0.071	0.016	<0.0001
Fat mass, kg	21.1 ± 10.3	29.9 ± 10.3	32.6 ± 11.2	<0.001	0.556	<0.0001	<0.0001
Muscle mass, kg	43.5 ± 4.4	46.2 ± 5.3	49.0 ± 6.2	<0.001	0.069	0.017	<0.0001
Bone mass, kg	2.33 ± 0.23	2.47 ± 0.28	2.61 ± 0.31	<0.001	0.105	0.011	<0.0001

Data are mean ± standard deviation
Abbreviations: BMI = body mass index, BSA = body surface area

Table 2: Left heart linear echocardiography measurements.

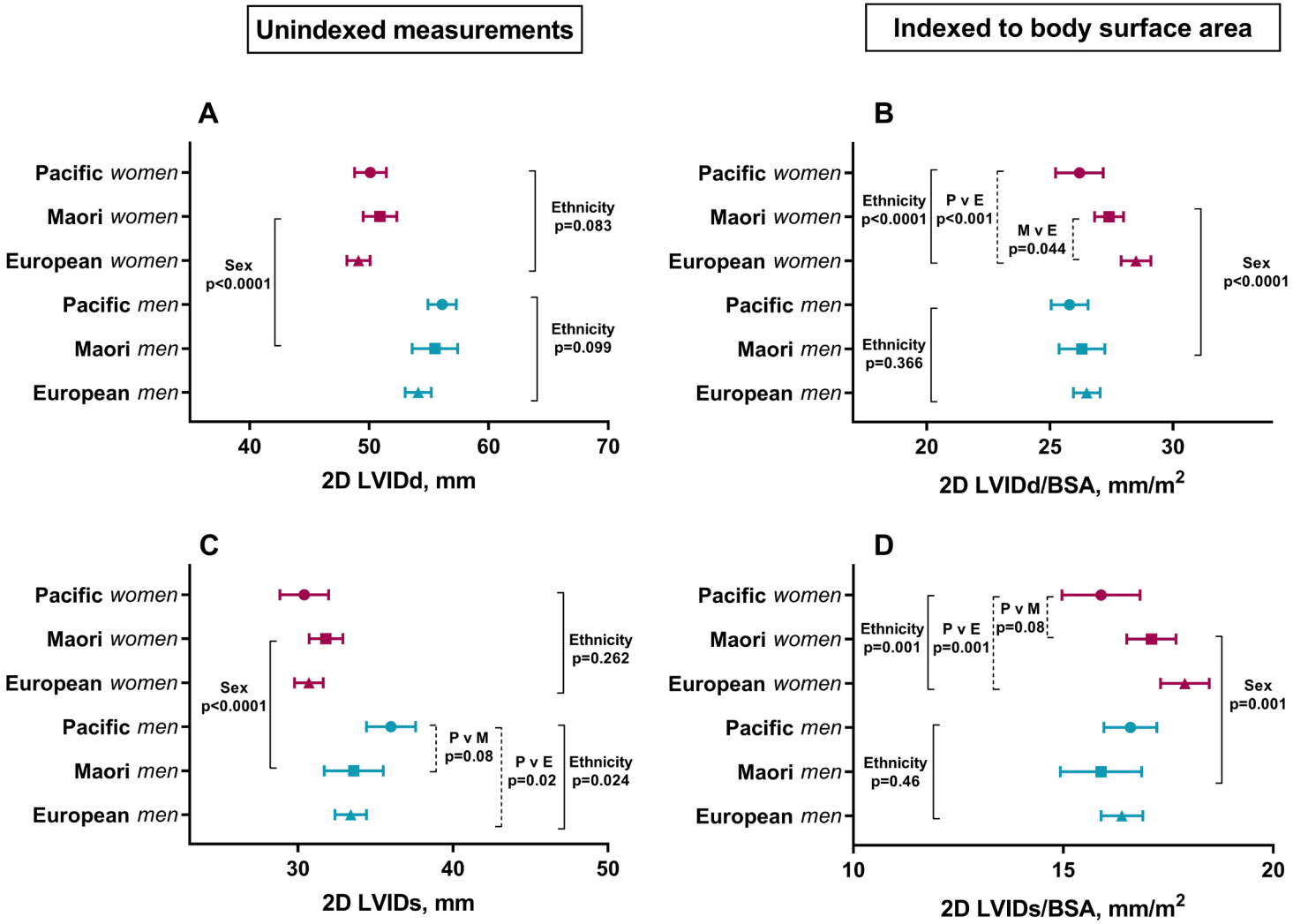
	NZ European ethnicity						Māori ethnicity						Pacific ethnicity						ANOVA		
	Male, N=65			Female, N=74			Male, N=28			Female, N=43			Male, N=27			Female, N=26					
Variable	**m ± sd**	**LLN**	**ULN**	**m ± sd**	**LLN**	**ULN**	**m ± sd**	**LLN**	**ULN**	**m ± sd**	**LLN**	**ULN**	**m ± sd**	**LLN**	**ULN**	**m ± sd**	**LLN**	**ULN**	**Ethnicity**	**Sex**	**Interaction**
LVIDd, mm	54.1 ± 4.4	47.1	61.8	49.1 ± 4.2	42.8	54.8	55.5 ± 4.9	46.6	61.4	50.9 ± 4.8	43.4	60.2	56.1 ± 3.0	51.1	60.0	50.1 ± 3.3	45.1	55.8	0.0142	<0.0001	0.7062
LVIDd /BSA, mm/m^2	26.5 ± 2.2	23.9	30.4	28.5 ± 2.6	24.5	32.5	26.3 ± 2.4	22.8	30.5	27.4 ± 2.0	24.0	30.5	25.8 ± 1.9	22.5	29.0	26.2 ± 2.4	22.5	30.3	0.0003	0.0003	0.0930
LVIDs, mm	33.4 ± 4.1	27.2	41.4	30.7 ± 4.0	23.2	36.8	33.6 ± 4.9	27.1	38.7	31.8 ± 3.7	26.5	37.9	36.0 ± 4.0	30.4	43.5	30.4 ± 3.89	24.5	35.3	0.1796	<0.0001	0.0269
LVIDs /BSA, mm/m^2	16.4 ± 2.0	13.7	20.4	17.9 ± 2.5	14.1	22.2	15.9 ± 2.5	12.7	18.8	17.1 ± 2.0	12.5	19.9	16.6 ± 1.6	13.8	19.1	15.9 ± 2.3	12.8	20.0	0.0280	0.0244	0.0109
LVOT, mm	22.7 ± 2.0	19.8	25.8	20.3 ± 1.6	18.0	23.5	24.3 ± 2.8	21.5	30.3	20.7 ± 1.5	18.1	23.7	24.1 ± 1.7	21.5	26.7	21.7 ± 2.2	18.5	26.1	<0.0001	<0.0001	0.0991
LVOT/BSA, mm/m^2	11.2 ± 1.1	9.4	12.6	11.7 ± 1.2	10.2	14.2	11.5 ± 1.6	9.5	14.0	11.2 ± 0.9	9.5	12.9	11.1 ± 1.2	9.5	12.9	11.3 ± 1.1	9.7	12.9	0.4426	0.3836	0.0294
Aortic root, mm	34.4 ± 3.7	29.5	39.5	30.2 ± 2.9	26.2	34.4	35.6 ± 4.5	30.7	42.8	30.8 ± 4.0	25.5	36.5	35.5 ± 5.0	24.9	43.3	32.7 ± 4.6	26.8	40.9	0.0161	<0.0001	0.3530
Aortic root/BSA, mm/m^2	16.8 ± 1.8	14.9	20.2	17.5 ± 2.2	14.3	20.1	16.0 ± 2.2	14.2	20.1	16.2 ± 2.2	13.7	20.2	16.4 ± 3.2	9.8	21.8	16.9 ± 2.4	13.7	21.7	0.2523	0.2983	0.4165
STJ, mm	28.4 ± 3.4	23.9	33.3	25.7 ± 2.6	21.7	30.3	29.3 ± 3.3	25.0	34.4	25.9 ± 2.8	22.0	30.1	29.4 ± 3.0	25.7	34.3	27.4 ± 3.5	23.4	32.9	0.0329	<0.0001	0.4936

Table 2 (contined): Left heart linear echocardiography measurements.

	NZ European ethnicity						Māori ethnicity						Pacific ethnicity						ANOVA		
	Male, N=65			Female, N=74			Male, N=28			Female, N=43			Male, N=27			Female, N=26					
Variable	**m ± sd**	**LLN**	**ULN**	**m ± sd**	**LLN**	**ULN**	**m ± sd**	**LLN**	**ULN**	**m ± sd**	**LLN**	**ULN**	**m ± sd**	**LLN**	**ULN**	**m ± sd**	**LLN**	**ULN**	**Ethnicity**	**Sex**	**Interaction**
STJ/BSA, mm/m^2	13.9 ± 1.6	11.5	16.6	14.9 ± 1.9	12.2	17.6	13.9 ± 1.6	12.2	15.9	14.0 ± 1.8	11.0	16.9	13.6 ± 1.8	10.9	16.3	14.2 ± 2.0	11.5	18.6	0.0776	0.0228	0.2943
Asc. Aorta, mm	31.1 ± 3.1	26.1	35.8	28.1 ± 3.1	23.3	33.4	31.3 ± 3.8	26.7	37.7	28.9 ± 3.2	24.8	35.5	32.3 ± 3.2	28.3	37.4	30.4 ± 2.7	27.1	33.6	0.0041	<0.0001	0.5737
Asc. Aorta/BSA, mm/m^2	15.2 ± 1.5	12.8	18.1	16.2 ± 1.9	12.7	18.7	14.8 ± 2.0	12.6	17.8	15.6 ± 1.7	13.3	19.1	15.0 ± 1.9	12.8	18.3	15.7 ± 1.9	12.0	18.2	0.1932	0.0008	0.8904

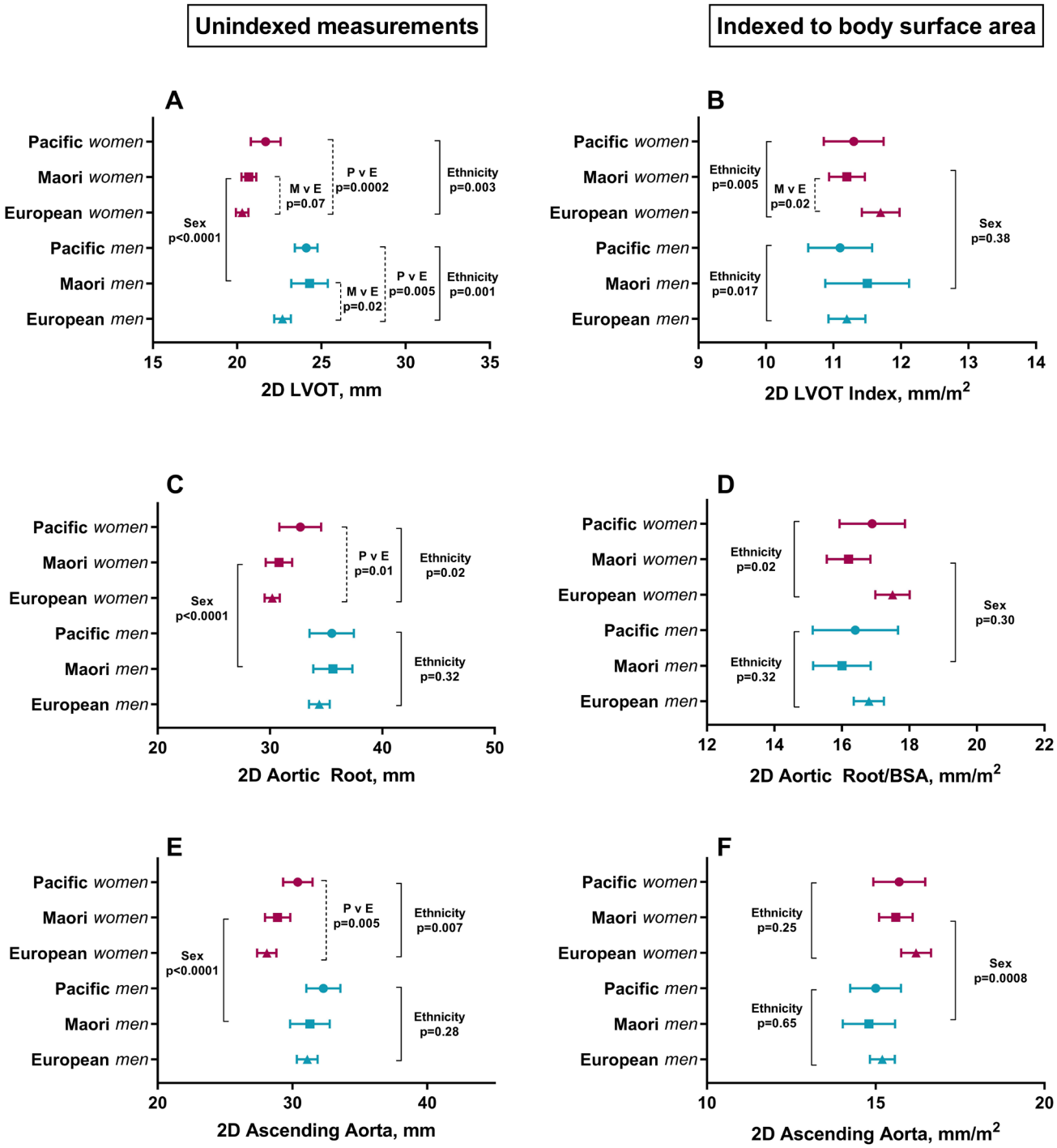
Data are mean ± standard deviation, LLN (lower limit of normal) is the 5% centile and ULN (upper limit of normal) is the 95% centile. ANOVA by ethnic groups overall (not within sex groups), sex and interaction ethnicity*sex.
Abbreviations: Asc = ascending, BSA = body surface area, IVS = interventricular septum, LVIDs = left ventricular end-diastolic dimension, LVIDs = left ventricular end-systolic dimension, LVOT = left ventricular outflow tract, STJ = sinotubular junction.

Figure 2: Left ventricular dimensions and the impact of indexation.



ANOVA for overall sex differences (solid lines); post hoc ethnicity differences within each sex group were tested using Tukey HSD (dashed lines).

Figure 3: Left ventricular outflow tract and aortic measurements and the impact of indexation.



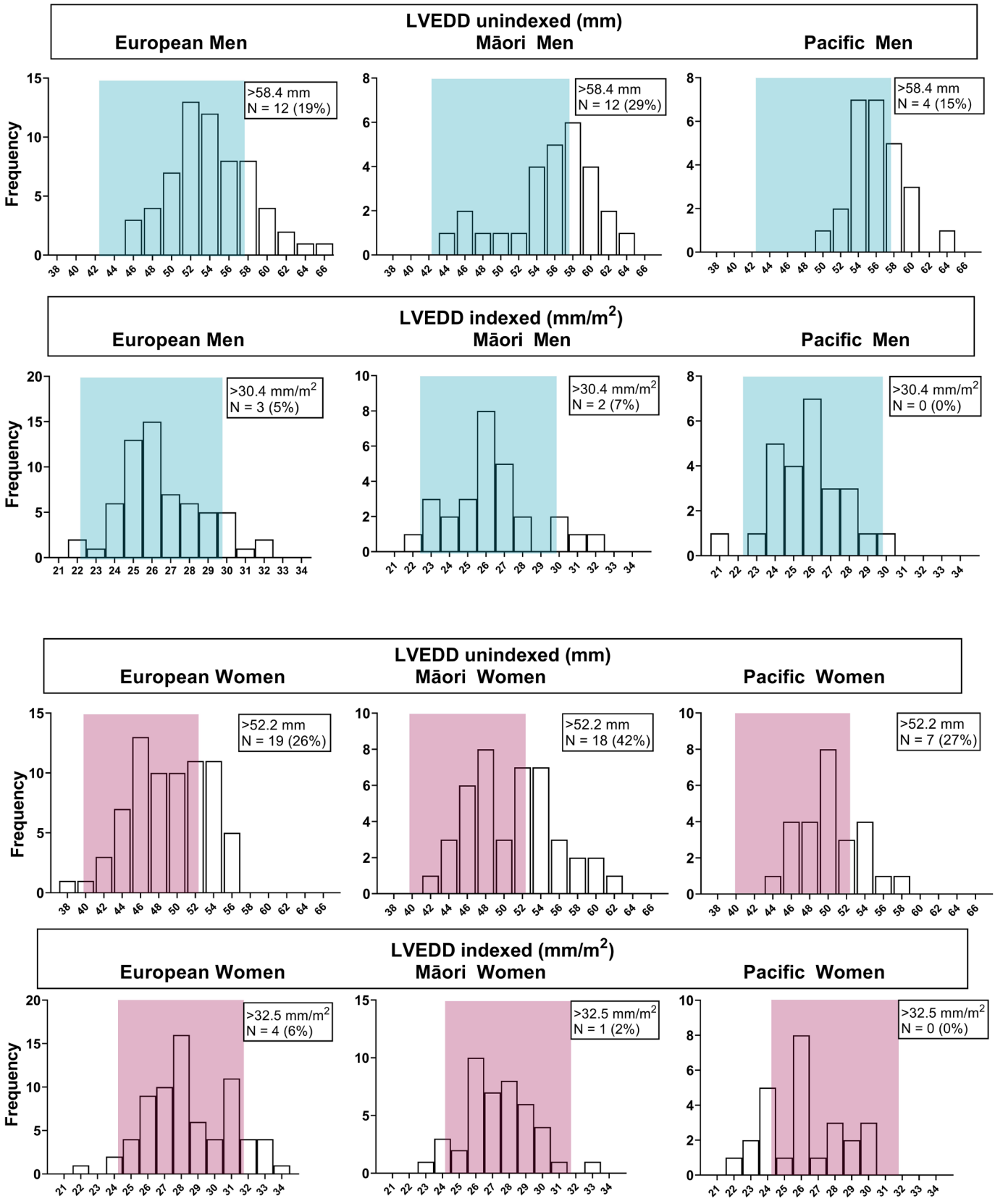
ANOVA for overall sex differences (solid lines); post hoc ethnicity differences within each sex group were tested using Tukey HSD (dashed lines).

Table 3: Comparison with other published reference values.

Echo Measurements	NewERA Reference ranges Age 18–50 European ethnicity only		ASE/EACVI Reference ranges All ages European ethnicity only[1]		EchoNoRMAL Reference ranges Age 30 years European ethnicity only[2]	
	Male	Female	Male	Female	Male	Female
	ULN	ULN	ULN	ULN	ULN	ULN
LVIDd, mm	61.8	54.8	58.4	52.2	59	53
LVIDd/BSA, mm/m^2	30.4	32.5	30	31	29	31
LVIDs, mm	41.4	36.8	39.8	34.8	42	37
LVIDs/BSA, mm/m^2	20.4	22.2	21	21	21	21
AoR, mm	39.5	34.4	40	36	na	na
AoR/BSA, mm/m^2	20.2	20.1	21	22	na	na
AscAo, mm	35.8	33.4	38	35	na	na
AscAo/BSA, mm/m^2	18.1	18.7	22	19	na	na

Data are ULN (upper limit of normal) based on the 95% centile for NewERA and EchoNoRMAL data and mean + 2 standard deviations for ASE/EACVI data. WASE used a combination of both methods.
Abbreviations: BSA = body surface area, LA = left atrium, LVIDd = left ventricular end-diastolic dimension, LVIDs = left ventricular end-systolic dimension.

Figure 4: Distribution of echo measurements compared to ASE/EACVI reference ranges.



Blue shading = ASE/EACVI reference ranges for men, pink shading = ASE/EACVI reference ranges for women.
Abbreviations: BSA = body surface area, LVEDD = left ventricular end-diastolic dimension.

in misclassification of abnormal heart size (such as with cardiomyopathy) as normal with subsequent under-treatment. This is systemic racism and puts Māori and Pacific peoples at higher risk of worse CVD outcomes but could be overcome if ethnic-specific references ranges were adopted in Aotearoa.

Globally, echocardiography is the main tool used to diagnose and monitor pathological cardiac changes, and its use will grow as the size and cost of equipment declines rapidly. However, normal echo reference ranges are yet to be determined for many ethnic groups. Given the dependence upon echocardiography, and in particular LV linear dimensions, to diagnose CVD, and guide interventions, timely and appropriate detection of abnormal heart size is paramount. Similar to other Indigenous populations, Māori and NZ Pacific peoples have the worst cardiovascular outcomes of all New Zealanders,[6,7] and are over-represented in almost every type of CVD. Further, CVD risk factors such as diabetes, hypertension and dyslipidaemia, are also more prevalent in Māori and NZ Pacific populations[7,15] as is rheumatic heart disease.[16] The results of this study indicate that the application of current normal reference indexed values, derived from mostly European individuals, is inappropriate and may lead to delayed diagnosis, especially if indexation to BSA is used.

Optimal identification of disease and provision of appropriate care requires appropriate reference ranges for each ethnic group and for both sexes. This is especially true given that many guidelines for evidence-based interventions incorporate thresholds based on echocardiographic measurements, such as those for valve replacement.[17] The impetus for the current study, was the lack of reference echocardiographic data on healthy Māori and Pacific populations. Differences in reference ranges have previously been demonstrated in other ethnicities and confirmed in the EchoNoRMAL study.[2] However, being an individual participant meta-analysis, it was limited by potentially different echo methods and analysis across the different countries. The World Alliance of Societies of Echocardiography Normal Values Study (WASE)[18] has recently reported a large international dataset (analysed centrally) to answer this question and provided more evidence that echo measurements are different between people of European ethnicity and others, especially Asian people who have smaller hearts. Unfortunately, the WASE study does not include Indigenous populations, nor any Pacific Island populations, nor indeed many populations anticipated to have different body composition than NZ Europeans.

It is likely that body composition is a key contributor to the ethnic differences in echocardiographic measurements observed in the current study and others since FFM has previously been linked to heart size.[3,4] Several studies have shown that for the same body mass index (BMI), Māori and Pacific people have a higher proportion of FFM for a given BMI than NZ Europeans of similar size.[8,19,20] Therefore, Māori and Pacific individuals could be expected to have larger hearts. However, if this is so, it is because of increased FFM, not increased BSA. Because BSA is a crude measure of body size, it is impossible to differentiate whether two people of similar BSA have the same body composition and using it as an indexing variable to minimise differences between individuals is flawed. Furthermore, a measurement that is essentially a surrogate for the surface, are of the skin that was derived initially from nine individuals over 100 years ago, and may have little relevance to modern humans. Verbraecken et al[21] have recently shown that the DuBois & DuBois BSA calculator underestimates BSA in traditionally-defined obese individuals by up to 5%, and they point out that differences in nutrition and exercise may have led to changes in body composition. However, this problem may not be limited to the DuBois & DuBois calculation. In a comparison of 25 BSA formulae an alarming discrepancy was noted such that the authors noted: *"Differences among calculations made by the formulae are so great that, in certain cases, they may considerably affect patients' mortality, especially for people with an abnormal physique or for children."*[22] To our knowledge, there have been no BSA derivation cohorts based in Aotearoa, nor indeed, any that included Māori and Pacific people who have different body composition. It is what the skin is covering that matters, and specifically how much fat free mass.

Historically, indexation to BSA was believed to remove the differences in heart size between men and women, but we now understand this not to be the case and the current guidelines provide different indexed values for men and women.[1] These differences in men and women can be explained by differences in body composition also. We believe that the difference between ethnicities can also be explained by differences in body composition. And by indexing echo measurements to

BSA, the ability to detect structural abnormalities is reduced in Māori and Pacific peoples. The differences seen in this study could also be explained by small differences in blood pressure observed between the ethnic groups in women (both systolic and diastolic) and men (diastolic only). But if the differences are linked to higher blood pressure in Māori and Pacific peoples, this provides even more compelling reason to not minimise the structural changes by dividing by BSA. It is unacceptable to apply reference ranges derived from one population to all other populations. Without appropriate reference ranges, timely and appropriate diagnosis and management is potentially compromised. In children, a different approach is used that measures the deviation from the mean (using standard deviations), and although FFM has also been shown to be the best predictor of heart size in children,[3] there is a paucity of data with regard to ethnicity and normal heart size in children and certainly none in Aotearoa.

Limitations

This study restricted the entry to adults 18–50 years because the risk of silent CVD increases with age, and careful (and potentially invasive) steps would have been needed to rule out CVD in older participants. This is an area for future research.

The results may have been influenced by the inclusion of overweight individuals. Initially we planned to exclude participants with BMI >35, but this would have excluded the majority of Pacific and some Māori participants. Therefore, a pragmatic decision was made to exclude participants with BMI >40. This also reflects the uncertainty of the use of BMI cutoffs in people of different ethnicity and different body composition, such as both the Māori and Pacific cohorts in the study, making the definition of obesity challenging. Furthermore, this population reflects a real-world cohort of healthy, younger individuals. Similarly, the results may have been influenced by physical activity, but self-reported activity was not different. Nevertheless, it would be useful to incorporate an objective measurement of physical fitness in future research to determine whether the increase in heart size seen in this cohort is linked to increased physical activity, as it has been in athletes in the past.

The study may be underpowered for some measurements and the smaller Māori and Pacific cohorts might have resulted in a failure to detect small, but clinically meaningful, differences for some variables. Nevertheless, the testing of our primary hypothesis remains robust. Furthermore, the number of observations over the age range presented is at least the same, if not greater than, reported in the WASE study.[18]

Another potential limitation is that measurements were made by one investigator (GAW), but this investigator is highly experienced and has led CORE lab analysis in several large trials. Measurements were made in random order, blinded to the participants' age, sex and ethnicity. Any measurement bias that remains applies to all three groups. We are also reassured by the similarity between our NZ European cohort reference limits and those published in the ASE/EACVI guidelines,[1] and the EchoNoRMAL Collaboration.[2]

Lastly, it is unclear what the impact of using these new ranges will impact on clinical management and outcomes: longitudinal data are needed. However, it is likely that under-recognition of pathology (by "indexing out" abnormalities using BSA) has occurred and to avoid this, indexed measurements should be used cautiously until we have longitudinal data.

Conclusion

Applying the current international echocardiography reference ranges indexed to BSA in Aotearoa will under-diagnose cardiac enlargement in some Māori and Pacific Island patients, and introduce unintentional bias that preferences the detection of pathology in NZ Europeans. In other words, the application of reference ranges developed in Caucasian to Māori and Pacific patients is an example of systemic racism. This study highlights the need for ethnic-specific normal ranges and highlights the unintended consequences that arise from using a one-size approach derived from European cohorts in different ethnic groups. Whilst it may seem ideal to index measurements to a measure of body size to enable comparison across people of different sizes, this study clearly shows there is potential for delayed diagnosis if ethnic-specific reference ranges are not used and applied. Ultimately, these new reference ranges need to be prospectively linked to clinical outcomes, but it's intuitive that if clinicians are following clinical guidelines that include linear echo measurements, and are making judgements about pathology based on international reference ranges derived from Europeans, misclassification is likely in Māori and Pacific peoples.

COMPETING INTERESTS

Nil.

ACKNOWLEDGEMENTS

This study was funded by a Health Research Council of New Zealand Research Partnerships for New Zealand Health Delivery grant (grant number 14/718).

AUTHOR INFORMATION

Gillian A Whalley: Department of Medicine and HeartOtago, Otago School of Medicine, The University of Otago, Dunedin, New Zealand; Unitec Institute of Technology, Auckland, New Zealand.

Allanah Harrington: Unitec Institute of Technology, Auckland, New Zealand; Dunedin Hospital, Southern District Health Board, Dunedin, New Zealand.

Jonathan Christiansen: Waitematā District Health Board, Auckland, New Zealand.

Bettina Ikenasio: Unitec Institute of Technology, Auckland, New Zealand.

Arun Deo: Unitec Institute of Technology, Auckland, New Zealand.

Greg D Gamble: Department of Medicinse, The University of Auckland, Auckland, New Zealand.

Sue Crengle: Department of Preventive and Social Medicine, Otago School of Medicine, The University of Otago, Dunedin, New Zealand.

CORRESPONDING AUTHOR

Professor Gillian A Whalley: Department of Medicine, Otago Medical School, University of Otago, PO Box 56 Dunedin 9054. 021306059. gillian.whalley@otago.ac.nz

URL

www.nzma.org.nz/journal-articles/new-echocardiography-reference-ranges-for-aotearoa-newera-study-the-application-of-international-echocardiographic-reference-values-to-linear-measurements-of-the-hearts-of-healthy-young-maori-and-pacific-adults-may-not-detect-cardiac-enlargement

REFERENCES

1. Lang RM, Badano LP, Mor-Avi V, et al. Recommendations for cardiac chamber quantification by echocardiography in adults: An update from the American society of echocardiography and the European association of cardiovascular imaging. Eur Heart J Cardiovasc Imaging. 2015;16(3):233-71.
2. The EchoNoRMAL Collaboration. Ethnic-specific normative reference values for echocardiographic LA and LV Size, LV Mass, and systolic function: The EchoNoRMAL study. JACC Cardiovasc Imaging. 2015;8(6):656-65.
3. Daniels SR, Kimball TR, Morrison JA, et al. Effect of lean body mass, fat mass, blood pressure, and sexual maturation on left ventricular mass in children and adolescents: Statistical, biological, and clinical significance. Circulation. 1995;92(11):3249-54.
4. Whalley GA, Gamble GD, Doughty RN, et al. Left ventricular mass correlates with fat-free mass but not fat mass in adults. J Hypertens. 1999;17(4):569-74.
5. Hull HR, Thornton J, Wang J, et al. Fat-free mass index: Changes and race/ethnic differences in adulthood. Int J Obes. 2011;35(1):121-7.
6. Chan WC, Wright C, Riddell T, et al. Ethnic and socioeconomic disparities in the prevalence of cardiovascular disease in New Zealand. N Z Med J. 2008;121(1285):11-20.
7. Sundborn G, Metcalf PA, Gentles D, et al. Ethnic differences in cardiovascular disease risk factors and diabetes status for Pacific ethnic groups and Europeans in the Diabetes Heart and Health Survey (DHAH) 2002-2003, Auckland New Zealand. N Z Med J. 2008;121(1281):28-39.
8. Rush EC, Freitas I, Plank LD. Body size, body composition and fat distribution: comparative analysis of European, Maori, Pacific Island and Asian Indian adults. Br J Nutr. 2009;102(04):632-41.
9. Whalley GA, Pitama S, Troughton RW, et al. Higher prevalence of left ventricular hypertrophy in two Māori cohorts: Findings from the Hauora Manawa/ Community Heart Study. Aust N Z J Public Health. 2015;39(1):26-31.
10. Du Bois, D. and Du Bois EF. A Formula to Estimate the Approximate Surface Area if Height and Weight Be Known. Arch Intern Med. 1916;17(6):863-71.
11. von Elm E, Altman DG, Egger M, et al. The strengthening the reporting of observational studies in epidemiology (STROBE) statement: Guidelines for reporting observational studies. Int J Surg. 2014;12(12):1495-9.
12. Ministry of Health, Health Information Standards Organisation. HISO 10001:2017 Ethnicity Data Protocols. Wellington; 2017.
13. Choi JO, Shin MS, Kim MJ, et al. Normal echocardiographic measurements in a Korean population study: Part I. cardiac chamber and great artery evaluation. J Cardiovasc Ultrasound. 2015;23(3):158-72.
14. Qureshi WT, Leigh JA, Swett K, et al. Comparison of echocardiographic measures in a hispanic/ latino population with the 2005 and 2015 American society of echocardiography reference limits (The Echocardiographic Study of Latinos). Circ Cardiovasc Imaging. 2016;9(1):1-8.
15. McDonald-Sundborn G, Metcalf P, Scragg R,

et al. Ethnic differences in the prevalence of new and known diabetes mellitus, impaired glucose tolerance, and impaired fasting glucose. Diabetes Heart and Health Survey (DHAH) 2002-2003, Auckland New Zealand. N Z Med J. 2007;120(1257):1-12.
16. Wilson N. Rheumatic Heart Disease in Indigenous Populations—New Zealand Experience. Hear Lung Circ. 2010;19(5–6):282-8.
17. Falk V, Baumgartner H, Bax JJ, et al. 2017 ESC/EACTS Guidelines for the management of valvular heart disease. Eur J Cardio-Thoracic Surg. 2017;52(4):616-64.
18. Asch FM, Miyoshi T, Addetia K, et al. Similarities and Differences in Left Ventricular Size and Function among Races and Nationalities: Results of the World Alliance Societies of Echocardiography Normal Values Study. J Am Soc Echocardiogr. 2019 Nov 1;32(11):1396-1406.e2.
19. Swinburn B, Ley S, Carmichael H, Plank L. Body size and composition in Polynesians. Int J Obes. 1999 Nov 11;23(11):1178-83.
20. Rush E, Plank L, Chandu V, et al. Body size, body composition, and fat distribution: A comparison of young New Zealand men of European, Pacific Island, and Asian Indian ethnicities. N Z Med J. 2004;117(1207):1-8.
21. Verbraecken J, Van De Heyning P, De Backer W, Van Gaal L. Body surface area in normal-weight, overweight, and obese adults. A comparison study. Metabolism. 2006;55(4):515-24.
22. Redlarski G, Palkowski A, Krawczuk M. Body surface area formulae: An alarming ambiguity. Sci Rep. 2016;6.

District health board engagement with the living wage movement: evidence from official information requests

Julie Douglas, Heather Came, Leah Bain and Grant Berghan

ABSTRACT

From a public health perspective, there is strong evidence that income is a major modifiable determinant of health. District health boards (DHBs), who were responsible for providing and/or funding regional health services across Aotearoa, are major employers. International literature suggests implementing a living wage strategy can improve health outcomes, contribute until July 2022 to the reduction of ethnic health inequities, and is ethical and socially responsible business practice.

In February 2021, official information requests were sent to all DHBs to determine engagement with the living wage movement. This was augmented through a content analysis of publicly available collective employment contracts to benchmark practice.

The review found no DHBs were registered living wage employers, nor is it a requirement of those whom they sub-contract. Two out of twenty DHBs are planning to become living wage employers, and several confirmed they were working collectively to improve working conditions of lower paid workers.

This paper makes a scholarly argument for DHBs to commit to becoming living wage employers. As significant regional employers this is an opportunity for DHBs to positively contribute to the alleviation of entrenched poverty a modifiable determinant of ethnic health inequities.

Living Wage Aotearoa (LWA) is part of the global living wage movement, ensuring workers can afford the necessities of life and can actively participate in communities.[1] LWA was launched in 2012 by 200 unions and community groups working across a bipartisan coalition.[2] They advocated for a living wage that covers food, shelter, utilities, transport, healthcare, childcare, and a small buffer for unforeseen events. The calculation assumes two adults working for 60 hours per week in total, with two children. The living wage is calculated each year by the New Zealand Family Centre Social Policy Unit, and the living wage hourly rate for 2021/22 is $23.65.[2] The median hourly rate in 2020 for all full-time employees was $27.00, but Māori and Pacific median rates were significantly lower at $24.98 and $24.00, respectively.[3]

LWA initially prioritised campaigning for the living wage within the local government sector. They argued that public money should not be used to entrench hardship and inequity in society.[4] Campaigns have been run in Britain where procurement, tendering practices for catering and cleaning jobs, and collective bargaining within public institutions have resulted in the successful introduction of a living wage to low paid public sector workers.[5]

Employers can obtain formal accreditation with LWA if they meet criteria focused on the terms and conditions of directly and indirectly employed workers. Within Aotearoa, more than a hundred private and public employers have committed to the programme (LWA, 2020). District health boards (DHBs) are of strategic importance in terms of the living wage movement, as they were major regional employers and they, often through their sheer size and the unionisation of their workforce, set the standard in regional employment conditions. Uptake by major health employers could encourage other employers to match this minimum benchmark.

The international literature provides a range of evidence to support employers becoming living wage employers. Much of the living wage work is voluntarily led by union activists, and so remains largely unevaluated with gaps in the evidence base. Research shows that health gain is likely from lifting household income, and that paying a living wage could contribute to reduced

ethnic inequities. Likewise, engagement with the living wage movement is a practical organisational demonstration of a commitment to ethical and socially responsible business practices. These are explored below.

Income is a key modifiable determinant of health[6] which is a universal right.[7] A World Health Organization survey found people in the poorest socio-economic status quintile were twice as likely to experience poor health than those in the wealthiest.[8] Eliminating poverty, by implementing a living wage policy alongside other system-wide initiatives, remains an important public health strategy to address health inequities.[9]

Some studies have captured specific health gains from the introduction of living wage initiatives. For example, Landefeld, Burmaster et al[10] found improvements in social status and self-rated health with particular improvements for women.

Decades of inaction on health equity in Aotearoa have meant limited improvement in Māori health outcomes despite targeted yet ultimately ineffective legislative and policy imperatives.[11] Systemic policy and practice failure[12] have heightened persistent ethnic socio-economic disparities.[13] Since Māori are over-represented in the lowest wage brackets, a living wage initiative could contribute to lifting Māori households out of poverty within the context of wider concerted action around addressing other critical determinants of health and the enduring legacies of colonisation.

Littman[14] has demonstrated that living wage-based procurement policies can impact positively for some of the lowest paid workers. Uptake across the public sector, could therefore make a significant long-term contribution to addressing health inequities. As DHBs are major regional employers, this is likely to provide concrete local benefits within their respective districts. This would also, in the long term, reduce demand on public health services as disease and consequences of poverty are reduced.

In recent years, businesses have become increasingly interested in ethical business practices and corporate social responsibility.[15] Becoming a living wage employer is one tangible way to demonstrate this social commitment. Proven benefits from such moves include reduced staff turnover and absenteeism, alongside productivity improvements, strengthened recruitment and organisational reputation.[4,16] Haar[15] found that organisational trust improved even if individual worker's salaries were not raised, and also that employees' attitudes and behaviours improved.

Accredited living wage employers are required to allow unionisation and collective processes, which further develop social integration and citizenship. These actions and consequences can deliver improved economic outcomes for the organisation offsetting the upfront wage cost.[17] However, it is also noted that human resource practices, including wage-setting, are often applied differentially. This results in some groups receiving socially responsible human resource management, while others experience socially irresponsible approaches, resulting in entrenched inequalities and the creation of deliberate in-work poverty.[18]

The health sector is currently being restructured and reimagined.[19] DHBs were dis-established and then recreated with the bulk of their funding and health delivery functions fulfilled by new entities. The Waitangi Tribunal[12] WAI 2575 health sector report directed the Crown and the health sector to urgently address systemic ethnic health inequities. The adoption of the living wage as a minimum requirement in any new entities could be an effective contribution to alleviating these inequities.

This paper makes the case for major health employers to become living wage employers. It then presents primary data examining to what extent DHBs engaged with the living wage campaign.

Method

Data for this article were collected through a narrative review of academic and grey literature, official information requests to DHBs and a content analysis of publicly available collective employment agreements. No organisational ethics approval was required for this study.

The Māori and Pākehā authors have all been union members and/or union delegates, with three having a professional background in public health and one in management studies.

At the time of writing there were twenty DHBs providing health services to their respective populations. We sent official information requests to DHB chief executives in February 2021, asking:

Ultimately, we got a 100% response rate from the DHBs but had to lodge a complaint with the ombudsman for initial non-compliance with one request. The content analysis of DHB collective employment contracts was to review the contracts' alignment with living wage salary benchmarks.

1. Is your DHB currently a registered living wage employer?
   If yes, what factors influenced that decision?
2. Are your contractors/sub-contractors currently living wage employers?
   Do you require them to be?
3. Does your DHB currently have plans to become a living wage employer?
   If so, can you describe how far you have progressed?
4. What do you see as the obstacles to becoming a living wage employer?

Findings

We undertook content analysis of the collective agreements between the DHBs and the Public Service Association (PSA) and E Tū, as major health sector unions covering lower-paid workers. The current multi-employer collective agreements covering clerical and administrative jobs (covered by the PSA) all had pay scales which were above the living wage. However, the collective agreements struck between E Tū and the DHBs continue to have pay scales below the living wage. The nature of the jobs at such levels includes orderlies, attendants, cleaners, laundry, kitchen hands, carpenters, painters, gardeners, stores and drivers, trade assistants and driving services. It is unclear how many workers are paid on the scales below the living wage.

Of the 20 DHBs, none were accredited living wage employers, and none required their contractors and sub-contractors to pay the living wage. Several noted they required procurement contracts to comply with current legislation which references the Minimum Wage Act 1983. One noted that staff of large on-site contracts are paid the living wage or better.

Seventeen of the DHBs had no plans to become living wage employers. One DHB reported that only 1.93% of their workforce were earning below the living wage in their base salaries, prior to allowances and penal rates which were routinely paid. Others noted that one group of employees had been moved to the living wage, and they were awaiting the outcome of a national pay equity claim, focused on historically underpaid workers from female-dominated professions, before taking further action. One shared they were supporting their workers to attain qualifications that would enable progression to higher levels of remuneration.

In response to questions about obstacles to become a living wage employer, most DHBs noted they were working with multi-employer and single employer collective employment agreements which were subject to robust collective bargaining processes. Many DHBs repeated the statement that *"any discussions about the living wage would progress in line with government expectations and through national discussion with health sector unions"*.

Some noted that once 2021 negotiations were completed, they expected minimum rates in most collectives to be close to or above the living wage. This was part of a commitment by all DHBs to improve the low wage conditions of their employees, which for most didn't require naming it as a living wage.

There were three DHBs that were moving toward becoming living wage employers. One had made the commitment as part of a strategy to reduce the gap between the lowest and highest incomes. By the end of 2021 they expect to have fewer than 2% of staff being paid under the living wage. The other had formally endorsed movement to the living wage for all current staff through collective agreements as part of a wider equity framework and state sector pay expectations.

Another DHB stated they were undertaking further analysis before deciding whether to proceed with the living wage.

Discussion

Neoliberalism, as embraced by political leaders in Aotearoa in 1980s and 1990s, is based on the notion that the market is the most efficient mechanism for determining the worth of something or someone.[20,21] This entails belief that society is a meritocracy, where character and tenacity combined with hard work brings success. It includes the assumption that society is a level playing field with everyone having fair chances to thrive.[22] Giroux[23] argues this phenomenon is a kind of collective denial of history and structural discrimination.

The passing of the Employment Contracts Act 1991 saw the transformation of employment relations. This legislation undermined collective bargaining, resulting in fewer multi-employer collective agreements, lowered union membership and reduced penal rates[24] meaning real reductions in earnings.

Seeing the rapid increase in inequities across New Zealand society, current political leaders have distanced themselves from these policies,[25]

but the legacy of decades of unrelenting hardship and massive wealth inequities remains. DHBs were imagined at the height of neoliberalism as a mechanism to contain health spending and with an imperative to run as effective businesses.[26] Presumably these imperatives made it difficult to prioritise ethnic pay parity. Research shows that the ethnic pay disparities remain entrenched[27] with fewer than 2.7% of Māori staff earning salaries over $100,000.

A living wage raises workers out of in-work poverty, enhances individual dignity and may avoid reliance on charity. Increased household income lifts all its members to a better standard of living, reducing poverty-related health issues, improving educational achievement, reducing deprivation, and enabling inclusion and citizenship.[28]

The living wage requires employers to pay an evidence-based fair wage rather than the lowest legal possibility, and the current minimum wage does not support human flourishing. The purpose of the minimum wage was not to reduce poverty on its own[28] relying instead on other government transfers (i.e., accommodation, health, and education) to support low-income families. Given the antipathy of sections of society fuelled by the media towards government top-ups and low-wage workers the minimum wage contravenes notions of decent work and a just society.[29]

Most of the DHBs in their responses are reluctant to take any initiative on their own sites and are followers of "government expectations". This passive position by most DHBs appears to contradict their own Employment Relations Strategy 2019–2024 document which states the DHBs are committed to "lifting the pay of the low-paid workforce" and importantly, "reducing poverty and inequalities by leveraging our employment footprint".[30] The DHBs' reference to collective agreements suggests they are unable to change the wage structures. The two main unions on sites at DHBs for non-medical employees, E Tū and the Public Service Association, both have a position on always presenting a living wage claim in bargaining.

Employers retain control over what step new employees begin on and could appoint above or at the living wage and in effect make lower rates functionally obsolete. While data on the actual number of employees on wages lower than the living wage were not collected, even small percentages represent individuals and families impacted by low incomes and too often in-work poverty. In a large workforce this can be a lot of employees.

Conclusion

The literature is very clear that the benefits of paying adequate wages to lift workers and their families out of poverty results in improvements for organisations through stronger commitment, self-esteem, productivity, and a reduction in absenteeism. As publicly funded health institutions DHBs are obliged to concern themselves with health outcomes within their region. Article three of Te Tiriti o Waitangi further emphasises the importance of equity.

Uptake of living wage accreditation within the health sector remains low behind other sectors within Aotearoa. If all major health employers paid living wages and became accredited living wage employers, they could be positive role models for other health sector employers and clearly demonstrate their commitment to best business practice. This accreditation would also provide security for employees, since their wages would be protected, and ongoing union involvement guaranteed.

The pending restructuring of the health sector signals an opportunity for the lowest wages in the sector to be reviewed. The variation across health providers may be moderated to contribute to the goal of reducing poverty and inequality to be realised. This is an opportunity for significant change in the thinking and practices of our health institutions, both in health delivery and in addressing the underlying issue that poor pay is inextricably linked with negative health outcomes.

COMPETING INTERESTS
Nil.

ACKNOWLEDGMENTS
Thanks to the health care and allied workers that have kept our health system running during a global pandemic.

AUTHOR INFORMATION
Julie Douglas: Senior lecturer, Auckland University of Technology, Private Bag 920006, Auckland 1142.
Heather Came: Associate Professor, Auckland University of Technology, Private Bag 920006, Auckland 1142.
Leah Bain: Policy Analyst, New Zealand Public Health Association, P O Box 11-243, Manners Street, Wellington 6142.
Grant Berghan: Chief Executive Officer, New Zealand Public Health Association, P O Box 11-243, Manners Street, Wellington 6142.

CORRESPONDING AUTHOR
Heather Came: Associate Professor, Auckland University of Technology, Private Bag 920006, Auckland 1142. heather.came@aut.ac.nz

URL
www.nzma.org.nz/journal-articles/district-health-board-engagement-with-the-living-wage-movement-evidence-from-official-information-requests

REFERENCES
1. Living Wage Aotearoa. Living wage 2020 [Available from: https://www.livingwage.org.nz/
2. Living Wage.(n.d) About. https://www.livingwage.org.nz/about
3. Statistics New Zealand. Earnings from wage and salary jobs by sex, age groups, ethnic groups, and full-time and part-time status 2021 [Available from: https://www.stats.govt.nz/information-releases/labour-market-statistics-income-june-2020-quarter.
4. Luce S. Living wages: A US perspective. Employee Relations. 2017;39(6):863-74.
5. Hirsch D. The 'living wage' and low income: Can adequate pay contribute to adequate family living standards? Critical Social Policy. 2018;38(2):367-86.
6. Lynch J, Smith G, Harper S, Hillemeir M, Ross N, Kaplan G, et al. Is Income inequality a determinant of population health? Part 1. A systematic review. The Milbank Quarterly. 2004;82(1):5-99.
7. United Nations. Universal Declaration of Human Rights. Geneva, Switzerland: Author; 1948 10 December.
8. Hosseinpoor AR, Stewart Williams, J.A., Itani, L., Chatterji, S. Socioeconomic inequality in domains of health: Results from the world health surveys. BMC Public Health. 2012;12(198).
9. Wilkinson R. Income distribution and life expectancy. British Medical Journal. 1996;304(6820):165-8.
10. Landefeld JC, Burmaster KB, Rehkopf DH, Syme SL, Lahiff M, Adler-Milstein S, et al. The association between a living wage and subjective social status and self-rated health: A quasi-experimental study in the Dominican Republic. Social Science & Medicine. 2014;121:91-7.
11. Came H, McCreanor T, Manson L, Nuku K. Upholding Te Tiriti: Ending institutional racism and Crown inaction on health equity. New Zealand Medical Journal. 2019;132(1492):62-6.
12. Waitangi Tribunal. Hauora report on stage one of the health services and outcomes inquiry: WAI 2575 Wellington, New Zealand: Author; 2019.
13. Ministry of Business Innovation and Employment. Māori in the labour market: June 2020 quarter (unadjusted) Wellington, New Zealand: Ministry of Business Innovation and Employment; 2020.
14. Littman D. The living wage: An idea whose time has come. New Zealand Journal of Employment Relations. 2014;151(3):70-7.
15. Haar J. Living wage employer status and job attitudes and behaviours. New Zealand Journal of Employment Relations. 2019;44(3):45-57.
16. Coulson A, Bonner J. Living wage employers: Evidence of UK business cases. London, England: Living Wage Foundation; 2015.
17. Maloney T, Gilbertson A. A literature review on the effects of living wage policies. Auckland: Auckland Council; 2013.
18. Richards J, Sang K. Socially irresponsible human resource management? Conceptualising HRM practice and philosophy in relation to in-work poverty in the UK. International Journal of Human Resource Management. 2021;32(10):2185-212.
19. Health and Disability System Review. Health and disability system review – Final report – Pūrongo Whakamutunga. Wellington, New Zealand: Author; 2020.
20. Kelsey, J. (1996). Life in the economic test-tube: New Zealand "experiment" a colossal failure. Radical Journal of Organization Theory, 2(1), 1-5.
21. Labonté, R., & Stuckler, D. (2016). The rise of neoliberalism: how bad economics imperils health and what to do about it. J Epidemiol Community Health, 70(3), 312-318. doi:10.1136/jech-2015-206295
22. McCreanor T. Challenging and countering anti-Maori discourse: Practices for decolonisation. New Zealand Psychological Society Conference; August;

Palmerston North, New Zealand 2009.
23. Giroux H. Spectacles of race and pedagogies of denial: Anti-black racist pedagogy under the reign of neoliberalism. Communication Education. 2003;52(3/4):191-211.
24. Rasmussen EJ. Employment relations in New Zealand. Auckland, New Zealand: Pearson; 2009.
25. Cooke H. Jacinda Arden says neoliberalism has failed. Radio New Zealand. Wellington, New Zealand, 12 Sept 2017.
26. Skegg, D. The health of the people. Wellington, New Zealand: Bridget Williams Books. 2019.
27. Came, H, Badu, E., Ioane, J, Manson, L, & McCreanor, T. (2020). Ethnic pay (dis)parities in the public sector leadership from 2001-2016 in Aotearoa New Zealand. International Journal of Critical Indigenous Studies, 13(1), 70-85.
28. Newman A. Precarious work and a living wage in our communities. New Zealand Journal of Employment Relations. 2014;38(2):64-9.
29. New Zealand Treasury. Living wage information release: New Zealand Government; 2013.
30. Edmonds, S. (2022). 'Kick in the guts for businesses': Minimum wage to rise to $21.20 https://www.stuff.co.nz/business/300515349/kick-in-the-guts-for-businesses-minimum-wage-to-rise-to-2120
31. Central Region Technical Advisory Services Limited. 20 DHB employment relations strategy 2019-2024 Wellington, New Zealand 2019.

Diabetes mellitus prevalence in Northland New Zealand schizophrenia patients on clozapine

Nicole M McGrath, Verity Humberstone, Ashley C Abraham

ABSTRACT

AIMS: Clozapine is a unique atypical anti-psychotic agent with best efficacy for treatment resistant schizophrenia compared to other agents, but with increased metabolic adverse effects. We sought to audit the prevalence of diabetes and pre-diabetes in Northland, New Zealand patients on clozapine.

METHOD: We captured all 287 patients in Northland, New Zealand who were prescribed clozapine in September 2021 and obtained demographic, clinical and laboratory data.

RESULTS: We discovered that 26.48% had diabetes (one patient type one, 75 type two diabetes) and 14.63% had pre-diabetes that developed after a median of six years' clozapine treatment. Diabetes prevalence is approximately 6% in the general population. NZ Māori made up 65.85% of the entire cohort (35.8% of the general population) and 85.53% of the diabetes patients. NZ Europeans represented most of the remaining 30.66% on clozapine, consistent with the largely bicultural ethnic mix of our region. Māori on clozapine were younger: mean age 42 years, compared to NZ Europeans, mean age 49 years. The average BMI was 37kg/m2 for Māori, 32 for Europeans (range 21–63, SD 8); there was a moderate relationship between clozapine use and increasing BMI (correlation coefficient of 0.74). For the diabetes patients, glycaemic control was overall suboptimal with a mean Hba1c of 66mmol/mol (range 41–117).

CONCLUSIONS: Culturally appropriate, flexible and accessible services which integrate both the mental and physical health needs of Northland, New Zealand people with treatment-resistant schizophrenia on clozapine are required to reduce the 41% rate of dysglycaemia in this predominantly Māori group.

Insulin resistance of unknown mechanism was first reported in patients with schizophrenia 55 years ago.[1] Modern atypical antipsychotics further increase the risk of diabetes through multiple mechanisms, but principally weight gain via central actions causing changes to leptin, adiponectin and ghrelin levels, and peripheral inhibition of glucose transport.[2,3] Clozapine and olanzapine are the atypical antipsychotics with the highest risk of causing diabetes.[4] Clozapine is unique in that it has superior efficacy for treatment resistant schizophrenia (failure to respond to at least two antipsychotic medications over at least six weeks each), and it is the only antipsychotic associated with decreased risk of attempted and completed suicide.[5] Meta-analysis shows lower long-term all-cause mortality compared with other antipsychotics, despite increased metabolic syndrome.[6] Furthermore, all patients on clozapine require long-term monthly lab tests to check for the rare, but potentially fatal, idiosyncratic side effect of neutropenia.[7] In New Zealand, a database is maintained to ensure all patients are monitored; therefore, all patients on clozapine in our region, Northland, New Zealand, are captured. As well as monthly full blood count, the recommendation is that patients on clozapine are screened for diabetes with HbA1c at baseline, three and six months after commencement of clozapine and then yearly.

Methods

We evaluated all Northland, New Zealand patients receiving clozapine in September 2021. We used the clozapine database that is an accurate record of all patients prescribed clozapine in our region, hospital and general practice records to obtain demographic data, including age, sex, ethnicity, duration of treatment; when available body mass index (BMI) and change of BMI using the formula BMI=kg/m2, where kg is a person's weight in kilograms, and m2 is their height in meters squared; co-administration of other antipsychotics; HbA1c results close to commencement of clozapine and most recent HbA1c. In New Zealand, diabetes is diagnosed with HbA1c of 50mmol/mol or greater on two occasions unless

symptomatic: pre-diabetes HbA1c 41–49 mmol/mol. The data analysis was performed in the R programming software. Results are reported as mean (range; standard deviation). Analysis of variance (ANOVA) and Pearson correlation coefficient was used to compare between two or more groups for any quantitative data.

Results

Two hundred and eighty-seven Northland patients with schizophrenia were prescribed clozapine at the time of the audit. Sixty-five point eight five percent were NZ Māori (Māori make up 35.8% of general Northland population), and 30.66% NZ European (NZE); 66.89% were male. Māori were younger—mean age 42 years (range 19–74; standard deviation (SD) 12)—compared to NZ Europeans—mean age 49 years (range 17-82; SD 15). Only 5.23% of the cohort had not obtained an HbA1c within the preceding two years. The majority of tests were requested by hospital mental health providers rather than through primary care.

The average current HbA1c of the entire cohort was 45mmol/mol (range 27–117, SD 17); in Māori the average current HbA1c was 48, in NZE 40mmol/mol (Figure 1).

The average HbA1c remained higher for females in the ethnicity group compared to males (Table 1, Figure 2).

Twenty-six point four eight percent of the cohort had diabetes: one patient had type one diabetes diagnosed before commencement of clozapine and 75 type two diabetes; an additional 42 patients (14.63 %) had pre-diabetes. In Northland's general population, approximately 6% have known diabetes.

Of the 118 patients with dysglycaemia, 19 (16.10 %) had diabetes or pre-diabetes at the time of commencement of clozapine; all those with pre-clozapine diabetes had a confirmed diagnosis. For the remaining 99 patients, diabetes/pre-diabetes was diagnosed 1–26 years after starting treatment (median six years; only six patients within the first year). For those with diabetes, 85.53% were Māori; control was overall suboptimal with a mean Hba1c of 66mmol/mol (range 41–117).

BMI data was available for 92% patients with diabetes/pre-diabetes. The average BMI was 37kg/m2 for Māori compared to 32kg/m2 in NZ Europeans (range 21–63, SD 8) (Figure 3).

There was a moderate relationship between clozapine use and increasing BMI (Pearson's correlation coefficient of 0.74); however, further studies are needed to establish a consistent relation between increase in BMI with clozapine for the Northland population.

Forty point four two percent of the entire cohort were co-prescribed an additional antipsychotic agent. Limitations in analysis did not determine

Figure 1: The box plot representing the HbA1c results in relation to each ethnicity. The dashed line represent the average HbA1c results of the entire sample (n =287).

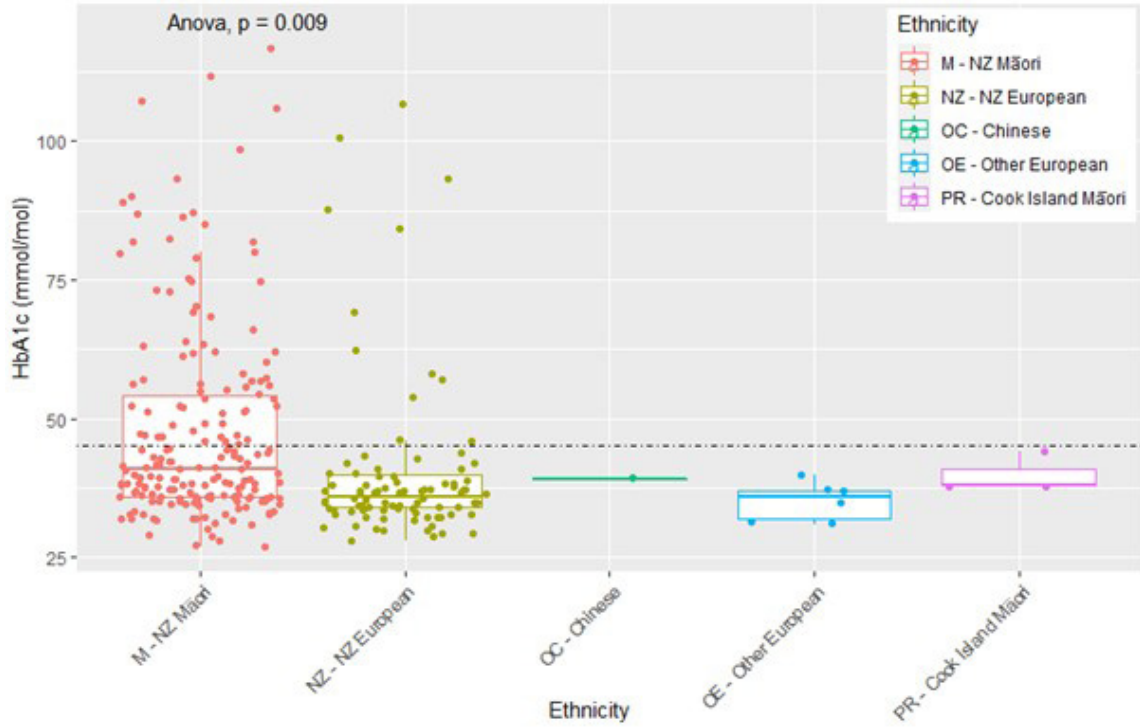


Table 1: Descriptive statistics of HbA1c results based on gender between Māori and NZ European.

Ethnicity	Average	Max	Min	Standard deviation	P value
NZ Māori	48	117	27	18	0.00027
F	50	117	27	21	0.021
M	47	106	28	16	0.0022
NZ European	40	107	28	15	0.00027
F	42	93	29	15	0.021
M	39	107	28	15	0.0022

Figure 2: Average HbA1c in relation to each ethnicity based on gender.

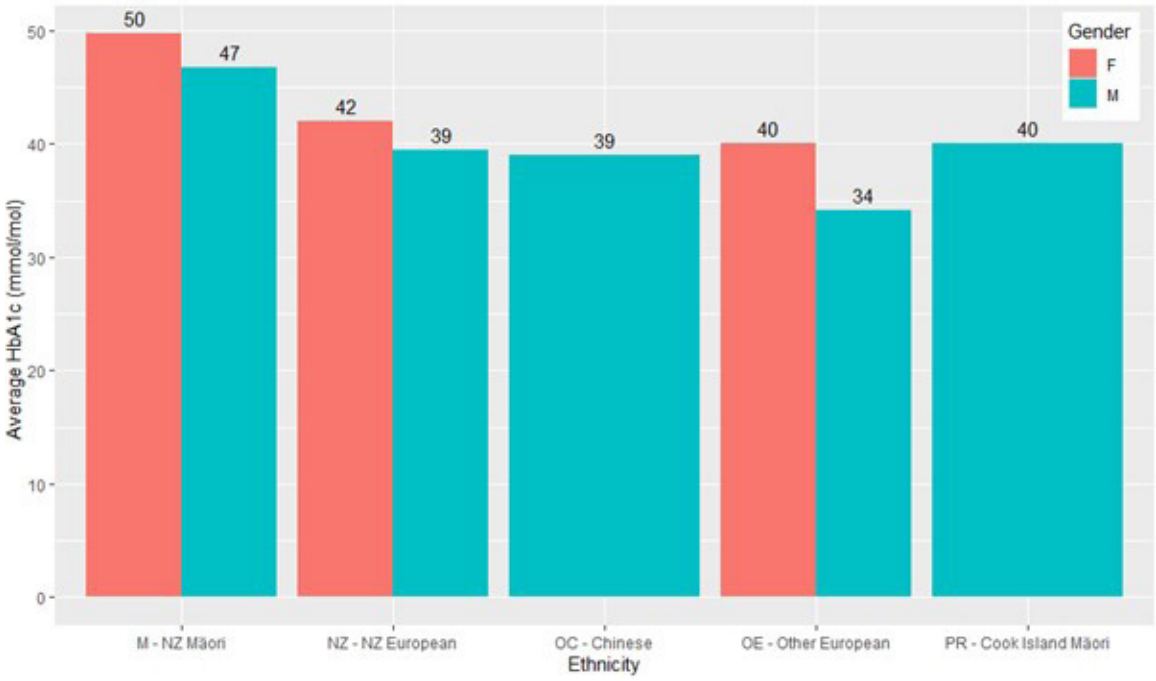
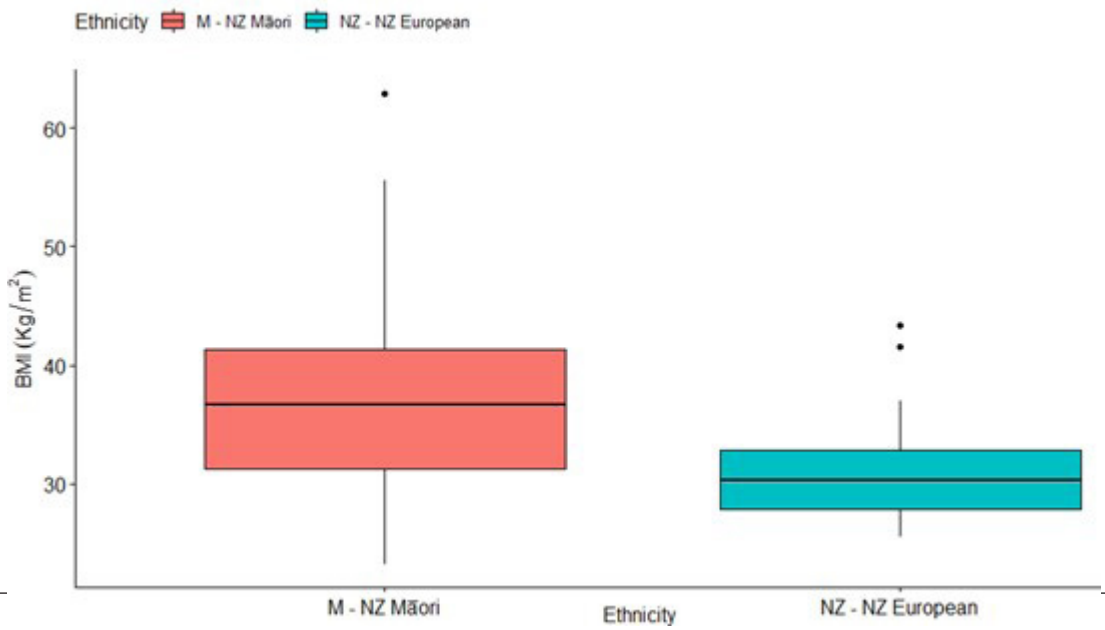


Figure 3: The box plot representing BMI between Māori and NZ Europeans.



whether the antipsychotic polypharmacy was as part of a time limited strategy or a maintenance regime. Of concern for 23 patients, olanzapine was prescribed with clozapine. Olanzapine has a high rate of weight gain and increased risk of diabetes. Of the patients prescribed both olanzapine and clozapine, four had diabetes, five pre-diabetes which was not an increased risk for dysglycaemia compared to the whole cohort.

Discussion

Forty-one percent of Northland schizophrenia patients on clozapine have either diabetes or pre-diabetes. The majority have type two diabetes, are obese and have poor glycaemic control. Māori are vastly over-represented and develop diabetes at a younger age than NZ Europeans. Given these results, the choice of clozapine does not appear to be influenced by pre-existing metabolic status, but rather on psychiatric indications. Our results are similar to a 21-year American study of 96 patients that showed a 43% rate of diabetes particularly in Hispanic and African Americans on clozapine.[8]

There are challenges to ensuring appropriate physical healthcare for patients with severe schizophrenia. Persistent psychotic symptoms can impact on the ability of patients to trust and engage with healthcare providers. The symptoms can also have an impact on the ability of the patients to engage with healthy lifestyle advice, or follow treatment plans involving adherence to complex medication regimes or monitoring blood glucose levels at home.

Working with primary care to try and ensure all patients on clozapine have a general practitioner is imperative. Unfortunately, a significant number of patients prescribed clozapine either are not enrolled in primary care or have not seen a general practitioner for over one year. Currently a pilot project is occurring with a community support worker attached to Te Roopu Whitiora, Māori mental health team Whangārei to try and practically help people with severe mental illness enrol and attend primary care and other specialists' reviews. Health improvement practitioners are attached to some primary care practices, and have a very broad brief involving health and wellbeing when a general practitioner wants additional support for a patient with mental health concerns. These could be an avenue to improve outcomes for people on clozapine who are engaged with primary care.

Northland nationally has a high proportion of people who are classified as being in the most deprived economic conditions. This directly impacts on access to healthy food options and primary care.[9] Māori and people with severe mental illness are more likely to experience social and economic deprivation.

Prevention of weight gain and weight loss strategies remain the priority for dealing with the adverse metabolic effects of clozapine and targeted intervention is required. GLP-1 agonists have only recently become funded in New Zealand and studies have shown they are likely to be the agent of choice after metformin.[10]

The increased percentage of Māori versus non-Māori prescribed clozapine can be seen as a proxy measure for an increased risk of severe schizophrenia in the Māori population. Although treatment resistant illness is associated with an increased risk of certain copy number variants there are also environmental risk factors associated with social deprivation that disproportionately affect Māori. Duration of untreated psychotic illness and the number of severe acute relapses contribute to persistent psychotic symptoms which require clozapine.

Culturally appropriate, flexible and accessible services which integrate both the mental and physical health needs of people with treatment-resistant schizophrenia are required. This is consistent with Māori models of healthcare such as Te Whare Tapa Whā.[11] Determining successful local strategies to optimally manage the physical health of this vulnerable group will involve review of "successful" patients who have managed to avoid weight gain and the development of dysglycaemia.

COMPETING INTERESTS
Nil.

AUTHOR INFORMATION
Nicole M McGrath: Physician, Department of Medicine, Northland District Health Board, Whangārei.
Verity Humberstone: Psychiatrist, Department of Psychiatry, Northland District Health Board, Whangārei.
Ashley C Abraham: Clinical Audit Facilitator, Northland District Health Board, Whangārei.

CORRESPONDING AUTHOR
Nicole M McGrath: Physician, Department of Medicine, Northland District Health Board, Private Bag 9748, Whangārei. 09 434100.
Nicole.mcgrath@northlanddhb.org.nz

URL
www.nzma.org.nz/journal-articles/diabetes-mellitus-prevalence-in-northland-new-zealand-schizophrenia-patients-on-clozapine

REFERENCES
1. Martin FI. Alford FP. Insulin sensitivity in schizophrenia. Br Med J 1970; 2:50.
2. De Hert M, Detraux J, Van Winkel R, Yu W, Correll CU. Metabolic and cardiovascular adverse effects associated with antipsychotic drugs. Nat Rev Endocrinol [Internet]. 2012 Feb.
3. Singh R, Bansal Y, Medhi B, Kuhad A. Antipsychotics-induced metabolic alterations: Recounting the mechanistic insights, therapeutic targets and pharmacological alternatives. Eur J Pharmacol. 2019 Feb 5;844:231-240.
4. Melkersson K, Dahl M-L. Adverse Metabolic Effects associated with Atypical antipsychotics: literature review and clinical implications. Drugs 2004;64(7):701-23.
5. Taipale H, Lähteenvuo M, Tanskanen A, Mittendorfer-Rutz E, Tiihonen J. Comparative Effectiveness of Antipsychotics for Risk of Attempted or Completed Suicide Among Persons With Schizophrenia. Schizophr Bull [Internet]. 2021 Jan 23 [cited 2021 Aug 23];47(1):23–30.
6. Vermeulen JM, Van Rooijen G, Van De Kerkhof MPJ, Sutterland AL, Correll CU, De Haan L. Clozapine and Long-Term Mortality Risk in Patients with Schizophrenia: A Systematic Review and Meta-analysis of Studies Lasting 1.1-12.5 Years. Schizophr Bull [Internet]. 2019 Mar 7 [cited 2021 Aug 23];45(2):315–29.
7. New Zealand data sheet CLOZARIL. Medsafe.govt.nz Available at: https://www.medsafe.govt.nz/profs/datasheet/c/Clozariltab.pdf [Accessed 12 January 2022].
8. Nemani KL, Greene C and Henderson DC. Clozapine, diabetes mellitus, cardiovascular risk and mortality: results of a 21-year naturalistic study in patients with schizophrenia and schizoaffective disorder. Clin Schizophr Relat Psychoses 2019;12(4): 168-176.
9. Population of Northland DHB. Ministry of Health NZ. 2021. Available at: https://www.health.govt.nz/new-zealand-health-system/my-dhb/northland-dhb/population-northland-dhb [Accessed 12 January 2022].
10. Cernea S, Dima L, Correll CU, Manu P. Pharmacological Management of Glucose Dysregulation in Patients Treated with Second-Generation Antipsychotics. Drugs [Internet]. 2020 Nov 1 [cited 2021 Aug 23];80(17):1763–81.
11. Durie M. 2001 Mauri ora: The dynamics of Māori health. Oxford University Press.

Can physical activity be simplified for health benefit?

Chey G Dearing, Carl D Paton

ABSTRACT

AIM: Physical activity (PA) offers protective benefits against at least 25 chronic conditions including psychological stress. The health benefits of PA may be largely attributed to improvements in cardiorespiratory fitness (CRF). However, current guidelines based on PA duration and intensity are controversial, and both are prone to measurement error. We designed a New Zealand specific physical activity frequency and type (PAFT) question, our aims were to examine if PAFT could predict CRF and psychological stress status.

METHODS: In experiment one, 20 subjects who regularly perfumed vigorous type PA completed PAFT prior to World Health Organization (WHO) recommended cardiorespiratory fitness (CRF) (VO_{2Peak}) estimation in a controlled exercise laboratory. In experiment two, 81 subjects completed PAFT and a reliable validated measure of stress (the ten-item Perceived Stress Scale (PSS-10)).

RESULTS: Vigorous type PA frequency had a strong association (R^2=0.71, p<0.01) with VO_{2Peak} and was also the most significant (p<0.01) predictor of low stress.

CONCLUSIONS: A simple quick PA type and frequency question predicts CRF and stress status. PA duration and intensity are not required to estimate the health benefits of PA. Two vigorous type PA activities per week can be recommended as a minimum PA dose to decrease risk of stress in similar populations.

Physical activity (PA) imparts clear health benefits and reduces risk (20–30%) of 25 or more chronic physical and mental health conditions.[1–3] PA is multi-faceted and can be characterised by several components: type, frequency, duration and intensity. There is a lack of knowledge and much controversy regarding how individual PA components combine to influence health. As weekly PA duration increases, all-cause mortality risk decreases in a non-linear relationship.[2–4] However, PA duration and risk varies by condition: 500 minutes of moderate intensity PA per week appears to be required for the largest observed decrease in cardiovascular disease risk, while greater than 1,200 minutes at the same PA intensity is required for the largest observed decrease in all-cancer risk.[4] While long PA duration is associated with the lowest mortality risk, the largest risk reduction is paradoxically observed at very low PA duration.[2,4] Essentially, the largest health benefit from PA is observed when "doing nothing" is compared with "doing something". One such benefit of regular PA is that it decreases psychological stress,[5] which can be defined as an individual's perception that their own personal capacity to cope with their environmental demands has been exceeded.[6] Psychological stress is itself associated with many physical diseases,[6] and in New Zealand psychological distress measures are worsening.[7] Psychological distress measures have also been recently compounded by the COVID-19 pandemic.[8] During COVID-19 restrictions, those who reported a reduction in PA behaviour reported significantly poorer mental health and wellbeing in New Zealand.[8] PA advice that can be provided to reduce and or limit stress and other health conditions is important for health in New Zealand.

The health-related components of physical fitness are cardiorespiratory fitness (CRF), muscular endurance, muscular strength, body composition and flexibility.[9] While all components are important, CRF has recently become the most valid vital sign for general health and function.[3,10,11] CRF is reliant on the contemporaneous performance of the respiratory, cardiovascular and musculoskeletal systems. When compared with traditional risk factors, CRF is the best single predictor of health outcomes in both healthy and clinical populations.[3,11] The World Health Organization (WHO) have long recommended cardiopulmonary exercise testing (CPX) as the gold standard method to assess CRF, as it allows direct measurement of VO_{2Peak}.[12] However, this is labour intensive, requiring a specialist exercise laboratory with advanced gas analysis equipment, trained personnel and subjects motivated to exercise until exhaustion. VO_{2Peak} can also be estimated via self-report questionnaires, which are a common method of measuring PA. However, when used to classify

subjects into just three CRF categories determined by the gold standard method, questionnaires will misclassify approximately half of all individuals.[13] This may be related to the quality of assessing PA duration and intensity from questionnaires which is particularly prone to error.[14] There is a need for self-reporting PA instruments that demonstrate good agreement with gold standard VO_{2Peak}.

PA guidelines for health in New Zealand are based on PA duration and intensity.[15] The guidelines recommend a minimum weekly PA dose of 150 minutes of moderate, or 75 minutes of vigorous, PA, and suggest aiming for 300 minutes of moderate, or 150 minutes of vigorous, PA for "extra health benefits". In contrast, the WHO[16] recommend that extra health benefits only occur at greater durations than these. PA duration and intensity differences are also apparent in recommendations from 23 European Union countries.[17] While all official guidelines contain a minimum weekly duration PA recommendation, these lack a robust evidence base. PA durations substantially below official recommendations show health benefits.[2,4] Many guidelines also recommend a minimum timeframe (often 10–15 minutes) for a single PA bout.[17] However, recent evidence suggests shorter duration single PA bouts are equally effective.[18] PA intensity is the most controversial of all PA components. Firstly, even highly objective PA intensity measurements such as the same percentages of VO_{2Peak} or maximal heart rate result in substantially different individual metabolic and cardio-circulatory responses.[19] Secondly, improving VO2Peak is shown to be possible from PA sessions that use a single 20–30 second bout at very high (sprint) intensity, and the largest improvements may occur with fewer (2–3) such bouts compared with more bouts per session.[20] Official PA guidelines are thus questionable, and may even be counter-productive by creating unnecessary barriers for some individuals.[1,2] For many health outcomes in many populations, PA type, frequency, duration and intensity thresholds to offer benefit remain unclear.

Current PA questionnaires are limited because they demonstrate particularly poor agreement with VO_{2Peak} (R^2=0.25–0.70).[13] As PA duration and intensity are both controversial and particularly prone to bias from questionnaires, we sought to examine if PA type and frequency alone could be useful to estimate CRF and health. We aimed to take a single question from a validated and reliable questionnaire, modify the PA types to match our local New Zealand populations PA preferences, and then to test the question. Specifically, we aimed to examine the associations between PA type and frequency data obtained from this one question with gold standard VO_{2Peak} and perceived stress. If such a question can predict VO_{2Peak} and stress, it may provide a simple guide for monitoring CRF and health in New Zealand populations. Additionally, it may encourage further research in designing a PA questionnaire that can reliably estimate VO_{2Peak}.

Material and methods

Physical activity frequency and type (PAFT) question

Question two from the validated and reliable five item physical activity questionnaire[21] was modified for the categories of PA. The categories of PA were initially chosen from the long forms of validated New Zealand Physical Activity Questionnaire (NZPAQ-LF). Categories were then refined during a test of the questionnaire on a small sample of 10 local residents. Five categories were moderate intensity PA and five were vigorous intensity PA, as defined by New Zealand guidelines. The final question contained 11 categories of PA. Each category uses a five-point Likert scale, categorised as "7 or more times/week", "5–6 times/week", "3–4 times/week", "1–2 times/week", and "0 times/week". The last category was the number of days per week with no PA, which also served as a cross-check answer validity check. The 11 categories of PA are scored as 7, 5.5, 3.5, 1.5 and 0, respectively. The sum of the first 10 items is used to calculate a total PA frequency score (PAF_{All}), a measure of total weekly moderate and vigorous PA frequency. A total PA vigorous score (PAF_{Vig}) was also calculated from the sum of the five vigorous PA activities. PAF_{Vig} is the number of total vigorous PA activities per week. The units for PAF_{All} and PAF_{Vig} are activities per week (AW). Activity days were also recorded as the reverse score of the last category.

Experiment 1
PAFT as a predictor of VO_{2Peak}

PAFT was completed by 20 subjects immediately prior to VO_{2Peak} testing. The cohort consisted of males (n=16), and females (n=4). Inclusion criteria of subjects were a resident of Hawkes Bay, willing and capable of performing VO_{2Peak} testing to exhaustion and free from injury and illness, and who was regularly performing vigorous style PA. Subjects completed a maximal cycling

or running test dependent upon their personal preference. All testing was conducted in an environmentally controlled laboratory (temperature 20±°C: relative humidity 36±4%). Prior to testing all subjects completed a 10 minute warm-up at a self-selected submaximal intensity.

Runners completed the test using a motorised treadmill (Cosmos pulsar 3p) with a gradient fixed at 1%. The maximal incremental test commenced at 8km/h and increasing by 1km/h each minute until subjects reached volitional exhaustion.

Cycling tests were performed on a calibrated Velotron Dynafit Pro cycle ergometer (RacerMate Inc., WA, USA). Subjects completed a maximal incremental test commencing at 75W with power output increasing at a rate of 25W·min^{-1} until the cyclist reached volitional exhaustion.

All participants achieved minimum test duration of eight minutes. Respiratory gases were continuously measured with a metabolic cart (Metalyser 3B, Cortex, Leipzig, Germany) calibrated in accordance with the manufacturer's instruction using Alpha gas standards. VO_{2Peak} was determined as the highest 30s oxygen uptake value recorded during the incremental test.

Experiment 2 PAFT as a predictor of perceived stress

Experiment two subjects were invited to participate in this study via posters and social media placed at the lead researchers' tertiary institution between February 2019 and December 2019. All subjects who consented completed the PAFT question followed with the ten item perceived stress scale (PSS-10).[22] Exclusion criteria were (1) a current residential address other than Hawkes Bay, (2) any data missing on any question on either of the two questionnaires, and (3) a lack of agreement between the first 10 categories of PA and the last reverse scored PA category.

The PSS-10 is a validated tool to measure perceived psychological stress over the preceding four weeks in many populations.[23] The PSS-10 was used to calculate a stress score as previously described.[22] Individual PSS-10 scores within the 0–13 range are considered low stress, the 14–26 range is considered moderate stress, while over 27 is considered high perceived stress.

Statistics

All variables were tested for Gaussian distributions with D'Agostino-Pearson normality omnibus K2 test to determine parametric statistic suitability. Correlation and regression were both performed to establish the relationship between VO_{2Peak} and PAF_{All}, PAF_{Vig} and activity days. One way ANOVA followed by *post hoc* Tukey was used in the following comparisons: (1) subjects were divided into low moderate and high stress groups (see PSS-10 above) and compared for age, activity days, PAF_{All}, PAF_{Vig}, and (2) subjects were compared for PSS across four groups based on the number of days of exercise per week (7 days, 6 or 5 days, 4 or 3 days and 2 or fewer days). The unpaired t-test was used in the following comparisons: (1) tertiary students were compared with non-tertiary students for age, activity days, PAF_{All}, and PAF_{Vig}. Low stress and high/moderate stress groups were examined for association using Pearson's Chi-squared test for identifying as a tertiary student or a specific gender. Receptor operating characteristic (ROC) analysis was used to examine if PSS could be predicted by activity days, PAF_{All}, PAF_{Vig}. The data was analysed and graphs constructed using Prism (Prism, Version 4.0 GraphPad Software, San Diego, CA, USA, www.graphpad.com).

Ethical approval

This study was approved by the local Research Committee on 11/12/2018 Reference (REF 18/17).

Results

Experiment one

Twenty subjects (mean ± SD age 41±8y; weight 72±11kg; height 176±11cm) volunteered for maximal aerobic testing and competed PAFT. PAF_{Vig} scores (mean ± SD age 5.9±2.8) correlated (r=0.68, p=0.002) with VO_{2Peak} (mean ± SD 57.5±9.1ml.kg^{-1}), while PAF_{All} did not. Activity days also correlated (r=0.71, p=0.002) with VO_{2Peak}; however, 65% of these subjects all recorded five or six days of activity per week limiting interpretation. A curvilinear relationship (Figure 1) best described the VO_{2Peak} PAF_{Vig} association.

Experiment two

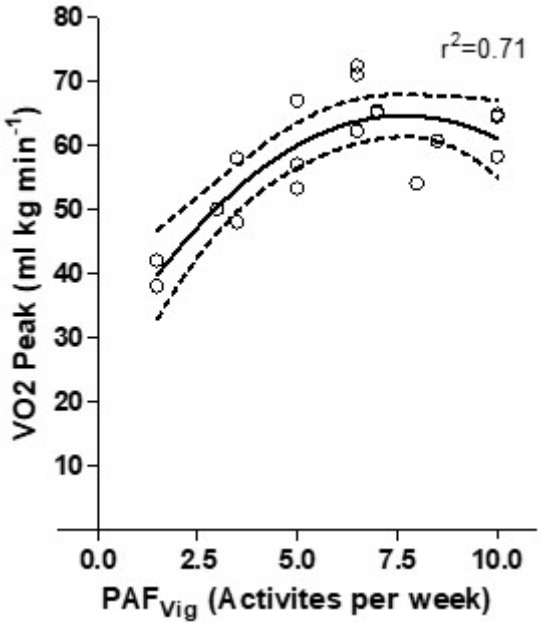
Eighty-seven subjects initially completed both PSS and PAFT. Six subjects were excluded as PAF_{All} or PAF_{Vig} were incompatible with activity days. Correlations between activity days and PAF_{All} (r=0.55, p<0.001) and PAF_{Vig} (r=0.40, p<0.001) provided a measure of cross-check answer validity. Tertiary students (n=44) compared with non-students were younger (p<0.001) (mean ± SD years 27.4±8.5 vs 45.5±14.5), reported greater (p<0.001) stress (20.7±5.6 vs 12.2±7.5) less (p=0.004) activ-

ity days (1.2±1.5 vs 2.3±1.9), lower (p=0.001) PAF_{All} (6.5±4.7 vs 11.4±6.7), and lower (p=0.001) PAF_{Vig} (6.5±4.7 vs 11.4±6.7). See Table 1.

To examine associations with categorical variables, high and moderate stress groups were combined into one higher stress group because a lack of subjects with high stress (n=8) prevented meaningful statistical analysis. Only identifying as a tertiary student (p<0.001, Chi-squared=34.72) was positively associated with higher stress.

PAF_{All} and PAF_{Vig} were examined as predictors of PSS using linear regression. PAF_{All} (R2=0.09, p=0.009) and PAF_{Vig} (R^2=0.12, p=0.002) explained only approximately 10% of the variance in PSS scores. Activity days was associated with perceived stress (Figure 2).

Figure 1: Maximal oxygen consumption vs PAF_{Vig} (n=20).



Activity days (the number of days subjects performed a minimum of one session of physical activity per week) are compared for PSS Score. Lines are Mean and 95% CI. Post hoc analysis (Tukey's Multiple Comparison Test) revealed only 7 days vs 3 or 4 days (p<0.01) and 7 days vs 2 or fewer days (p<0.01) were different between groups.

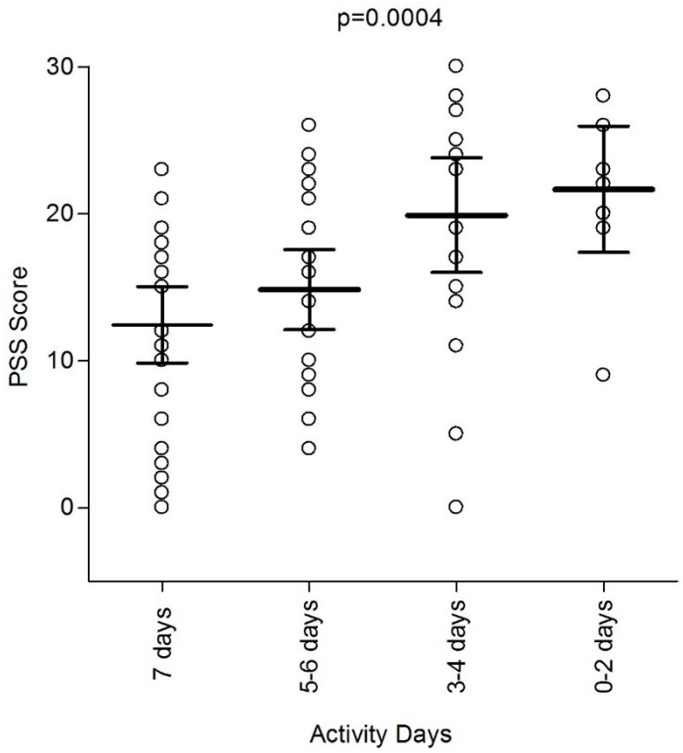
Table 1: ANOVA results from subjects grouped by stress level.

	One way ANOVA results		**Low stress (n=30)**		**Moderate stress (n=43)**		**High stress (n=8)**	
	p	**F**	**Mean**	**Std. dev.**	**Mean**	**Std. dev.**	**Mean**	**Std. dev.**
Subject age (y)	<0.001	12.65	45.4	15.4	30.7	11.8	28.0	10.9
PAF_{Days}	0.007	5.23	5.9	1.3	4.9	1.8	4.0	2.1
PAF_{All}	0.019	4.17	11.7	6.6	7.4	5.7	8.8	8.0
PAF_{Vig}	0.076*	2.66	4.3	4.4	2.3	3.8	1.6	2.7

Table 1 compares study variables for stress categories and presents means values and standard deviations for the subjects by stress category.
* not significant

ROC analysis revealed that activity days, PAF_{All} and PAF_{Vig} were all predictive of low stress in this population (Table 2). Several cut-off thresholds were available for PAF_{All} and PAF_{Vig}. A PAF_{Vig} score of two has a sensitivity of 60.0% (95% CI 40.6% to 77.3%) and a specificity of 70.4% (95% CI 56.4% to 82.0%) to predict low stress. A PAF_{All} score of eight has a sensitivity of 62.5% (95% CI 43.69% to 78.9%) and a specificity of 74.1% (95% CI 60.4% to 85.0%) to predict low stress.

Figure 2: Exercise frequency and stress.



The relationship between maximum oxygen consumption and PAF_{Vig} is shown. Equation; Polynomial: Second Order (Y=A+B*X-+C*X2) Best-fit values (A=26.31, B=10.03, C=-0.6552) 95% Confidence Intervals (A 14.23 to 38.39, B 5.646 to 14.41, C -1.018 to -0.2927).

Table 2: ROC area under the curves for activities that are significant independent predictors of low stress.

Test result variable(s)	Area	Significance	95% Confidence interval	
			Lower bound	Upper bound
PAF_{All}	0.689	0.004	0.573	0.806
PAF_{Vig}	0.702	0.002	0.588	0.816
Active days	0.673	0.009	0.558	0.789
Active days = number of days per week with a minimum of one session of physical activity.				

Table 2 displays ROC area under the curve, significance and confidence intervals for activities that are significant independent predictors of low stress.

Discussion

We sought to examine if questions on PA type and frequency alone could be used to estimate CRF and stress. We modified a single question from a validated and reliable questionnaire, to match our local populations PA frequency and type preferences. We then examined this PAFT question in two local populations. Vigorous style PA as estimated by the novel PAF_{Vig} from PAFT had a strong association (R^2=0.71, p=0.001) with VO_{2Peak} determined by the WHO recommended method in the first population. PAF_{Vig} was also the most significant predictor (ROC area 0.70, p=0.002) of low stress in the second population. ROC analysis identified that two vigorous PA sessions or eight moderate PA sessions per week can be recommended as thresholds to decrease the risk of stress in this and similar populations.

The strength of our study is that we used direct CPX which is the gold standard WHO approach to assessing CRF and allowed us direct measurement of VO_{2Peak}.[12] This is now considered the most valid vital sign for general health and function.[3,10,11] The method is labour intensive and only 20 subjects were assessed which may be considered a limitation. Nevertheless, the use of CPX does give PAFT a measure of validity that is rare in PA questionnaire validation. PAF_{Vig} agreement with VO_{2Peak} (R^2=0.71) compared well (R^2=0.25–0.70) with existing PA questionnaires.[13] Therefore, we suggest that it is not necessary to estimate PA intensity and duration as specific questions in order to predict PA health benefit. Additionally, we believe PAF_{Vig} may offer less bias as a PA metric as it is established that PA duration and intensity from questionnaires is particularly prone to this error.[14] Also, the controversies of minimum single PA bout durations[18] and intensity[20] are removed with PAF_{Vig}. PAF_{Vig} appears to offer potential as a useful and particularly simple prescription for PA.

Age, tertiary study, PA frequency and type were all factors associated with increased psychological stress in our study population. The perception of psychological stress is markedly higher in younger individuals and those undergoing tertiary study compared with other individuals in the studied population. Unfortunately, the size of this exploratory study did not allow separate analysis of these groups. However, we should note this is an important finding, as psychological stress encountered when young appears to impart an increased risk of chronic diseases of ageing.[24] The younger subjects in this study may be at higher risk many physical diseases.[6,25,26] A growing body of evidence[27] demonstrates that stress is a major concern with higher education students. Strategies to reduce stress in younger individuals undertaking tertiary study would likely benefit long-term health outcomes.

Our study supports that regular PA participation decreases stress, which is similar to consensus.[5,28] However, only approximately half of studies suggest that higher PA or higher CRF levels are associated with attenuated responses to psychosocial stress.[28] As such, there is little consensus on which types of exercise have the strongest impact on psychological stress.[5] We found that PAF_{Vig} were associated with a more profound reduction in stress when compared with PAF_{All}. Additionally, we found that the greater number of sessions per week that an individual performs PAF_{Vig} activities is also associated with increased reductions in perceived stress. We suggest that a reduction in stress with increased PAF_{Vig} may be directly related to increases in VO_{2Peak}. It is interesting to speculate that the optimum dose of PA to reduce stress may in fact be the same dose that improves VO_{2Peak}. This would support the growing consensus that VO_{2Peak} is an important health variable.[3,10,29] One limitation is that health benefits from PA are specific to the population studied,[5] and to the health outcome being measured. Indeed, given that that the tertiary students compared to other subjects reported significantly greater stress (mean ± SD 20.7±5.6 vs 12.2±7.5) the levels of PA to reduce risk of stress may only be consistent with our specific population.

Our findings suggest that simple frequency PA information can be used to estimate both CRF and health. PA frequency recommendations appear simple when compared with the minimum 75 minutes of vigorous physical activity, or 150 minutes of moderate PA durations recommended by many official guidelines. We suggest that two vigorous PA style sessions per week with no bout duration limit may be a simple recommendation for improving CRF and health. For extra health benefit, this may be increased into the range of 5–8 vigorous PA sessions per week which appears to be associated with the highest VO_{2Peak} in our current study. We suggest future research should focus on the relationships between PA frequency and all five components of physical fitness for health. If this valid, easy-to-use, rapid assessment of PA can be used with a wide range of patient populations, it may benefit many health professionals and their patients.

COMPETING INTERESTS
Nil.

ACKNOWLEDGEMENTS
We acknowledge the Eastern Institute of Technology for providing financial support.

AUTHOR INFORMATION
Chey G Dearing: The Eastern Institute of Technology, School of Health and Sport Science, Napier, New Zealand. ORCID 0000-0002-6546-1647.
Carl D Paton: The Eastern Institute of Technology, School of Health and Sport Science, Napier, New Zealand. ORCID 0000-0002-7418-7213.

CORRESPONDING AUTHOR
Chey G Dearing: The Eastern Institute of Technology, School of Health and Sport Science, Napier, New Zealand. ORCID 0000-0002-6546-1647. 64 6 9748000. cdearing@eit.ac.nz

URL
www.nzma.org.nz/journal-articles/can-physical-activity-be-simplified-for-health-benefit

REFERENCES
1. Warburton DE, Bredin SS. Health benefits of physical activity: a systematic review of current systematic reviews. Current opinion in cardiology. 2017;32(5):541-56.
2. Warburton DE, Bredin SS. Health benefits of physical activity: A strengths-based approach. Multidisciplinary Digital Publishing Institute; 2019.
3. Ross R, Blair SN, Arena R, Church TS, Després J-P, Franklin BA, et al. Importance of assessing cardiorespiratory fitness in clinical practice: a case for fitness as a clinical vital sign: a scientific statement from the American Heart Association. Circulation. 2016;134(24):e653-e99.
4. Burtscher J, Burtscher M. Run for your life: tweaking the weekly physical activity volume for longevity. BMJ Publishing Group Ltd and British Association of Sport and Exercise Medicine; 2020.
5. Gerber M, Pühse U. Do exercise and fitness protect against stress-induced health complaints? A review of the literature. Scandinavian journal of public health. 2009;37(8):801-19.
6. Cohen S, Janicki-Deverts D, Miller GE. Psychological stress and disease. Jama. 2007;298(14):1685-7.
7. Mulder R, Rucklidge J, Wilkinson S. Why has increased provision of psychiatric treatment not reduced the prevalence of mental disorder. Australian and New Zealand Journal of Psychiatry. 2017;51:1176-7.
8. Faulkner J, O'Brien W, McGrane B, Wadsworth D, Coulter M, Draper N, et al. Physical activity, mental health and well-being of adults during early COVID-19 containment strategies: A multi-country cross-sectional analysis. 2020.
9. Caspersen CJ, Powell KE, Christenson GM. Physical activity, exercise, and physical fitness: definitions and distinctions for health-related research. Public health reports. 1985;100(2):126.
10. Arena R, Canada JM, Popovic D, Trankle CR, Del Buono MG, Lucas A, et al. Cardiopulmonary exercise testing–refining the clinical perspective by combining assessments. Expert Review of Cardiovascular Therapy. 2020;18(9):563-76.
11. Imboden MT, Harber MP, Whaley MH, Finch WH, Bishop DL, Fleenor BS, et al. The association between the change in directly measured cardiorespiratory fitness across time and mortality risk. Progress in cardiovascular diseases. 2019;62(2):157-62.
12. Shephard RJ, Allen C, Benade A, Davies C, Di Prampero P, Hedman R, et al. The maximum oxygen intake: An international reference standard of cardio-respiratory fitness. Bulletin of the World Health Organization. 1968;38(5):757.
13. Peterman JE, Whaley MH, Harber MP, Fleenor BS, Imboden MT, Myers J, et al. Comparison of non-exercise cardiorespiratory fitness prediction equations in apparently healthy adults. European journal of preventive cardiology. 2021;28(2):142-8.
14. Nigg CR, Fuchs R, Gerber M, Jekauc D, Koch T, Krell-Roesch J, et al. Assessing physical activity through questionnaires–A consensus of best practices and future directions. Psychology of sport and exercise. 2020;50:101715.
15. Ministry of Health. How much physical activity is needed? 2020 [Available from: https://www.health.govt.nz/your-health/healthy-living/food-activity-and-sleep/physical-activity/how-much-activity-recommended.
16. World Health Organization. WHO guidelines on physical activity and sedentary behaviour. 2020.
17. Gelius P, Tcymbal A, Abu-Omar K, Mendes R, Morais ST, Whiting S, et al. Status and contents of physical activity recommendations in European Union countries: a systematic comparative analysis. BMJ open. 2020;10(2):e034045.
18. Piercy KL, Troiano RP, Ballard RM, Carlson SA, Fulton JE, Galuska DA, et al. The physical activity guidelines for Americans. Jama. 2018;320(19):2020-8.
19. Hofmann P, Tschakert G. Special needs to prescribe exercise intensity for scientific studies. Cardiology research and practice. 2011;2011.

20. Vollaard N, Metcalfe R, Williams S. Effect of number of sprints in a SIT session on change in VO2max: a meta-analysis. Medicine and science in sports and exercise. 2017;49(6):1147-56.
21. Cho M-H. Preliminary reliability of the five item physical activity questionnaire. Journal of physical therapy science. 2016;28(12):3393-7.
22. Cohen S, Kamarck T, Mermelstein R. Perceived stress scale. Measuring stress: A guide for health and social scientists. 1994;10.
23. Lee E-H. Review of the psychometric evidence of the perceived stress scale. Asian nursing research. 2012;6(4):121-7.
24. Miller GE, Chen E, Parker KJ. Psychological stress in childhood and susceptibility to the chronic diseases of aging: moving toward a model of behavioral and biological mechanisms. Psychological bulletin. 2011;137(6):959.
25. Mathur MB, Epel E, Kind S, Desai M, Parks CG, Sandler DP, et al. Perceived stress and telomere length: A systematic review, meta-analysis, and methodologic considerations for advancing the field. Brain, behavior, and immunity. 2016;54:158-69.
26. Penedo FJ, Dahn JR. Exercise and well-being: a review of mental and physical health benefits associated with physical activity. Current opinion in psychiatry. 2005;18(2):189-93.
27. Wunsch K, Fiedler J, Bachert P, Woll A. The Tridirectional Relationship among Physical Activity, Stress, and Academic Performance in University Students: A Systematic Review and Meta-Analysis. International Journal of Environmental Research and Public Health. 2021;18(2):739.
28. Mücke M, Ludyga S, Colledge F, Gerber M. Influence of regular physical activity and fitness on stress reactivity as measured with the trier social stress test protocol: A systematic review. Sports Medicine. 2018;48(11):2607-22.
29. Harber MP, Kaminsky LA, Arena R, Blair SN, Franklin BA, Myers J, et al. Impact of cardiorespiratory fitness on all-cause and disease-specific mortality: advances since 2009. Progress in cardiovascular diseases. 2017;60(1):11-20.

Revised Guidelines for smoking cessation in New Zealand, 2021

Jessica McCormack, Natalie Walker, Hayden McRobbie, Karen Wright, Vili Nosa, Basil Fernandes, Chris Bullen

ABSTRACT

AIMS: To summarise the literature underpinning key recommendations made in the 2021 revision of the Ministry of Health's *New Zealand Guidelines for Helping People to Stop Smoking*.

METHODS: A comprehensive literature review of smoking cessation interventions was undertaken in July 2021. Recommendations were formulated from the findings of the literature review and expert advice.

RESULTS: Healthcare professionals should ask and briefly advise all people who smoke to stop smoking, regardless of whether they say they are ready to stop smoking or not. They should offer smoking cessation support, which includes both behavioural and pharmacological (e.g., nicotine replacement therapy, nortriptyline, bupropion or varenicline) interventions. The Guidelines also include advice around the use of vaping in smoking cessation. Recommendations are also formulated for priority populations of smokers: Māori, Pacific, pregnant women, and people with mental illness and other addictions.

CONCLUSIONS: The guidelines will assist healthcare professionals in providing evidence-based smoking cessation support to people who smoke. To be effective and equitable, the ABC model requires organisational commitment, integration into routine practice, and increased attention to the upstream determinants of smoking and quitting.

Helping people who smoke tobacco to quit is an important strategy towards achieving New Zealand's smokefree 2025 goal,[1] and in improving health equity. In 2021, the Ministry of Health published *The New Zealand Guidelines for Helping People to Stop Smoking: 2021 Update* to contribute to this high-priority strategy by providing health workers with the information they need to encourage people to stop smoking.[1] In this paper, we summarise the 2021 Guidelines and outline the process of developing them.

Methods

Guidelines development process

New Zealand's guidelines for stopping smoking were first published in 1999, with revisions in 2002, 2007 and 2013. The current (2021) update was prompted by substantial changes to the New Zealand tobacco environment; specifically, the increased availability and use of vaping devices (e-cigarettes), new evidence on the effectiveness of smoking cessation treatments, amendments to the Smokefree Environments and Regulated Products Act 1990, and the development of the Action Plan for Smokefree 2025.

Literature review

The guideline development process included an updated literature review (January 2014 to March 2021). We sought evidence on the following interventions: nicotine replacement therapy, pharmacotherapy, e-cigarettes and heat-not-burn products, alternative therapies (e.g., acupuncture, hypnosis), behaviour/psychosocial interventions, and community-led smoking cessation programmes. Population level interventions and oral tobacco products were excluded. Sources included the Cochrane Database of Systematic Reviews, PubMed and PsycINFO databases and the US Preventive Services Task Force report on Tobacco cessation[2] (N=45). Additional evidence from high-quality randomised control trials (RCTs) was sought where no meta-analyses or systematic reviews existed on a topic. Where available, we report long-term smoking abstinence rates; that is, verified continuous smoking abstinence over a period of at least 6-months from the stop-smoking date.

Findings

Key changes from previous guidelines

The basis for the 2021 Guidelines continues to be the ABC pathway (Figure 1). The guidelines differ from the 2013 version in the following ways:

- inclusion of evidence about vaping as a cessation tool,
- updated information about other approaches that people may use to try to quit,
- risk ratio with 95% confidence intervals

reported, and the number of studies and number of participants, contributing to the evidence where available,
- inclusion of information on barriers and facilitators for smoking cessation that might affect individuals,
- use of GRADE system for guiding recommendations about the quality of evidence wherever possible and a new approach to signal the strength of the evidence.

Providing behavioural support

Behavioural support involves targeted activities designed to maximise motivation to remain smokefree, minimise motivation to smoke, enhance the skills and capacity needed to avoid and resist urges to smoke, and optimise effective use of stop smoking medication.[3] Behavioural support can increase long-term smoking cessation, both with and without pharmacotherapy.[4] Network meta-analysis suggested that the components with the most benefit are "counselling of any kind, guaranteed financial incentives for quitting, and text-messaging based delivery".[4]

Brief advice

Brief advice can have a large impact at the population level due to the potential reach of the intervention. Brief opportunistic advice from a doctor increases the rate of quitting by 76% compared with doing nothing,[5] with similar findings reported for nurses, community pharmacists, and oral health workers.[4] More intensive advice (>20 minutes) and the addition of follow-up are more effective than minimal advice.[3,5,6] Brief advice should ideally be combined with an offer of cessation support because offering cessation support is more effective than simply giving brief advice;[4,7] both should be regarded as best practice for all health professionals.

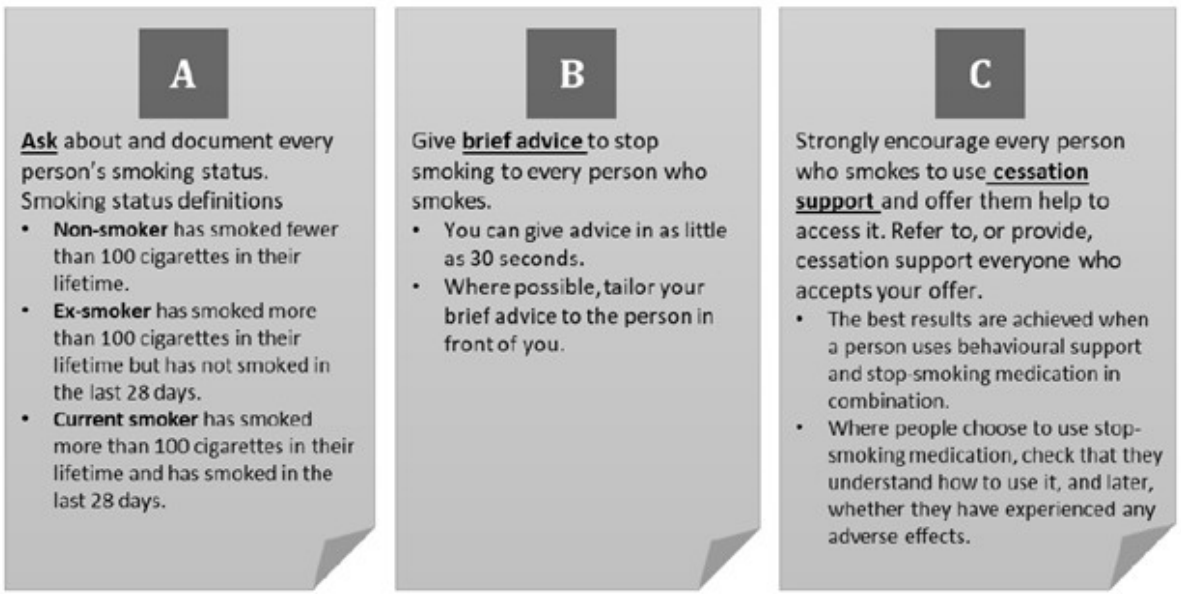
Counselling

Counselling can be delivered face-to-face, over the phone, via real-time video-counselling, individually or in a group. There is no evidence that any one method is better than another.[4] Compared to controls (i.e., usual care, brief advice, and self-help) counselling increases long-term abstinence by more than 50% for individual and group counselling, and almost 40% for telephone counselling.[4] The New Zealand Quitline (https://quit.org.nz/) is an example of a telephone counselling service that has been shown to be effective, and that has expanded its range of modalities to include text messaging and online support.[8] More intensive counselling is more effective in increasing long-term abstinence than less intensive counselling.[9]

Technology-based support

Internet-based interventions—includes web pages (e.g., online self-help guides, user forums and blogs) and social media platforms.[10] Internet-based interventions that are tailored and interactive have been shown to increase long-term

Figure 1: The ABC pathway.



abstinence rates compared to self-help guides or usual care; however, the effect is small, and should be interpreted with caution.[10] There is no evidence of benefit for internet-based interventions compared to active controls (e.g., counselling).[10]

Automated text messaging support—delivers a mix of information, advice, and motivational messages. Text messaging support increases long-term abstinence rates by 54% compared to minimal support controls.[11] When added to other smoking cessation support (such as counselling and pharmacotherapy) text messaging support is more effective than other smoking cessation support alone.[11] No difference was found for high-frequency versus low-frequency text messaging.[11]

Smartphone applications—have been trialled in providing smoking cessation support; however, there is insufficient evidence of their effectiveness and further evidence from RCTs is needed.[11]

Providing stop-smoking medicines

Nicotine replacement therapy

When compared to controls, nicotine replacement therapy (NRT) can improve long-term abstinence rates by around 50%, regardless of the type of NRT.[12] Higher-dose NRT products are more effective than lower-dose products (e.g., 42 mg patch versus 14mg patch).[13] Most people should use NRT for 8 to 12 weeks. A small number of smokers may need to use it for longer; however, there is insufficient evidence that long-term NRT use is more effective than short-term use.[13] NRT is effective at helping people reduce the number of cigarettes they smoke before stopping. This is an effective method of stopping smoking long-term, and improves long-term abstinence compared to standard NRT use by 25%.[13] NRT use is associated with an increased risk of chest pains that are categorised as "cardiovascular adverse events" compared to placebo, but not with an increased risk of serious cardiovascular effects.[14]

Partial agonists

Varenicline, a nicotinic acetylcholine receptor (nAChR) partial agonist, helps people to stop smoking primarily by reducing the severity of tobacco withdrawal symptoms, but it also reduces the rewarding properties of nicotine. Long-term abstinence rates when using varenicline more than double, compared to a placebo.[15] Varenicline is more effective than other smoking cessation medications including bupropion and NRT.[15] There is a 25% increase in the risk of serious adverse events when using varenicline compared to placebo; however, the adverse events include comorbidities or illness events (e.g., cancer diagnosis) not considered to be associated with the use of varenicline.[15] There is no evidence to suggest increased risk of cardiovascular events or neuropsychiatric events.[15]

Cytisine is a plant-based alkaloid that works in a similar way to varenicline by reducing the severity of cravings and the reward properties of nicotine.[15] Although there is good evidence for cytisine's efficacy and effectiveness, it is not yet licensed for use in New Zealand. If approved, cytisine has potential to be highly acceptable, particularly to Māori, because of its presence in the kōwhai tree.[16] Cytisine is more effective than placebo in increasing long-term abstinence rates.[15] Two New Zealand non-inferiority trials comparing cytisine to varenicline[17] and cytisine to NRT[18] found cytisine was just as effective in increasing long-term abstinence. Cytisine is well tolerated: participants taking cytisine were less likely to report adverse events, such as nausea, than those taking varenicline,[17] but studies with longer follow-up are needed.[6]

Antidepressants

Bupropion, an atypical antidepressant, helps people to stop smoking by reducing the severity of withdrawal symptoms. Bupropion is as effective as NRT and nortriptyline but less effective than varenicline. Bupropion improves long-term abstinence rates by 64%, compared to a placebo.[19] A large multi-site RCT (N=8,144) found no increase in psychiatric adverse events in people using bupropion compared to placebo, regardless of diagnosis.[20]

Nortriptyline, a tricyclic antidepressant, helps people to stop smoking by reducing the severity of withdrawal symptoms. Nortriptyline improves long-term abstinence, compared to a placebo.[19] In studies comparing nortriptyline to bupropion, there was no significant difference in quit rates.[19] There is insufficient evidence on adverse events,[6] but there are a number of contraindications and precautions with its use.

Combining smoking cessation interventions

In most cases, behavioural support and pharmacotherapy are most effective when delivered together.[9,21] Combined behavioural treatment and pharmacotherapy (in most studies, NRT) increases long-term abstinence rates by 83% compared to usual care, brief advice, or less intensive

behavioural support.[21] There is also evidence that combining pharmacotherapies improves smoking cessation outcomes. For example, combining patch with a faster-acting gum or lozenges increases long-term abstinence by 25% compared with a single NRT product.[13] There are no safety concerns with combining NRT products compared to single NRT. Using varenicline in combination with NRT may improve long-term abstinence compared varenicline alone, although more evidence is needed.[22]

Vaping products

Vaping products (electronic cigarettes, also known as e-cigarettes or vapes) are electronic devices that heat a liquid to form an aerosol inhaled by the user. Vaping liquids often contain nicotine. Vaping products containing nicotine are effective in increasing long-term quit rates by 69%, compared to NRT, and by 71% compared to non-nicotine vaping products.[23] Nicotine-containing vaping products more than double long-term abstinence compared to behavioural support; however, estimates should be interpreted with caution.[23]

In New Zealand, vaping products are *not* licensed medicines or devices, but they are regulated tobacco products subject to smokefree provisions and prohibition of sale to minors. They are a less harmful way of delivering nicotine when compared to traditional cigarettes, but they are not harmless. They produce a range of toxicants, including some carcinogens, but the literature points to these generally being at much lower levels than those found in cigarette smoke and less likely to cause harm.[24,25] Available evidence suggests that risk of adverse events is no different from NRT; however, more long-term (>12 months) follow-up data are needed.[23] Vaping products are typically used over a longer time than most smoking cessation medications (e.g., 12 weeks)[8] so more information is needed about the health effects of long-term use. They may have a particular appeal to people who have had difficulty quitting with conventional support, both because of their favourable pricing compared to cigarettes and behavioural replacement characteristics.

Smoking cessation interventions for priority groups

In general, interventions effective in the general population are also effective in priority population groups. However, significant ethnic inequalities in the socio-economic determinants of health, access to treatment, and quality of care[26] affect both smoking prevalence and smoking cessation support.

Providing stop-smoking support to Māori

Since 2006, daily smoking prevalence in the general adult population has fallen from 22% to 9.4%,[27] and from 42% to 22% among Māori.[27] Māori men and women are more than twice as likely to be daily smokers than non-Māori (adjusted ratio 2.60 [95% CI 2.14–3.16] and 3.58 [95% CI 3.01–4.26] for men and women, respectively).[27] Healthcare workers should demonstrate culturally safe practice and understand that systematic and structural factors, including racism, colonisation and the Crown's failure to meet obligations under Te Tiriti o Waitangi, have contributed to the high prevalence of smoking in Māori compared to non-Māori.[26] Inequitable access to health services has contributed to disparities in health between Māori and non-Māori. Financial cost, pervasive smoking among whānau and peers, environments accepting of smoking, and perceived cultural inappropriateness of treatments, are all barriers to Māori using available stop-smoking support.[16] Stop-smoking interventions for Māori must therefore be culturally appropriate, multi-faceted, address cigarette dependence, provide support, partner with Māori, and be inclusive of whānau.[28,29]

Interventions that work in the general population (e.g., behavioural support and stop-smoking medicines) are at least as effective for Māori.[30] For example, one randomised controlled trial (N=134) showed bupropion was effective in assisting Māori to stop smoking.[31] Likewise, subgroup analyses of RCTs have found no differences in quit rates for Māori compared to non-Māori for vaping devices[32] or text message support.[33] A recent trial comparing cytisine and varenicline in Māori and whānau of Māori found 12 weeks of cytisine was at least as effective as varenicline in increasing long-term abstinence.[17]

Several small studies have implemented behavioural support programmes for Māori, including incentive programmes,[34,35] exercise interventions[36] and peer support.[37] Such programmes have had promising results, and high acceptability, but more evidence is needed to determine their effectiveness.

Providing stop-smoking support to Pacific people

Since 2006, smoking prevalence has decreased from 30% to 16% among Pacific peoples.[27] Smoking prevalence amongst Pacific people varies by Pacific nation, especially by sex. Systemic factors also contribute to relatively high smoking among Pacific peoples, including barriers in access to care and quality of care.[38] Services and organisa-

tions must identify and address barriers to equitable care for Pacific peoples to address health disparities between groups and improve health equity. Health workers who provide support to Pacific smokers should seek training to ensure they are both technically and culturally safe in this role.

There are limited data on effective interventions for Pacific smokers. However, interventions known to work in the general population are likely to be just as effective for Pacific peoples. Some small studies of culturally tailored smoking cessation behavioural interventions have shown success in helping people quit smoking including text message support [39] and online training programmes.[40]

Providing stop-smoking support to pregnant women

Stopping smoking as early as possible during pregnancy can reduce the risk of adverse birth outcomes (such as premature birth and low-birth weight) and infant mortality.[41] Pregnant women need services that are appropriate and meaningful, and that deliver support in a timely manner. Offering partner and wider whānau referral to a stop-smoking service also helps the pregnant woman to stop.[42] Women should be offered ongoing support to remain smokefree after birth, as rates of relapse after birth are high.[43]

The following interventions are effective in improving abstinence in pregnant women:[44] counselling; incentives; and feedback in conjunction with other strategies, although these latter findings should be interpreted with caution due to small sample size. NRT with behavioural support has also been shown to increase abstinence rates in pregnant women compared to behavioural support alone.[45] There is insufficient evidence to determine the effectiveness of other pharmacological interventions for pregnant women, and varenicline is contraindicated for pregnancy.[46] Expert opinion suggests that pregnant women can use NRT once they have been advised of the potential risks and benefits.[47] The use of NRT in pregnancy carries a small potential risk to the fetus, but using NRT is far safer than smoking while pregnant, as blood nicotine levels are typically lower and NRT does not contain harmful substances in tobacco smoke (such as carbon monoxide). There is insufficient evidence to determine the risk of adverse birth outcomes between those using NRT and placebo.[45] There is insufficient evidence to determine the safety or effectiveness of e-cigarettes to support abstinence during pregnancy.[6]

Providing stop-smoking support to children and young people

The prevalence of daily smokers in people aged between 15 and 24 years has halved from 20.1% in 2006 to 10.1% in 2021.[27] Group counselling is effective at increasing long-term abstinence rates in young people who smoke compared to control interventions, but there is insufficient evidence to determine the effectiveness of individual counselling.[48] There is insufficient evidence to confirm the effectiveness of interventions specifically aimed at helping young people to stop smoking, or to recommend integrating any particular model into standard practice.[48,49] Interventions that may be acceptable for young people include support from family, friends and community, and incentives, physical activity and group support.[50] There is insufficient evidence that using NRT improves long-term abstinence rates among young smokers.[48] Nevertheless, expert opinion is that NRT may be considered for use by young people who want help to stop smoking. The safety and efficacy of other pharmacological interventions in patients under 18 years of age have not been established.[48,49]

Providing stop-smoking support to people who use mental health and addiction treatment services

People with mental health disorders have particularly high smoking rates. People who smoke are 1.5 times more likely than non-smokers to be diagnosed with at least one mental health condition (25% in smokers and 15% in non-smokers).[51]

Previous reviews of effective interventions for adults with mental health conditions have been mixed in their findings; however, these are based on several small studies.[52–54] A recent, large multisite RCT compared varenicline, bupropion and NRT to placebo, and found pharmacological interventions increased long-term abstinence compared to the placebo in patients with psychiatric disorders.[20] The trial found no increased risk of moderate or severe adverse events.[20]

There is insufficient evidence to conclude that using NRT improves long-term abstinence rates among people with mental illness who smoke,[3] or people with substance use disorders, although there is some evidence of effectiveness for short-term abstinence.[55] Nevertheless, expert opinion is that NRT may be considered for use by people in this group who want help to stop smoking.

Other treatments and interventions

Table 1 summarises other treatments and interventions that people may ask about, or want to use, to help them stop smoking.

Discussion

The updated *New Zealand Guidelines for Helping People to Stop Smoking*[1] provide current evidence on effective interventions for smoking cessation and make recommendations based on this evidence. These guidelines will be updated in future as more research evidence becomes available.

In addition to these recommendations, the guidelines identify barriers and facilitators to providing smoking cessation. Healthcare professionals can have a positive or negative role in people's smoking behaviour, and barriers and facilitators to delivering smoking cessation (Table 2).

Providing support for people who smoke should always be done with an understanding of the broader context in which people start smoking,

Table 1: Other smoking cessation interventions.

Effective
Reduction-to-quit[56]
Written self-help materials[57]
Financial incentives[58]
Insufficient evidence
Acupuncture[59]
Other antidepressants (i.e., SSRI, MAOI)[60]
Anti-anxiety medication[61]
Competitions[62]
Heated tobacco products[2]
Hypnotherapy[63]
NicoBloc and NicoBrevin
Physical activity[64]
St John's Wort[60]
Harmful
Clonidine[65]

Table 2: Healthcare workers' barriers and facilitators to implementing the ABC pathway.

Barriers	**Facilitators**
Health workers who smoke	Ongoing training
Lack of time, knowledge, and skills	System supports, including leadership
Health workers not engaging if they assume a lack of patient motivation	Provision of a rationale specific to their area of work
Health workers' misperception that smoking cessation interventions are not effective	System prompts (e.g., automated systems, medical chart stickers)
Health workers' concerns that providing smoking cessation advice will adversely affect their relationship with a patient	Audits and feedback

why they continue to smoke and why they try to stop, such as their level of exposure to tobacco products, access to smoking cessation services and support, and their level of exposure to people who have successfully quit.

These guidelines highlight gaps in evidence. More research relevant to New Zealand priority populations is needed to investigate and evaluate interventions operating at the level of social groups and systems, and on the upstream determinants of smoking and quitting. Information on the relative cost-effectiveness of the interventions is also needed to inform decision-makers and clinicians about the "best buys" to achieve cessation outcomes.

Finally, individual-level smoking cessation interventions are important but should always be seen as one strategy among a comprehensive package of mutually reinforcing population-level tobacco control interventions aimed at tackling smoking in New Zealand.

COMPETING INTERESTS
Nil.

ACKNOWLEDGEMENTS
This work was funded through a contract with the New Zealand Ministry of Health.

AUTHOR INFORMATION
Dr Jessica McCormack: National Institute for Health Innovation, School of Population Health, The University of Auckland, New Zealand.
Associate Professor Natalie Walker: National Institute for Health Innovation, School of Population Health, The University of Auckland, New Zealand.
Professor Hayden McRobbie: National Drug and Alcohol Research Centre, University of New South Wales, Australia.
Dr Karen Wright: Te Kupenga Hauora Māori, The University of Auckland, New Zealand.
Associate Professor Vili Nosa: Pacific Health, School of Population Health, The University of Auckland, New Zealand.
Basil Fernandes: Counties Manukau Health Living Smokefree Service.
Professor Chris Bullen: National Institute for Health Innovation, School of Population Health, The University of Auckland, New Zealand.

CORRESPONDING AUTHOR
Chris Bullen: National Institute for Health Innovation, School of Population Health, The University of Auckland. c.bullen@auckland.ac.nz

URL
www.nzma.org.nz/journal-articles/revised-guidelines-for-smoking-cessation-in-new-zealand-2021

REFERENCES
1. Ministry of Health. The New Zealand Guidelines for Helping People to Stop Smoking: 2021 Update. 2021. Wellington: Ministry of Health.
2. United States Public Health Service Office of the Surgeon General and National Center for Chronic Disease Prevention and Health Promotion (US) Office on Smoking and Health. Smoking Cessation: A Report of the Surgeon General. Washington DC United States Public Health Service, 2020.
3. West R, Raw M, McNeill A, et al. Health-care interventions to promote and assist tobacco cessation: a review of efficacy, effectiveness and affordability for use in national guideline development. Addiction (Abingdon, England) 2015; 110: 1388-1403. DOI: https://doi.org/10.1111/add.12998.
4. Hartmann-Boyce J, Livingstone-Banks J, Ordóñez-Mena JM, et al. Behavioural interventions for smoking cessation: an overview and network meta-analysis. Cochrane Database of Systematic Reviews 2021. DOI: 10.1002/14651858.CD013229.pub2.
5. Stead LF, Buitrago D, Preciado N, et al. Physician advice for smoking cessation. Cochrane Database of Systematic Reviews 2013. DOI: 10.1002/14651858.CD000165.pub4.
6. Patnode CD, Henderson JT, Melnikow J, et al. Interventions for Tobacco Cessation in Adults, Including Pregnant Women: An Evidence Update for the US Preventive Services Task Force. 2021.
7. Aveyard P, Begh R, Parsons A, et al. Brief opportunistic smoking cessation interventions: a systematic review and meta-analysis to compare advice to quit and offer of assistance. Addiction (Abingdon, England) 2012; 107: 1066-1073.
8. Nghiem N, Cleghorn CL, Leung W, et al. A national quitline service and its promotion in the mass media: modelling the health gain, health equity and cost–utility. Tobacco Control 2018; 27: 434-441. DOI: 10.1136/tobaccocontrol-2017-053660.
9. Lancaster T and Stead LF. Individual behavioural counselling for smoking cessation. Cochrane Database of Systematic Reviews 2017. DOI: 10.1002/14651858.CD001292.pub3.
10. Taylor GMJ, Dalili MN, Semwal M, et al. Internet-based interventions for smoking cessation. Cochrane Database of Systematic Reviews 2017. DOI: 10.1002/14651858.CD007078.pub5.
11. Whittaker R, McRobbie H, Bullen C, et al. Mobile phone text messaging and app-based interventions for smoking cessation. Cochrane Database of Systematic Reviews 2019. DOI: 10.1002/14651858.CD006611.pub5.
12. Hartmann-Boyce J, Chepkin SC, Ye W, et al. Nicotine replacement therapy versus control for smoking cessation. Cochrane Database of Systematic Reviews 2018. DOI: 10.1002/14651858.CD000146.pub5.
13. Lindson N, Chepkin SC, Ye W, et al. Different doses, durations and modes of delivery of nicotine replacement therapy for smoking cessation. Cochrane Database of Systematic Reviews 2019. DOI: 10.1002/14651858.CD013308.
14. Mills EJ, Thorlund K, Eapen S, et al. Cardiovascular Events Associated With Smoking Cessation Pharmacotherapies. 2014; 129: 28-41. DOI: doi:10.1161/CIRCULATIONAHA.113.003961.
15. Cahill K, Lindson-Hawley N, Thomas KH, et al. Nicotine receptor partial agonists for smoking cessation. Cochrane Database of Systematic Reviews 2016. DOI: 10.1002/14651858.CD006103.pub7.

16. Thompson-Evans TP, Glover MP and Walker N. Cytisine's Potential to Be Used as a Traditional Healing Method to Help Indigenous People Stop Smoking: A Qualitative Study With Māori. Nicotine & Tobacco Research 2011; 13: 353-360. DOI: 10.1093/ntr/ntr002 %J Nicotine & Tobacco Research.
17. Walker N, Smith B, Barnes J, et al. Cytisine versus varenicline for smoking cessation in New Zealand indigenous Māori: A randomized controlled trial. Addiction (Abingdon, England) 2021; n/a. DOI: https://doi.org/10.1111/add.15489.
18. Walker N, Howe C, Glover M, et al. Cytisine versus Nicotine for Smoking Cessation. 2014; 371: 2353-2362. DOI: 10.1056/NEJMoa1407764.
19. Howes S, Hartmann-Boyce J, Livingstone-Banks J, et al. Antidepressants for smoking cessation. Cochrane Database of Systematic Reviews 2020. DOI: 10.1002/14651858.CD000031.pub5.
20. Evins AE, Benowitz NL, West R, et al. Neuropsychiatric Safety and Efficacy of Varenicline, Bupropion, and Nicotine Patch in Smokers With Psychotic, Anxiety, and Mood Disorders in the EAGLES Trial. J Clin Psychopharmacol 2019; 39: 108-116. DOI: 10.1097/JCP.0000000000001015.
21. Stead LF, Koilpillai P, Fanshawe TR, et al. Combined pharmacotherapy and behavioural interventions for smoking cessation. Cochrane Database of Systematic Reviews 2016. DOI: 10.1002/14651858.CD008286.pub3.
22. Chang P-H, Chiang C-H, Ho W-C, et al. Combination therapy of varenicline with nicotine replacement therapy is better than varenicline alone: a systematic review and meta-analysis of randomized controlled trials. BMC public health 2015; 15: 689. DOI: 10.1186/s12889-015-2055-0.
23. Hartmann-Boyce J, McRobbie H, Lindson N, et al. Electronic cigarettes for smoking cessation. Cochrane Database of Systematic Reviews 2020. DOI: 10.1002/14651858.CD010216.pub4.
24. Ministry of Health. Position Statement of Vaping, https://www.health.govt.nz/our-work/preventative-health-wellness/tobacco-control/vaping-smokefree-environments-and-regulated-products/position-statement-vaping#:~:text=The%20Ministry%20of%20Health%20encourages,the%20help%20of%20vaping%20products. (2020, accessed 6 April 2020).
25. Wilson N, Summers JA, Ait Ouakrim D, et al. Improving on estimates of the potential relative harm to health from using modern ENDS (vaping) compared to tobacco smoking. BMC Public Health 2021; 21: 2038. 2021/11/10. DOI: 10.1186/s12889-021-12103-x.
26. Health Quality & Safety Commission. He Matapihi Ki Te Kounga o NgĀ Manaakitanga Ā-hauora o Aotearoa 2019: A Window on the Quality of Aotearoa New Zealand's Health Care 2019. 2019. Wellington: Health Quality & Safety Commission.
27. Ministry of Health. Annual Update of Key Results 2020/21: New Zealand Health Sruvey. 2021. Wellington: Ministry of Health.
28. Chamberlain C, Perlen S, Brennan S, et al. Evidence for a comprehensive approach to Aboriginal tobacco control to maintain the decline in smoking: an overview of reviews among Indigenous peoples. Systematic reviews 2017; 6: 135. 2017/07/12. DOI: 10.1186/s13643-017-0520-9.
29. Fernandez C and Wilson D. Maori women's views on smoking cessation initiatives. Nursing Praxis in New Zealand 2008; 24: 27-40.
30. Ministry of Health. Evaluation of Culturally Appropriate Smoking Cessation Programme for Mäori Women and Their Whänau: Aukati Kai Paipa 2000. Ministry of Health Wellington, New Zealand, 2003.
31. Holt S, Timu-Parata C, Ryder-Lewis S, et al. Efficacy of bupropion in the indigenous Maori population in New Zealand. Thorax 2005; 60: 120-123. DOI: 10.1136/thx.2004.030239 %J Thorax.
32. Walker N, Parag V, Verbiest M, et al. Nicotine patches used in combination with e-cigarettes (with and without nicotine) for smoking cessation: a pragmatic, randomised trial. The Lancet Respiratory Medicine 2020; 8: 54-64. DOI: https://doi.org/10.1016/S2213-2600(19)30269-3.
33. Bramley D, Riddell T, Whittaker R, et al. Smoking cessation using mobile phone text messaging is as effective in Maori as non-Maori. The New Zealand medical journal 2005; 118: U1494.
34. Glover M, Kira A, Walker N, et al. Using incentives to encourage smoking abstinence among pregnant indigenous women? A feasibility study. Maternal and child health journal 2015; 19: 1393-1399. 2014/11/28. DOI: 10.1007/s10995-014-1645-2.
35. Kira A, Glover M, Walker N, et al. Recruiting Pregnant Indigenous Women Who Smoke into a High Contact Incentivized Cessation Trial: A Feasibility Study. Nicotine & tobacco research : official journal of the Society for Research on Nicotine and Tobacco 2016; 18: 2036-2040. 2016/05/08. DOI: 10.1093/ntr/ntw106.
36. Roberts V, Glover M, McCowan L, et al. Exercise to Support Indigenous Pregnant Women to Stop Smoking: Acceptability to Māori. Maternal and child health journal 2017; 21: 2040-2051. 2017/07/14. DOI: 10.1007/s10995-017-2303-2.
37. Glover M, Kira A and Smith C. Enlisting "Aunties" to Support Indigenous Pregnant Women to Stop

Smoking: Feasibility Study Results. Nicotine & tobacco research : official journal of the Society for Research on Nicotine and Tobacco 2016; 18: 1110-1115. 2015/08/09. DOI: 10.1093/ntr/ntv146.
38. Ryan D, Grey C and Mischewski B. Tofa Saili: A review of evidence about health equity for Pacific Peoples in New Zealand. 2019. Wellington: Pacific Perspecitives Ltd.
39. Whittaker R, Umali E, Tanielu H, et al. TXTTaofiTapaa: pilot trial of a Samoan mobile phone smoking cessation programme. Journal of Global Health Reports 2019; 3.
40. Kwan P, Sabado-Liwag M, Lee C, et al. Development of an Online Smoking Cessation Curriculum for Pacific Islanders: A Community-Based Participatory Research Approach. Prog Community Health Partnersh 2017; 11: 263-274. DOI: 10.1353/cpr.2017.0031.
41. Pineles BL, Park E and Samet JM. Systematic Review and Meta-Analysis of Miscarriage and Maternal Exposure to Tobacco Smoke During Pregnancy. American Journal of Epidemiology 2014; 179: 807-823. DOI: 10.1093/aje/kwt334.
42. Allen M, Barnes C, Dalley A, et al. 2012. Best Practice Framework for Dedicated Pregnancy Smoking Cessation Services: Report for the Ministry of Health. Wellington: Allen & Clarke.
43. Rockhill KM, Tong VT, Farr SL, et al. Postpartum Smoking Relapse After Quitting During Pregnancy: Pregnancy Risk Assessment Monitoring System, 2000–2011. Journal of Women's Health 2016; 25: 480-488. DOI: 10.1089/jwh.2015.5244.
44. Chamberlain C, O'Mara-Eves A, Porter J, et al. Psychosocial interventions for supporting women to stop smoking in pregnancy. Cochrane Database of Systematic Reviews 2017. DOI: 10.1002/14651858.CD001055.pub5.
45. Claire R, Chamberlain C, Davey MA, et al. Pharmacological interventions for promoting smoking cessation during pregnancy. Cochrane Database of Systematic Reviews 2020. DOI: 10.1002/14651858.CD010078.pub3.
46. Karnieg T and Wang X. Cytisine for smoking cessation. CMAJ 2018; 190: E596-E596. DOI: 10.1503/cmaj.171371.
47. Bar-Zeev Y, Lim LL, Bonevski B, et al. Nicotine replacement therapy for smoking cessation during pregnancy. The Medical journal of Australia 2018; 208: 46-51. 2018/01/11. DOI: 10.5694/mja17.00446.
48. Fanshawe TR, Halliwell W, Lindson N, et al. Tobacco cessation interventions for young people. Cochrane Database of Systematic Reviews 2017. DOI: 10.1002/14651858.CD003289.pub6.
49. Selph S, Patnode C, Bailey SR, et al. Primary Care–Relevant Interventions for Tobacco and Nicotine Use Prevention and Cessation in Children and Adolescents: Updated Evidence Report and Systematic Review for the US Preventive Services Task Force. JAMA 2020; 323: 1599-1608. DOI: 10.1001/jama.2020.3332 %J JAMA.
50. Marsh L, Dawson A and McGee R. What Do Young New Zealanders Want in Terms of Smoking Cessation? Journal of Smoking Cessation 2014; 9: 98-108. 2013/10/23. DOI: 10.1017/jsc.2013.30.
51. Ministry of Health. Tobacco Use 2012/13: New Zealand Health Survey. . 2014. Wellington: Ministry of Health.
52. Lightfoot K, Panagiotaki G and Nobes G. Effectiveness of psychological interventions for smoking cessation in adults with mental health problems: A systematic review. British journal of health psychology 2020; 25: 615-638. 2020/07/18. DOI: 10.1111/bjhp.12431.
53. Siskind DJ, Wu BT, Wong TT, et al. Pharmacological interventions for smoking cessation among people with schizophrenia spectrum disorders: a systematic review, meta-analysis, and network meta-analysis. The lancet Psychiatry 2020; 7: 762-774. 2020/08/24. DOI: 10.1016/s2215-0366(20)30261-3.
54. Secades-Villa R, González-Roz A, García-Pérez Á, et al. Psychological, pharmacological, and combined smoking cessation interventions for smokers with current depression: A systematic review and meta-analysis. PloS one 2017; 12: e0188849. 2017/12/06. DOI: 10.1371/journal.pone.0188849.
55. Apollonio D, Philipps R and Bero L. Interventions for tobacco use cessation in people in treatment for or recovery from substance use disorders. Cochrane Database of Systematic Reviews 2016. DOI: 10.1002/14651858.CD010274.pub2.
56. Lindson N, Klemperer E, Hong B, et al. Smoking reduction interventions for smoking cessation. Cochrane Database Syst Rev 2019; 9: Cd013183. 2019/10/01. DOI: 10.1002/14651858.CD013183.pub2.
57. Livingstone-Banks J, Ordóñez-Mena JM and Hartmann-Boyce J. Print-based self-help interventions for smoking cessation. Cochrane Database Syst Rev 2019; 1: Cd001118. 2019/01/10. DOI: 10.1002/14651858.CD001118.pub4.
58. Notley C, Gentry S, Livingstone-Banks J, et al. Incentives for smoking cessation. Cochrane Database Syst Rev 2019; 7: Cd004307. 2019/07/18. DOI: 10.1002/14651858.CD004307.pub6.
59. White AR, Rampes H, Liu JP, et al. Acupuncture and related interventions for smoking cessation. Cochrane Database Syst Rev 2011: Cd000009.

2011/01/21. DOI: 10.1002/14651858.CD000009.pub3.
60. Howes S, Hartmann-Boyce J, Livingstone-Banks J, et al. Antidepressants for smoking cessation. Cochrane Database Syst Rev 2020; 4: Cd000031. 2020/04/23. DOI: 10.1002/14651858.CD000031.pub5.
61. Hughes JR, Stead LF and Lancaster T. Anxiolytics for smoking cessation. Cochrane Database Syst Rev 2000; 2000: Cd002849. 2000/10/18. DOI: 10.1002/14651858.Cd002849.
62. Fanshawe TR, Hartmann-Boyce J, Perera R, et al. Competitions for smoking cessation. Cochrane Database Syst Rev 2019; 2: Cd013272. 2019/02/21. DOI: 10.1002/14651858.Cd013272.
63. Barnes J, McRobbie H, Dong CY, et al. Hypnotherapy for smoking cessation. Cochrane Database Syst Rev 2019; 6: Cd001008. 2019/06/15. DOI: 10.1002/14651858.CD001008.pub3.
64. Ussher MH, Faulkner GEJ, Angus K, et al. Exercise interventions for smoking cessation. Cochrane Database Syst Rev 2019; 2019 2019/11/07. DOI: 10.1002/14651858.CD002295.pub6.
65. Gourlay SG, Stead LF and Benowitz NL. Clonidine for smoking cessation. Cochrane Database Syst Rev 2004; 2004: Cd000058. 2004/07/22. DOI: 10.1002/14651858.CD000058.pub2.

Acute alcohol use and suicide deaths: an analysis of New Zealand coronial data from 2007–2020

Rose Crossin, Lana Cleland, Annette Beautrais, Katrina Witt, Joseph M Boden

ABSTRACT

AIMS: Acute alcohol use is a proximal risk factor for suicide. However, the proportion of suicide deaths involving acute alcohol use has not been quantified in New Zealand. We sought to quantify and characterise the association between acute alcohol use and suicide.

METHODS: Data for all suicides (≥15 years) between July 2007 and December 2020 were drawn from the National Coronial Information System. Acute alcohol use was defined as blood alcohol concentration (BAC) >50mg/100mL. Logistic regression was used to compare characteristics between suicide deaths with and without acute alcohol use.

RESULTS: Twenty-six point six percent of suicide deaths involved acute alcohol use. No difference in the association was found by sex (male AOR: 0.87 (95%CI: 0.74,1.02)). Ethnicity differences were identified (Māori AOR: 1.20 (95%CI: 1.01,1.42), Pacific AOR: 1.46 (95%CI: 1.10,2.00)). Those aged 15–54 years had similar risks of suicide involving acute alcohol use, with a lower association in older age groups.

CONCLUSIONS: Acute alcohol use was identified in approximately one quarter of suicides, with stronger associations in those of Māori and Pasifika ethnicity, and those aged <55 years. Acute alcohol use is a significant but modifiable risk factor for suicide in New Zealand.

Acute alcohol use is a known proximal risk factor for suicide,[1] and has been shown to significantly increase risk of suicide attempt, particularly at high levels of acute consumption.[2] For suicide deaths, reviews find the prevalence of acute alcohol use range from 10% to 69%, differing by population demographics including age and sex.[3] Alcohol may neurocognitively trigger suicide attempts by increasing impulsivity and disinhibition,[4] weakening psychological barriers to suicide attempts,[5] or by increasing despair, and cognitively impairing efforts to mitigate despair.[6] Acute use of alcohol is associated with use of more lethal suicide means,[4,5] and may potentiate the effects of other drugs consumed in overdose,[3] thereby reducing the likelihood of surviving an attempt. These findings suggest that acute alcohol use should be a focus for suicide prevention.

Recent coronial data studies in Australia and South Korea provide data about characteristics of acute alcohol use in suicide.[7–9] In Australia, around one quarter (26.7%) of suicide decedents had a blood alcohol concentration (BAC) of ≥0.05g/100mL (the legal drink-driving limit in Australia); alcohol use prior to suicide was associated with male sex and use of more lethal means.[7] In South Korea, a study of 683 suicide decedents found that almost one third (28.7%) had a BAC ≥0.08g/100mL (the legal drink-driving limit in that country, and defined as "intoxication"); acute alcohol intoxication was associated with having no underlying medical or psychiatric diagnosis.[8] This negative association between intoxication and psychiatric history has also been identified in Australia: alcohol use prior to suicide was associated with acute stress (e.g., relationship breakdown), but not with psychiatric illness.[9] These studies suggest that acute alcohol use may increase impulsive suicide risk in those without psychiatric risk factors but who are exposed to an acute stressor.

Suicide is a significant public health issue in New Zealand. The suicide rate in June 2021 was 11.6/100,000 population.[10] This rate is higher for Māori (15.8/100,000), and for those aged 15–24 (11.4 and 22.2 per 100,000 for females and males, respectively).[10] The World Health Organization emphasises that almost one in five of all suicides can be attributed to alcohol use,[11] highlighting alcohol policy as a point of intervention for reducing suicide.[12] Not targeting alcohol represents a missed opportunity for suicide prevention efforts.[13] This is pertinent, as New Zealand has high levels of alcohol use; 80% of New Zealanders ≥15 years have drunk alcohol in the past year;

20% drink at hazardous levels.[14] However, the relationship between alcohol and suicide has not been examined systematically in New Zealand, and the national Suicide Prevention Strategy fails to identify alcohol harm reduction strategies as a means of suicide prevention.[15]

We sought to inform suicide prevention by improving understanding of a potentially significant and modifiable risk factor, using New Zealand-specific data. The objective of this research was to quantify and characterise the association between acute alcohol use and suicide death in New Zealand, to provide a baseline against which future interventions or trends can be assessed. Specifically, we asked: 1) how prevalent is acute alcohol use within suicide deaths in New Zealand; 2) has the proportion of suicides involving acute alcohol use changed over time, and 3) what are the characteristics of suicides involving acute alcohol use?

Methods

Data were drawn from the National Coronial Information System (NCIS), which compiles cases from the Coronial Service of New Zealand. This project was approved by the University of Otago Human Research Ethics Committee (HD20/102) with a second level of review and approval by NCIS (NZ019).

Case identification and inclusion criteria

New Zealand suicide data are available from NCIS for 1 July 2007 onwards. Cases were extracted from this date to 31 December 2020, with the search last run on 7 September 2021. Eligibility criteria were closed cases, coded in NCIS as intentional self-harm (i.e., suicide), where the person was ≥15 years at death. The rationale for this age cut-off recognises that suicidal intent differs in individuals, and while intent may be determined in children as young as 12,[16] the World Health Organization uses 15 as the lower age group in global statistics and reporting. As cases can take up to two years to be closed, not all suicide deaths from 2019 and 2020 were included in the sample of eligible cases. NCIS reports quarterly on case closure percentages across all deaths,[17] based on information provided by the Coronial Services of New Zealand; the report for all deaths (not specific to suicide) that most closely matches the data collection period of this study was published on 1 October 2021, and it indicated that case closure percentages for 2019 and 2020 at that time were 70.5% and 55.8%, respectively. Inclusion criteria were then applied in the following sequence:

1. Is toxicology data available?
2. Was alcohol measured in blood post-mortem in toxicological analysis?
3. If an additional ante-mortem blood sample was taken, post-mortem and ante-mortem samples must concur.
4. If decomposition was noted, alcohol concentration must also have been confirmed through measurement in vitreous humour.

The rationale for criterion 4 (above) is that alcohol can be produced endogenously through decomposition; however, vitreous humour is less prone to microbial invasion and post-mortem effects.[18] These criteria are consistent with those of a recent Australian study,[7] and facilitate comparison of results.

Characteristics of suicide deaths

The following characteristics were extracted, primarily using NCIS-coded data with any missing data searched for in the linked coronial reports:

- Age – age in years at death, subsequently grouped into ten-year intervals
- Sex – female, male
- Employment status – employed, unemployed, student, retired/pensioned, other (including categories of home duties, prisoner, still enquiring, child not at school), unknown
- Marital status – Never married, widowed, divorced/separated, married/de facto, unknown
- Ethnicity – European, Māori, Pacific peoples, Asian, Middle Eastern/Latin American/African, other ethnicity (consistent with 2018 Census ethnic group summaries)[19]
- Method of death – as follows, based on International Classification of Diseases ICD-10-AM code;
    - Poisoning – X40-X49, X60-X69, X85-X90, Y10-Y19
    - Hanging – W75-W84, X70, X91, Y20
    - Drowning – W65-W74, X71, X92, Y21
    - Firearm – W32-W34, X72-X74, X93-X95, Y22-Y24
    - Sharp object – W25-W29, X78, X99, Y28
    - Falls – W00-W19, X80, Y01, Y30

    - Other – W22-W23, X00, X30-X31, X75-X79, X81-X84, Y23, Y31
- Year of death.

Risk factors such as mental health history, chronic pain, or financial problems are not coded in NCIS. These factors were therefore excluded from analyses, because it cannot be assumed that the absence of these factors in Coronial or police reports means that they were not present.

Post-mortem BAC was extracted from toxicological and coronial reports and then dichotomised as:

- No acute alcohol use – BAC ≤50mg/100mL of blood
- Acute alcohol use – BAC >50mg/100mL of blood.

This categorisation is consistent with the current legal BAC for adults (20 years and older) when driving in New Zealand (i.e., 0.05%). As a sensitivity test, analyses were run using two additional BAC levels to define acute alcohol use: >30mg/100mL (where some individuals may show signs of impairment) and >80mg/100mL (New Zealand's legal driving limit until December 2014). Whether alcohol was identified in NCIS records as a contributory cause of death was also determined by use of ICD-10-AM codes (F10.0, F10.1–10.9, R78.0, T51, X45 or X65) and searching for the word "alcohol" at all levels of the cause of death fields. If any one of these codes was identified, we deemed alcohol had been identified as a contributory cause of death. In many instances, blood alcohol was the only toxicological test on record. Therefore, data on other psychoactive substances were not extracted.

Statistical analysis

Statistical analysis was conducted in Stata (version 16.1 for Windows).[20] Fields with n<5 were blinded to minimise risk of individuals being identified, with associated cell counts suppressed to prevent blinded cells from being calculated.

For each year of the study period, the proportion of suicide deaths involving acute alcohol use was calculated, to avoid the effects of population change over that time. Data are presented visually, without statistical analysis. These data are included to enable assessment of any future intervention relative to baseline trends.

To test for differences between included and excluded cases, and to compare characteristics of suicide deaths with and without acute alcohol use, logistic regression modelling was undertaken. Multivariate logistic regression models were used to compute unadjusted and adjusted odds ratios (OR, AOR; 95% CIs) controlling for the effects of all other significant variables (age, sex, employment status, marital status, ethnicity and method of death).

Results

Between 1 July 2007 and 31 December 2020, 6,072 New Zealanders aged ≥15 years died by suicide and had NCIS records. No toxicology data were available for 651 cases (10.7%); no measurement of BAC was undertaken post-mortem (n=235; 3.9%); ante-mortem and post-mortem BAC levels did not concur (n=4; 0.1%); and decomposition was noted but alcohol concentration was not confirmed in vitreous humour (n=524; 8.6%). These 1,414 cases were, therefore, excluded leaving a total sample of 4,658 cases (76.7%) eligible for inclusion. The percentage of cases excluded per year of the study period are shown in Supplementary Table 1.

Table 1 compares characteristics of excluded and included cases. There was no significant difference between excluded and included cases in relation to sex. Older age groups were less likely to be included than those aged 15–24. Those who were widowed were less likely to be included than those who were never married, while those who were married were more likely to be included.

Of included suicides, 1,238 (26.6%) involved acute alcohol use, BACs are shown in Table 2.

Figure 1 shows the proportion of suicides involving acute alcohol use across the 14-year study period. This fraction ranged from 21.7% to 33.3% across the 14 years (2007–2020), with no clear trend over time.

Of the 1,238 suicides involving acute alcohol use, 416 (33.6%) were coded in NCIS as alcohol being a contributory cause of death (the most commonly identified codes were F10.0 (acute alcohol intoxication) and F10.1 (harmful use of alcohol)). In addition, 154 suicides where acute alcohol use was not identified (BAC ≤50mg/100mL) also had alcohol coded as a contributory cause of death, occurring predominantly in the context of alcohol dependence and/or a low level of BAC considered contributory to a poly-drug overdose.

The characteristics of suicides without and with acute alcohol use are described in Table 3. The proportion of suicides involving acute alcohol use declined with increasing age; however,

Table 1: Descriptive characteristics of included cases compared to excluded cases and results of logistic regression modelling showing characteristics associated with inclusion.

Characteristic		**Excluded n (%)**	**Included n (%)**	**OR (95% CI)**	**AOR (95% CI)**
Age	15–24	240 (18.2)	1,081 (81.8)	REF	REF
	25–34	236 (22.0)	836 (78.0)	0.79 (0.64–0.96) *	0.73 (0.59–0.91) **
	35–44	239 (23.0)	802 (77.0)	0.75 (0.61–0.91) **	0.67 (0.54–0.85) **
	45–54	279 (23.7)	897 (76.3)	0.74 (0.59–0.87) **	0.64 (0.51–0.81) ***
	55–64	208 (26.7)	571 (73.3)	0.61 (0.49–0.75) ***	0.56 (0.43–0.72) ***
	65–74	7 (25.9)	20 (74.1)	0.63 (0.27–1.52)	0.62 (0.25–1.54)
	75+	205 (31.3)	451 (68.8)	0.49 (0.39–0.61) ***	0.61 (0.42–0.90) *
Sex	**Female**	**360 (22.9)**	**1,211 (77.1)**	**REF**	**REF**
	Male	1,054 (23.4)	3,447 (76.6)	0.97 (0.85–1.11)	0.97 (0.84–1.12)
Employment status	**Employed**	**602 (22.3)**	**2,101 (77.7)**	**REF**	**REF**
	Unemployed	377 (23.2)	1,248 (76.8)	0.95 (0.82–1.10)	1.01 (0.87–1.17)
	Student	83 (18.2)	372 (81.8)	1.28 (1.00–1.66)	1.11 (0.84–1.49)
	Retired/ pensioner	240 (32.3)	504 (67.7)	0.60 (0.50–0.72) ***	0.71 (0.52–0.96) *
	Other	47 (16.8)	233 (83.2)	1.42 (1.03–1.97) *	1.48 (1.06–2.06) *
	Unknown	65 (24.5)	200 (75.5)	0.88 (0.66–1.18)	0.95 (0.71–1.29)
Marital status	**Never married**	**610 (24.0)**	**1,930 (76.0)**	**REF**	**REF**
	Widowed	82 (34.3)	157 (65.7)	0.61 (0.46–0.80) ***	1.07 (0.77–1.49)
	Divorced/ separated	224 (25.8)	646 (74.3)	0.91 (0.76–1.09)	1.20 (0.99–1.46)
	Married/ de facto	410 (19.5)	1,695 (80.5)	1.31 (1.13–1.50) ***	1.66 (1.41–1.95) ***
	Unknown	88 (27.7)	230 (72.3)	0.83 (0.64–1.07)	0.97(0.74–1.27)

Table 1 (continued): Descriptive characteristics of included cases compared to excluded cases and results of logistic regression modelling showing characteristics associated with inclusion.

Characteristic		Excluded n (%)	Included n (%)	OR (95% CI)	AOR (95% CI)
Ethnicity	**European**	**1,023 (24.4)**	**3,174 (75.6)**	**REF**	**REF**
	Māori	258 (20.8)	983 (79.2)	1.23 (1.05–1.43) **	0.93 (0.78–1.10)
	Pacific peoples	61 (23.3)	201 (76.7)	1.06 (0.79–1.43)	0.79 (0.58–1.07)
	Asian	62 (19.8)	252 (80.3)	1.31 (0.98–1.74)	1.14 (0.85–1.53)
	Middle Eastern/Latin American/African	5 (19.2)	21 (80.8)	1.35 (0.51–3.60)	1.18 (0.44–3.18)
	Other ethnicity	5 (15.6)	27 (84.4)	1.74 (0.67–4.53)	1.74 (0.66–4.62)
Method of death	**Poisoning**	**369 (28.4)**	**932 (71.6)**	**REF**	**REF**
	Hanging	746 (20.4)	2,911 (79.6)	1.55 (1.34–1.79) ***	1.34 (1.15–1.57) ***
	Drowning	33 (28.7)	82 (71.3)	0.98 (0.65–1.50)	1.02 (0.67–1.57)
	Firearm	119 (25.0)	358 (75.1)	1.19 (0.94–1.51)	1.13 (0.88–1.45)
	Sharp object	38 (31.2)	84 (68.9)	0.86 (0.59–1.31)	0.83 (0.55–1.25)
	Falls	38 (22.8)	129 (77.3)	1.34 (0.92–1.97)	1.24 (0.84–1.83)
	Other	71 (30.5)	162 (69.5)	0.90 (0.67–1.22)	0.83 (0.61–1.13)

NB: Multivariate logistic regression models were used to compute both unadjusted odds ratios (OR), and adjusted odds ratios (AOR) controlling for the effects of all other significant variables (age, sex, employment status, marital status, ethnicity and method of death). Data are reported with 95% confidence intervals (CI). REF – reference group. * p<0.05, ** p<0.01, *** p<0.001.

the 65–74 age group data could not be reported due to small numbers. The fraction of male and female suicides involving acute alcohol use were almost identical. Of these, males were 26.5%; median BAC 142mg/100mL; interquartile range 101–188mg/100mL); and females were 26.7%; median BAC 155mg/100mL; interquartile range 109–203mg/100mL). Māori (32.3%) and Pacific peoples (35.3%) had higher proportions of suicides involving acute alcohol use than Europeans (25.4%) and Asians (11.9%).

Table 4 summarises the logistic regression model comparing suicide deaths with and without acute alcohol use, and shows ORs for each independent variable, unadjusted and adjusted (for age, sex, employment status, marital status, ethnicity, suicide means). This analysis confirms the association between suicide involving acute alcohol use, and between being young/middle aged (<55 years), employed, of Māori or Pacific ethnicity, and using hanging as the suicide method. Overall, there was minimal effect on the ORs after adjustment, except for being widowed (120 (76.4%) of those who were widowed were aged 75+). Sensitivity tests of the two additional BACs utilised for logistic regression modelling are presented in the Supplementary File; there was a minimal impact on the ORs; however, some covariates showed an alteration in significance level.

Table 2: Identified blood alcohol concentrations (BAC) in included suicide deaths.

BAC range	n	%
≤50mg/100mL	3,420	73.4%
51–100mg/100mL	289	6.2%
101–150 mg/100mL	363	7.8%
151–200 mg/100mL	322	6.9%
mg/100mL	175	3.8%
> 250mg/100mL	89	1.9%

NB: BAC – blood alcohol concentration reported in milligrams per 100 millilitres of blood.

Figure 1: The proportion of suicide deaths with acute alcohol use from 2007–2020 (shown as a percentage by year) show no consistent increasing or decreasing trend over the study period.

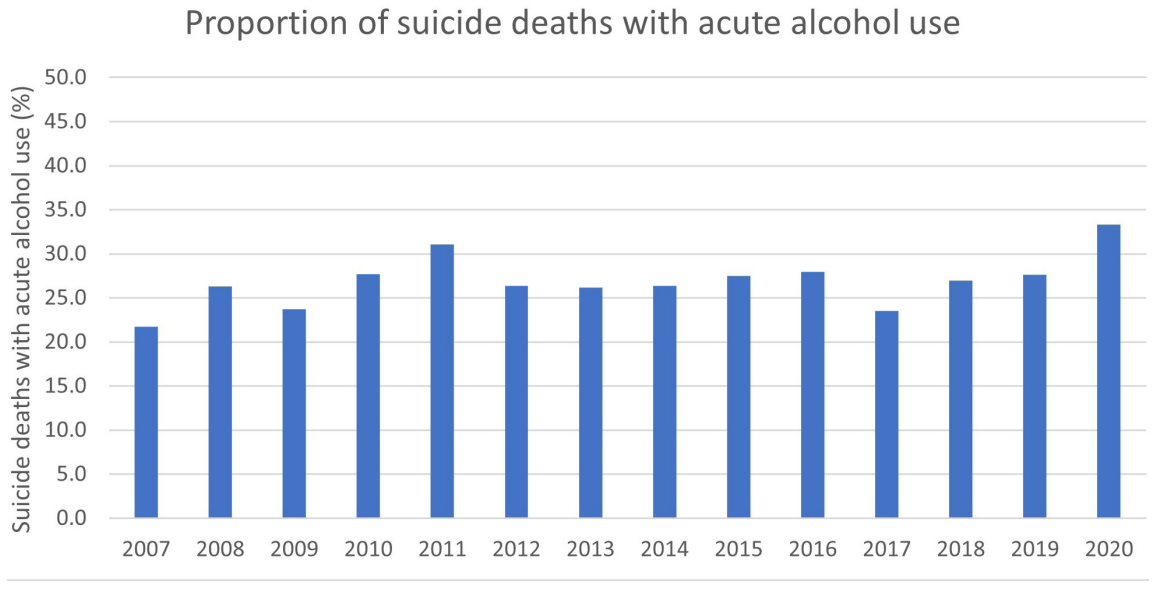


Table 3: Characteristics comparison between suicide deaths without and with acute alcohol use (AAU).

Characteristic		No AAU n (%)	AAU n (%)	Total
Age	15–24	771 (71.3)	310 (28.7)	1,081
	25–34	572 (68.4)	264 (31.6)	836
	35–44	553 (69.0)	249 (31.0)	802
	45–54	656 (73.1)	241 (26.9)	897
	55–64	448 (78.5)	123 (21.5)	571
	65–74	Blinded for confidentiality	n<5	20
	75+	404 (89.6)	47 (10.4)	451
Sex	**Female**	**888 (73.3)**	**323 (26.7)**	**1,211**
	Male	2,532 (73.5)	915 (26.5)	3,447
Employment status	**Employed**	**1,439 (68.5)**	**662 (31.5)**	**2,101**
	Unemployed	911 (73.0)	337 (27.0)	1,248
	Student	296 (79.6)	76 (20.4)	372
	Retired/pensioner	448 (88.9)	56 (11.1)	504
	Other	185 (79.4)	48 (20.6)	233
	Unknown	141 (70.5)	59 (29.5)	200
Marital status	**Never married**	**1,393 (72.2)**	**537 (27.8)**	**1,930**
	Widowed	125 (79.6)	32 (20.4)	157
	Divorced/separated	467 (72.3)	179 (27.7)	646
	Married/de facto	1,272 (75.0)	423 (25.0)	1,695
	Unknown	163 (70.9)	67 (29.1)	230

Table 3 (continued): Characteristics comparison between suicide deaths without and with acute alcohol use (AAU).

Characteristic		No AAU n (%)	AAU n (%)	Total
Ethnicity	**European**	**2,368 (74.6)**	**806 (25.4)**	**3,174**
	Māori	665 (67.7)	318 (32.3)	983
	Pacific peoples	130 (64.7)	71 (35.3)	201
	Asian	222 (88.1)	30 (11.9)	252
	Middle Eastern/ Latin American/African	Blinded for confidentiality	n<5	21
	Other ethnicity	17 (63.0)	10 (37.0)	27
Method of death	**Poisoning**	**722 (77.5)**	**210 (22.5)**	**932**
	Hanging	2,044 (70.2)	867 (29.8)	2,911
	Drowning	67 (81.7)	15 (18.3)	82
	Firearm	272 (76.0)	86 (24.0)	358
	Sharp object	71 (84.5)	13 (15.5)	84
	Falls	110 (85.3)	19 (14.7)	129
	Other	134 (82.7)	28 (17.3)	162

NB: Results are not shown when numbers are less than five (n<5) and related cells are blinded to prevent calculation of suppressed cells (which would increase the likelihood that individual cases could be identified).

Table 4: Summary of logistic regression modelling for risk of suicide death involving acute alcohol use (AAU) by case characteristics.

Characteristic		OR	95% CI	p value	AOR	95% CI	p value
Age	**15–24**	**REF**			**REF**		
	25–34	1.15	0.94, 1.40	0.169	1.11	0.90, 1.38	0.325
	35–44	1.12	0.92, 1.37	0.266	1.11	0.88, 1.40	0.370
	45–54	0.91	0.75, 1.11	0.371	0.93	0.73, 1.19	0.575
	55–64	0.68	0.54, 0.87	0.002	0.74	0.56, 0.99	0.041
	65–74	0.62	0.21, 1.87	0.399	0.90	0.29, 2.86	0.863
	75+	0.29	0.21, 0.40	<0.001	0.42	0.25, 0.72	0.002
Sex	**Female**	**REF**			**REF**		
	Male	0.99	0.86, 1.15	0.931	0.87	0.74, 1.02	0.087
Employment	**Employed**	**REF**			**REF**		
	Unemployed	0.80	0.69, 0.94	0.006	0.73	0.62, 0.85	<0.001
	Student	0.56	0.43, 0.73	<0.001	0.49	0.36, 0.66	<0.001
	Retired/pensioner	0.27	0.20, 0.36	<0.001	0.49	0.31, 0.76	0.002
	Other	0.56	0.41, 0.78	0.001	0.51	0.36, 0.71	<0.001
	Unknown	0.91	0.66, 1.25	0.559	0.86	0.62, 1.20	0.375
Marital status	**Never married**	**REF**			**REF**		
	Widowed	0.66	0.44, 0.99	0.045	1.79	1.10, 2.90	0.019
	Divorced/separated	0.99	0.81, 1.21	0.955	1.05	0.84, 1.31	0.654
	Married/de facto	0.86	0.74, 1.00	0.051	0.92	0.77, 1.10	0.329
	Unknown	1.07	0.79, 1.44	0.676	1.19	0.86, 1.63	0.289

Table 4 (continued): Summary of logistic regression modelling for risk of suicide death involving acute alcohol use (AAU) by case characteristics.

Characteristic		OR	95% CI	p value	AOR	95% CI	p value
Ethnicity	**European**				**REF**		
	Māori	1.40	1.20, 1.64	<0.001	1.20	1.01, 1.42	0.043
	Pacific peoples	1.60	1.19, 2.17	0.002	1.46	1.10, 2.00	0.018
	Asian	0.40	0.27, 0.59	<0.001	0.42	0.28, 0.63	<0.001
	Middle Eastern/Latin American/African	0.49	0.14, 1.67	0.253	0.45	0.13, 1.56	0.208
	Other ethnicity	1.73	0.79, 3.79	0.172	1.68	0.75, 3.77	0.209
Method of death	**Poisoning**	**REF**			**REF**		
	Hanging	1.46	1.23, 1.73	<0.001	1.30	1.07, 1.56	0.007
	Drowning	0.77	0.43, 1.38	0.377	1.04	0.57, 1.89	0.891
	Firearm	1.09	0.82, 1.45	0.569	1.10	0.81, 1.48	0.544
	Sharp object	0.63	0.34, 1.16	0.138	0.65	0.35, 1.21	0.174
	Falls	0.59	0.36, 0.99	0.045	0.58	0.34, 0.98	0.040
	Other	0.72	0.46, 1.11	0.136	0.67	0.43, 1.05	0.078

NB: Multivariate logistic regression models were used to compute both unadjusted odds ratios (OR), and adjusted odds ratios (AOR) controlling for the effects of all other significant variables (age, sex, employment status, marital status, ethnicity and method of death). Data are reported with 95% confidence intervals (CI). REF – reference group.

Discussion

We quantified and characterised the association between acute alcohol use and suicide in New Zealand, by analysing coronial data from 2007 to 2020, in order to provide a baseline dataset for the association. We found that around one quarter (26.6%) of all suicides over the study period involved acute alcohol use. While this is the first time that the proportion of suicide deaths involving acute alcohol use has been quantified in New Zealand, these findings are consistent with international studies: meta-analytic findings show the prevalence of acute alcohol use in suicides internationally ranged from 26.5% to 44.4%,[2] and a recent Australian study found 26.7% of suicides between 2010 and 2015 involved acute alcohol use.[7] The proportion of New Zealand suicides involving acute alcohol use was stable over the 14-year study period, indicating that acute alcohol use has a strong, persistent and long-standing association with suicide.

While the overall proportion of suicides involving acute alcohol use in New Zealand was comparable with other similar countries, we found key differences in demographic characteristics. Equal fractions of male and female suicides in New Zealand involved acute alcohol use, in contrast to international studies which have consistently identified males as having a higher fraction of suicides involving acute alcohol use.[7–9] This difference may reflect New Zealand's alcohol culture, but is difficult to explain given that data from the New Zealand Health Survey shows that hazardous drinking rates in males are approximately double those of females.[14] However, New Zealand has rates of foetal alcohol spectrum disorder substantially higher than the global prevalence estimate,[21] which suggests that female alcohol consumption may be higher than found in current data sources. In a number of OECD countries, including Australia and New Zealand, suicides in young females have increased, particularly among young indigenous females.[22] Given that risk factors for binge drinking differ between males and females,[23] there is a need for further research focussed on female alcohol use, ethnicity, drinking patterns and suicidal behaviour, in order to inform development of interventions specific to female needs, and which are culturally appropriate and responsive.

We found that those aged between 15 and 54 years had similar risks of suicide involving acute alcohol use, in contrast to the Australian study that found middle age groups (ages 35–44) had increased risk.[7] This finding is of concern given New Zealand's high teenage suicide rate,[24] and points to alcohol use being an important point of intervention in reducing teenage suicide. However, these findings were pooled across the study period, and adolescent hazardous drinking declined overall in New Zealand between 2001 and 2012,[25] while hazardous drinking in older people is of increasing concern.[26] These time-dynamic changes suggest the need to monitor consumption patterns in different demographic groups, as well as the relationship between acute alcohol use and suicide. We also found significant ethnicity differences, with Māori and Pacific peoples more likely to die by suicide involving acute alcohol use than European and Asian ethnicities. This observation is a substantial health equity issue, and may reflect multiple risk factors for hazardous alcohol use that disproportionately impact Māori and Pacific peoples, including; neighbourhood availability of alcohol,[27] experiences of discrimination,[28] and the effects of trauma.[29] There are well-established inequities in New Zealand for both alcohol-related harm[30] and suicide;[10] this study adds to that body of knowledge and supports the need for addressing alcohol as a contributor to health inequities.

This study provides the first known quantification of acute alcohol use in New Zealand suicides, but limitations need to be acknowledged. Some differences in the characteristics of included and excluded cases may be a potential source of bias. In particular, older age groups were more likely to be excluded from the final sample of cases, with almost half of exclusions due to a lack of toxicology data. Reasons for this are unclear but the characteristics of the decedent may influence testing decisions and contribute to possible bias. Additionally, BAC was the only toxicological test ordered in many cases, which means that the contribution of other psychoactive substances could not be evaluated. We recommend that toxicology should be ordered, and BAC analysed, for every suspected suicide. This recommendation is important, since NCIS-coding of alcohol as a contributory cause of death cannot be solely relied upon as a definition of alcohol's contribution to suicide. We found that only one third of suicides involving acute alcohol use (as defined by BAC results) in New Zealand had alcohol coded as contributory only. A comparable Australian study found that half of suicides involving acute alcohol use had alcohol coded as a contributory cause of death.[31] We acknowledge that defining acute alco-

hol use at a set BAC does not reflect that alcohol's effects may differ by individual. However, our approach was consistent with previous studies,[7,8] and our sensitivity testing suggests that the presence of alcohol is more relevant than the cut-off used to define acute alcohol use. Results are current, as at 7 September 2021, acknowledging that cases may still be closed and added after this date given that there is a lag between year of death and coronial cases being closed, particularly for the years of 2019 and 2020. As such, it would be beneficial to re-run this study a few years in the future, to add to long-term trends, and to identify any pandemic-related impacts.

The design of this study does not allow consideration of the mechanism of association between acute alcohol use and suicide,[3] nor can we determine whether alcohol was used as a deliberate, facilitatory means of suicide.[32] Another limitation is that not all relevant variables are consistently available within the NCIS dataset e.g., socio-economic status, co-morbid mental disorders (particularly alcohol use disorder and other substance use disorders), and acute stressors prior to death. Based on international findings, we hypothesise that those who die by suicide involving acute alcohol use are more likely to die impulsively following acute stressful events, rather than having psychiatric or physical co-morbidities.[8,9] Future New Zealand research should investigate prior service contact for those who die by suicide involving acute alcohol use.

We have identified that just over a quarter of suicide deaths in New Zealand involve acute alcohol use, and this is particularly prevalent in population groups known to have higher suicide rates (including young people and Māori). Thus, we conclude that alcohol use is a significant but modifiable risk factor for a substantial group of suicide deaths in New Zealand. International evidence shows that actions taken to reduce alcohol consumption at a population-level are associated with reduced suicidal behaviour.[33] Therefore, we recommend that interventions targeted at alcohol be included in New Zealand's suicide prevention strategy. Our findings provide baseline data for the development of interventions targeting suicide associated with acute alcohol use in New Zealand.

Appendix:
https://uploads-ssl.webflow.com/5e332a62c703f6340a2faf44/62ccecc35b92a363774f0311_5693%20-%20appendix-final.pdf

COMPETING INTERESTS
Nil.

ACKNOWLEDGEMENTS
This research was funded by the Oakley Mental Health Foundation (grant awarded to Rose Crossin and Joseph M Boden). Author Katrina Witt is funded by an emerging leader fellowship from the National Health and Medical Research Council of Australia (1177787). We acknowledge the Victorian Department of Justice and Community Safety as the organisation source of the data, and the National Coronial Information System (NCIS) as the database source of the data. The authors thank the staff of the National Coronial Information System for their assistance throughout this project, including providing feedback on the draft manuscript.

AUTHOR INFORMATION
Rose Crossin: Department of Population Health, University of Otago (Christchurch), Christchurch, New Zealand.
Lana Cleland: Department of Population Health, University of Otago (Christchurch), Christchurch, New Zealand; Department of Psychological Medicine, University of Otago (Christchurch), Christchurch, New Zealand.
Annette Beautrais: South Canterbury District Health Board, Timaru, New Zealand.
Katrina Witt: Orygen, Parkville, Australia; Centre for Youth Mental Health, The University of Melbourne, Parkville, Australia.
Joseph M Boden: Department of Psychological Medicine, University of Otago (Christchurch), Christchurch, New Zealand.

CORRESPONDING AUTHOR
Rose Crossin: Department of Population Health, University of Otago (Christchurch), Christchurch, New Zealand. rose.crossin@otago.ac.nz

URL
www.nzma.org.nz/journal-articles/acute-alcohol-use-and-suicide-deaths-an-analysis-of-new-zealand-coronial-data-from-2007-2020

REFERENCES
1. Turecki G, Brent DA, Gunnell D, O'Connor RC, Oquendo MA, Pirkis J, et al. Suicide and suicide risk. Nature reviews Disease primers. 2019;5(1):1-22.
2. Borges G, Bagge C, Cherpitel CJ, Conner K, Orozco R, Rossow I. A meta-analysis of acute alcohol use and the risk of suicide attempt. Psychological medicine. 2017;47(5):949.
3. Cherpitel CJ, Borges GL, Wilcox HC. Acute alcohol use and suicidal behavior: a review of the literature. Alcoholism: clinical and experimental research. 2004;28:18S-28S.
4. Sher L. Alcohol consumption and suicide. QJM. 2006;99(1):57-61.
5. Hufford MR. Alcohol and suicidal behavior. Clinical psychology review. 2001;21(5):797-811.
6. Norström T, Rossow I. Alcohol consumption as a risk factor for suicidal behavior: a systematic review of associations at the individual and at the population level. Archives of Suicide Research. 2016;20(4):489-506.
7. Chong D, Buckley N, Schumann J, Chitty K. Acute alcohol use in Australian coronial suicide cases, 2010-2015. Drug and alcohol dependence. 2020:108066.
8. Lee JW, Park CHK, Kim EY, Kim SH, Yoo SH, Ahn YM. Characteristics of completed suicide in different blood alcohol concentrations in Korea. Forensic science international. 2017;281:37-43.
9. Kõlves K, Koo YW, De Leo D. A drink before suicide: analysis of the Queensland Suicide Register in Australia. Epidemiology and psychiatric sciences. 2020;29.
10. Coronial Services of New Zealand. Annual Suicide Statistics. Wellington: Ministry of Justice; 2021.
11. World Health Organization. Global status report on alcohol and health 2018. World Health Organization; 2019. Report No.: 9241565632.
12. World Health Organisation. Preventing suicide: a global imperative. Geneva: World Health Organization; 2014.
13. Witt K, Lubman DI. Effective suicide prevention: Where is the discussion on alcohol? Australian & New Zealand Journal of Psychiatry. 2018;52(6):507-8.
14. Ministry of Health. New Zealand Health Survey 2019/20 Wellington: Ministry of Health; 2019 [Available from: https://minhealthnz.shinyapps.io/nz-health-survey-2018-19-annual-data-explorer/_w_da15d6ce/#!/explore-indicators.
15. Ministry of Health. Every Life Matters - He Tapu te Oranga o ia tangata: Suicide Prevention Strategy 2019-2029 and Suicide Prevention Action Plan 2019-2024 for Aotearoa New Zealand. Wellington: Ministry of Health; 2019.
16. Ridge Anderson A, Keyes GM, Jobes DA. Understanding and treating suicidal risk in young children. Practice Innovations. 2016;1(1):3.
17. National Coronial Information System. NCIS Operational Statistics Australia: National Coronial Information System; 2022 [updated April 2022; cited 2022 3 May 2022]. Available from: https://www.ncis.

org.au/about-the-data/operational-statistics/.
18. Kugelberg FC, Jones AW. Interpreting results of ethanol analysis in postmortem specimens: a review of the literature. Forensic science international. 2007;165(1):10-29.
19. Statistics New Zealand. 2018 Census ethnic group summaries Wellington, New Zealand2018 [cited 2021. Available from: https://www.stats.govt.nz/tools/2018-census-ethnic-group-summaries.
20. StataCorp. Stata Statistical Software: Release 16. . College Station, TX: StataCorp LLC.; 2019.
21. Lange S, Probst C, Gmel G, Rehm J, Burd L, Popova S. Global prevalence of fetal alcohol spectrum disorder among children and youth: a systematic review and meta-analysis. JAMA pediatrics. 2017;171(10):948-56.
22. Stefanac N, Hetrick S, Hulbert C, Spittal MJ, Witt K, Robinson J. Are young female suicides increasing? A comparison of sex-specific rates and characteristics of youth suicides in Australia over 2004–2014. BMC Public Health. 2019;19(1):1-11.
23. Wilsnack RW, Wilsnack SC, Gmel G, Kantor LW. Gender differences in binge drinking: Prevalence, predictors, and consequences. Alcohol research: current reviews. 2018.
24. UNICEF Office of Research. Building the future: Children and the sustainable development goals in rich countries. Innocenti, Florence: UNICEF Office of Research 2017.
25. Ball J, Edwards R, Sim D, Cook H, Denny S. What explains the decline in adolescent binge-drinking in New Zealand? International Journal of Drug Policy. 2020;84:102826.
26. Stevenson BS, Stephens C, Dulin P, Kostick M, Alpass F. Alcohol consumption among older adults in Aotearoa/New Zealand: a comparison of 'baby boomers' and 'over-65s'. Health Psychology and Behavioral Medicine. 2015;3(1):366-78.
27. Ayuka F, Barnett R, Pearce J. Neighbourhood availability of alcohol outlets and hazardous alcohol consumption in New Zealand. Health & Place. 2014;29:186-99.
28. Winter T, Riordan BC, Surace A, Scarf D. Association between experience of racial discrimination and hazardous alcohol use among Māori in Aotearoa New Zealand. Addiction. 2019;114(12):2241-6.
29. Reid J, Taylor-Moore K, Varona G. Towards a social-structural model for understanding current disparities in Māori health and well-being. Journal of loss and trauma. 2014;19(6):514-36.
30. Walker K. Issues of tobacco, alcohol and other substance abuse for Māori. Wellington; 2019.
31. Chitty KM, Schumann JL, Moran LL, Chong DG, Hurzeler TP, Buckley NA. Reporting of alcohol as a contributor to death in Australian national suicide statistics and its relationship to post-mortem alcohol concentrations. Addiction. 2020.
32. Conner KR, Bagge CL, Goldston DB, Ilgen MA. Alcohol and suicidal behavior: what is known and what can be done. American journal of preventive medicine. 2014;47(3):S204-S8.
33. Kõlves K, Chitty KM, Wardhani R, Värnik A, De Leo D, Witt K. Impact of alcohol policies on suicidal behavior: a systematic literature review. International journal of environmental research and public health. 2020;17(19):7030.

Innovation in Aotearoa New Zealand's healthcare system—how to make it happen

Robyn Whittaker, Penny Andrew, Rosie Dobson, Dale Bramley

ABSTRACT

To date, innovation in Aotearoa New Zealand healthcare services has varied around the country. As we move into a health system restructure, it is important to reflect on what has worked to date and how we can take these elements into the new system. In this paper we describe the approach at Waitematā District Health Board (DHB) including the establishment of an Institute for Innovation and Improvement. We highlight what we view as the key elements of an innovation enabling environment and suggest measures of success.

There are many different definitions of innovation, although most include the elements of novelty, application and benefit.[1,2] In health services, innovation can simply be doing something differently, and better than how it is generally done or has previously been done—it could be a new process, device, technology, system or service. It is not just having the idea of how to do something differently (the idea or invention) but also getting it embedded into standard clinical practice (the implementation). If it is not in practice and having an impact, then it is still just an idea.

It is often acknowledged that the implementation and dissemination of innovation is the most difficult part of the process.[3,4] This is said to be impacted by three clusters of influence: (1) perceptions of the innovation including uncertainty, salience, complexity, trialability and observability; (2) characteristics of the people who need to adopt it—often depicted on a scale from early adopters through to laggards; and (3) "contextual" or organisational and system factors.[4] Some of the specific barriers to innovation implementation in Aotearoa New Zealand healthcare identified recently were: disconnection between industry, research and the health system; inability to prioritise funding for innovation; government rules of procurement; clinical and organisational resistance to change; a high burden of proof for new treatments in evidence-based medicine; and, limited innovation capability and opportunities within Aotearoa New Zealand.[5]

Many of these barriers lie beyond the ability of those in health services to change. In a recent report, the Productivity Commission stated that district health boards (DHBs) are important but mostly inactive in supporting healthtech innovation, and that opportunities for mutual benefits for the healthtech sector and the health system are being lost as a result.[6] They state that:

> *"The main reasons for lack of support from DHBs are their lack of mandate and incentive to participate in innovation, the lack of targeted innovation funding, and rigidities in their procurement processes. Also, health policy provides no effective strategy on innovation and learning to guide DHBs."*

Some aspects of the enabling environment, however, sit within the health services themselves.[7,8] Berwick (2003) developed seven critical success factors for the dissemination of healthcare innovation: surveillance to find sound innovations; find and support innovators; invest in early adopters; make early adopter activity observable; trust and enable reinvention; create slack for change; lead by example.[4] At Waitematā DHB, we have been creating an enabling environment for innovation implementation with our Institute for Innovation and Improvement (known as "i3"). This paper outlines what we have focused on to date, measures for how we can assess success, and what we have learnt. It is hoped that this may usefully inform how we deliberately structure and embed an enabling innovation environment in a reformed healthcare system for Aotearoa New Zealand.

Innovation at Waitematā DHB

In 2014 Waitematā DHB initiated the Leapfrog Programme—a Chief Executive sponsored programme of strategic innovation projects that would make a large impact in the medium term across the entire organisation. Learning from visits to international exemplar organisations and leaders (including Intermountain Healthcare, Beth Israel Deaconess Medical Center, the Scripps Research Institute, an innovation hub in Norway, the Qulturum Jönköping County in Sweden, Trafford Community Care, and the Scottish Patient Safety Programme), the Institute for Innovation and Improvement (i3) was established by the DHB in 2016, creating an engine room of people-resource focused on digital, data, design, and clinical leadership, to support services to improve patient outcomes and patient and whānau experience.[9] The i3 intentionally integrated innovation and improvement to ensure innovation is not about technology for technology's sake, rather that process and service improvement drive everything we do, focusing on ensuring high quality of care and improvement of health outcomes. The innovation- and improvement-enabling environment was extended across the organisation including other programmes, notably a Māori Health Pipeline and primary-community programmes.

Over the ensuing years, through multiple projects and workstreams, the steps towards an innovation enabling environment have included the following key features:

- A vision of where we are heading with clear priorities aligned with the organisation's priorities and values, and a requirement that partners have an aligned sense of purpose.
- Executive leadership with a Chief Executive (CE) committed to the i3's vision and purpose, the Director of the i3 reporting to the CE and being a member of the Executive Leadership Team, and CE sponsorship that ensures innovation and improvement is protected and prioritised and not overshadowed by "the requirements of the day".
- Integration of innovation, quality improvement and clinical governance to ensure the focus of innovation is on systems and processes that improve the reliability, safety and quality of care, and strong engagement of clinicians. For all innovations we ask "how will this help deliver better, high quality care and health outcomes?", and every project is sponsored by a clinical leader.
- Funding and support—consistent leadership (Chief Executive and Board) support even in times of austerity when others may view i3 as non-essential, along with committed baseline funding for a critical mass of staff reflecting the scale of the entity (i.e., no requirement for the i3 to self-fund), and business case approval for projects based on value add to the organisation (which has included reductions in paper, postage, storage and reducing long term spend on large expensive IT systems).
- The removal of silos and building partnerships—in particular, the integration of innovation, service design, quality improvement, data, digital/IT and research/evaluation—all working together on initiatives moving us towards the same vision. This is underpinned by i3 leaders that combine managerial, clinical, operational, and digital and data experience and who are closely connected internally with clinical governance (patient safety and quality) structures, and externally with a broad range of national and international networks.
- A continuous pipeline of new ideas and people—this includes staff on the ground within health services, fresh perspectives from students, new graduates, other disciplines and industries, academics, companies and start-ups, a diversity of people in our communities, and patient groups. This has been achieved through a Fellows Programme of 12-month roles in i3, internships, studentships, academic partnerships, consumer representation, co-design projects and programmes such as "Engineers in Clinical Residence". It also includes horizon scanning for the best innovations that have been implemented internationally and nationally with significant impact.
- A network of frontline healthcare workers ready for change and willing to lead it—a broad and diverse network of people working at the frontlines of healthcare who are not only interested and open to new ideas, but who are able to ground them in

the reality of their daily working lives. They are also able to improve ideas to ensure that they will work in our context. This has been fostered through Senior Medical Officer (SMO) roles and sabbaticals in i3, prioritising clinical leads for projects, clinical IT experts who are available to listen and work alongside frontline workers, the i3 Fellows Programme, and the establishment of a Clinical Digital Academy (CDA) to train clinicians in data and digital health.
- An engine room of people with a diverse range of skills including change management, quality improvement, systems engineering, co-design, project management and clinical experience, who are closely connected to people working at the frontlines, with local relationships and understanding of both the ideas and local contexts, who make things happen supported by our IT and data teams.
- Data to drive the identification and quantification of the issues to measure the impact of innovations, and feedback loops to the staff and services through accessible dashboards, analytics support, the integration of artificial intelligence to support clinical decision making, user-friendly data tools integrated with electronic clinical records in the hands of clinicians, along with active use of population health registers to identify gaps in systems and connect people to preventive services (screening, immunisation and treatment).
- Early quick wins focused on providing value for clinicians, in terms of making their daily work lives easier and having well designed clinical systems to deliver safe, high quality care—establishing their support and acceptance of further change.

Measures of success

Measuring whether this model is successful in creating an innovation enabling environment within the DHB is not straightforward. Existing implementation science frameworks tend to focus on two aspects: (1) the implementation of an individual initiative with respect to aspects such as adoption, fidelity, penetration, effectiveness and sustainability;[10,11] or (2) whether determinants of implementation were supportive for a particular innovation, such as champions, innovation-values fit (extent to which targeted users perceive that use of the innovation will foster fulfilment of their values), management support, implementation policies and practices (the extent actions ensure user skills, create incentives and/or identify and address barriers to use), financial resource availability, implementation climate (employees' shared perceptions of the importance of innovation implementation within the organisation), and implementation effectiveness.[12]

To measure an innovation enabling environment we describe below a more pragmatic set of measures that take into account exisiting frameworks and critical success factors but assess innovation as a system rather than discrete parts. The proposed measure set reflects our innovation definition: an environment that continues to enable new or different things/ways of working to be put into standard practice and have a positive benefit. This includes:

1. "new" things (systems, processes, tools, technologies) have been put into practice and changed the way people work or services are delivered;
2. there is a pipeline of new ideas and trials underway;
3. new staff want to work there or to lead initiatives due to a culture of innovation and continuous improvement;
4. improvements in population and individual health outcomes alongside positive patient and whānau experience of their health services, particularly reductions in health inequities;
5. responsiveness to Māori and equity.

Additionally, the global pandemic adds the opportunity to look at the ability to adapt to changes in context or new threats to health. These proposed measures of success are considered for Waitematā DHB in Table 1. We acknowledge that the population and individual outcome measures described below cannot be causally linked to an innovation environment; these measures are merely descriptive of improvements over time or compared with other DHBs.

It is important to note that Waitematā DHB's innovation and improvement programme has not required extraordinary financial investment. Waitematā DHB is one of the only DHBs that has been able to deliver a break-even budget and, at the same time, has delivered an exceptional strategic innovation programme (the Leapfrog Programme) for under approximately $15m, at least one sixth of the cost of implementing a single vendor electronic health record system.

Table 1: Proposed measures of success in establishing an enabling environment within Aotearoa New Zealand health services.

Proposed success measure	Examples from across Waitematā DHB (referenced in public Board Reports[13] and the i3 website[9])
Significant new systems/ processes/services/ tools/ technologies embedded in clinical practice that have changed the way things are done	The implementation of: ward nurses using iPad minis for drug administration and vital signs/nursing assessments that underpin the Patient and Whānau Care Standards Programme, an electronic eVitals system linked to communication tools enabling a comprehensive deteriorating patient programme with automated electronic early warning scores for all patients, decision support (e.g., sepsis prompt) and alerts in electronic whiteboards and clinician devices, electronic ordering systems for tests and procedures with integrated clinical decision support (including Choosing Wisely[14] recommendations), data-driven, evidence-based clinical pathways (for example appendicitis, acute cholecystitis, chest pain, and fractured neck of femur) supporting continuous quality improvement, a one page digital inpatient summary ("Snapshot") pulling from multiple different systems that is quicker than accessing the individual systems, with digital notes for ward rounds and consultations that are searchable, an outpatients improvement programme that includes new models of care (telehealth, patient self referral on symptoms (SOS), clinical pathways) enabled by robust clinical data (eOutcomes), digital tools (patient online booking and electronic clinic room booking and scheduling), and paperless clinics meaning clinicians can conduct clinics from anywhere and send e-orders to community laboratories and prescriptions to community pharmacies, improvement of patient experience through digital post, emailing letters, questionnaires and helpful information to patients using an in-house designed Emailer tool, improvement of clinical handover and communication with smartphone systems for paging with two way communication between the ward and clinician that integrate patient safety tools (e.g., ISBAR communication tool and early warning scores), and between ward/clinical area for Orderlies task management, aggregated data that links multiple datasets which can be visualised and interrogated directly by clinicians and services, and can be used to inform service redesign (e.g., establishing an orthogeriatric service), process improvement (e.g., streamlining clinical document transcription), clinician decision making and continuous quality improvement (e.g., implementing a multidisciplinary fractured neck of femur pathway). Our digital data environment has enabled the development and implementation of artificial intelligence (AI) (e.g., mortality risk and rehabilitation response algorithms) and spurred the development of an AI governance framework, electronic patient experience and patient-reported outcomes measures (PROMs) that can be entered electronically by patients and results are embedded in the clinical portal (patient's electronic health record) and seen in real time, community clinicians able to access and enter data into all systems from patient homes.

Table 1 (continued): Proposed measures of success in establishing an enabling environment within Aotearoa New Zealand health services.

A pipeline of new ideas and trials underway with academics/ universities and start-ups/ companies	Trials with companies including Orion Health, The Clinician, BlueMirror, Data Robot, Aranz Medical Ltd, Zoom, Smartpage, Fronde, Trials of internal new developments such as apps and a paediatric device, Academic partnerships with PrecisionDrivenHealth, the MedTech Centre of Research Excellence, Good Health Design AUT, National Institute for Health Innovation (NIHI) – research projects under these partnerships and separately, including student projects Internal Artificial Intelligence (AI) development projects and governance, and development of an AI Lab.
Great people wanting to work with us and a culture of innovation and continuous improvement amongst all staff	Since conception there have been: ~40 i3 fellows, 10 Masters interns, 47 summer students (>120 apply for studentships each year), The Clinical Digital Academy (CDA) has trained 32 clinicians in IT and led to 7 digital fellows, 7 Senior Medical Officers (SMOs) have had part-time roles and sabbaticals in i3, The DHB is consistently rated by Resident Medical Officers (RMOs) as the best digital experience,[15] i3 fellows, SMOs, and CDA alumni go back into their service and are supported to innovate and improve, work on i3 projects, and be champions within their service.
Improvements in patient outcomes and equity, patient and whānau experience	Each project is evaluated on its own merit (e.g., average of ~$150 savings to patients for telehealth outpatient appointments, 88% would use telehealth again, and time/paper/cost savings for digital systems),[16] Waitematā DHB has some of the best health outcomes across DHBs eg. highest life expectancy in New Zealand at 84.2 years and increasing, with the gap between Māori and non-Māori closing;[17] the lowest hospital standardised mortality (HDxSMR ratio of 0.65 across both hospitals 2020-21);[18] second-lowest rate of amenable mortality with rates more than halving for Māori over the past decade;[17] one of the lowest rates of hospital-acquired complications including bloodstream infections, pressure injuries surgical complications, neonatal birth trauma (2.4% of admitted patients vs 3.4% for peer hospitals);[19] the top performer in hip fracture clinical care 2021 (ANZHFR 2021 New Zealand Golden Hip Award).[20]

Table 1 (continued): Proposed measures of success in establishing an enabling environment within Aotearoa New Zealand health services.

Responsiveness to Māori and equity	Growth in Māori workforce by 31% (from 368 to 484 over five years) due to multiple initiatives including scholarship programmes, paid Health Care Assistant (HCA) training, and dedicated Clinical Nurse Specialist roles, Similar workforce initiatives, including ten Pacific Science Academies in schools, have seen the Pacific workforce increase by 33% (356 to 476) over the last five years, A Māori Health Pipeline Programme of projects with academic and community partners that are governed and led by Māori to accelerate Māori health gain and close the life expectancy gap, including the abdominal aortic aneurysm (AAA)[21] and atrial fibrillation (AF) screening programme (first screening programme to be designed and targeted for Māori and only programme internationally to have screened women); Te Oranga Rūkahukahu lung cancer screening (LCS) (first Indigenous-led LCS programme in the world); [22] alternative models for cardiac and pulmonary rehabilitation; HPV self-testing; breast cancer data match "500 women campaign",[23] The establishment of Kōtui Hauora, Northern Region Iwi-DHB Partnership Board, and the first DHB Chief Advisor Tikanga role, which has led to the development of a Māori research framework for the implementation of Māori-led research and innovation, The DHB has the second highest Māori life expectancy in New Zealand (80.8yrs), with a rate of increase in Māori life expectancy that is twice that of non-Māori. The life expectancy gap for Māori is 3.8 years, Māori mortality rates for cancer and cardiovascular disease have decreased by 27% over 10 years (2008–2018), housing related hospital admission rates for Māori have decreased by 77% (2010-2020), and Māori wahine maternal birth injury rates have decreased by 40% (2009–2018).[14,24]
Ability to adapt to COVID-19	Trained i3 staff were immediately deployed to COVID-19 projects in our DHB, and also regional and national developments such as: adapting the clinical portal to include a COVID-19 pathway and banner alerts for COVID-19 status and vaccination status, establishing community laboratory test e-ordering from all sites (testing stations, hotels, GPs, hospitals) and community e-prescribing for paperless clinics for hospital specialists, establishing a regional datastore and dashboards for managing COVID-19 across the region and linked nationally, initially tracking testing, inpatient COVID-19 status and hospital/ICU occupancy, followed by the national vaccination dashboard and most recently dashboards to manage COVID-19 in the community including the development and integration of a hospitalisation risk algorithm, involved in the clinical design for national developments including the Border Clinical Management System/COVID Community Care Module, national electronic ordering system for COVID-19 swabs at testing centres, the self-recording of rapid antigen test (RATs) results in My COVID Record plus the national collection of point-of-care RATs from all channels (consumer, GP, pharmacist, others).

Discussion

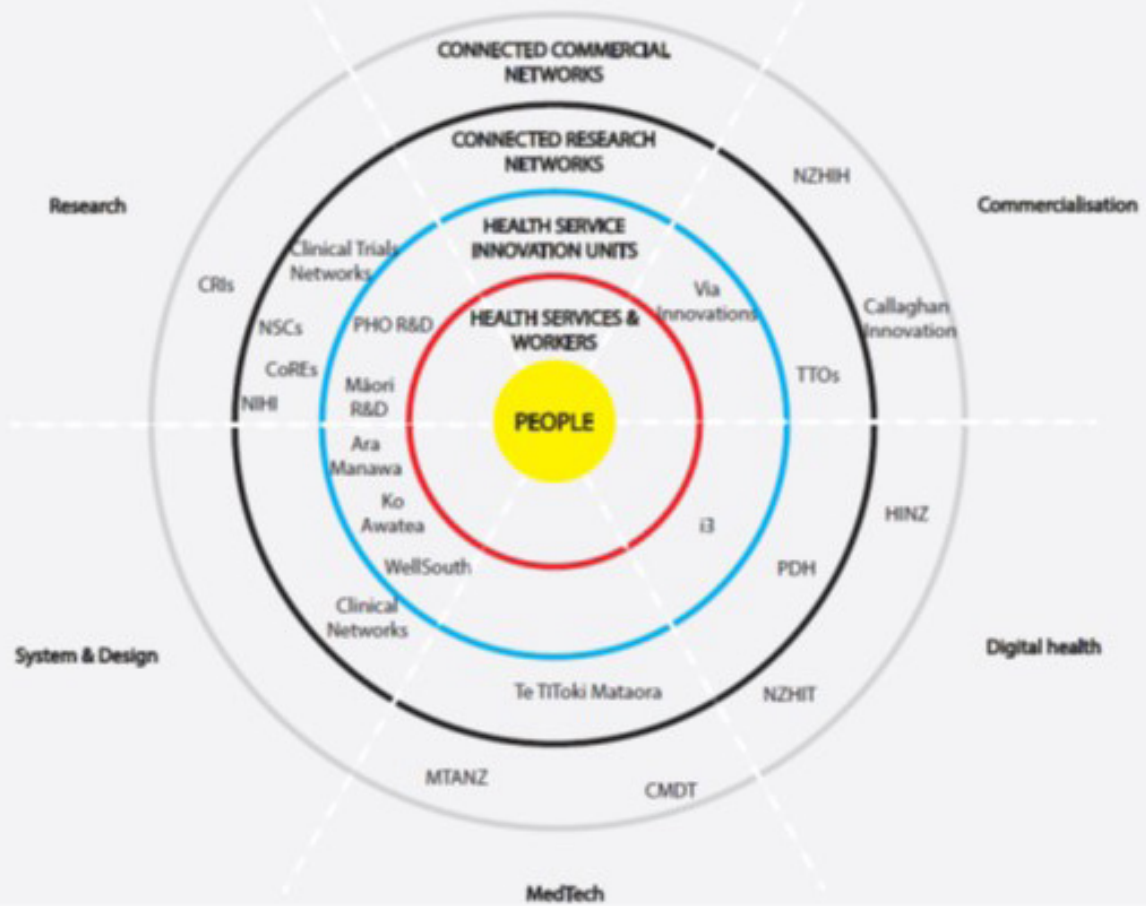
The planning phase for major health system reform and restructure is an opportune time to reflect on what we think works and should be embedded in Aotearoa New Zealand's new health system. The health reform vision is: "to build a system that achieves pae ora | healthy futures for all New Zealanders" with five areas of focus to achieve this vision including: "Excellence,ensuring consistent, high-quality care everywhere, supported by clinical leadership, innovation and new technologies to continually improve services."[25]

To do this, we need to create an overarching continuous improvement environment with people working together to innovate and improve systems and processes that underline high quality care and patient experience.

From Waitematā DHB's experience, the key elements for creating such an environment are: executive leadership and clinical governance; provision of a door into the health service for those with aligned public good purpose; pipelines for new people, perspectives and ideas; career pathways, training and support for clinicians and others to lead innovation implementation; an engine room of people with diverse skills to support development and implementation that is deeply connected with the frontline health services; integration of data, digital, service design, quality improvement, innovation and research, all working towards shared goals; and strong networks with the broader innovation ecosystem (Figure 1).

We have described measures to evaluate the benefits and to inform continuous improvement of an innovation enabling environment at Waitematā DHB. We reiterate that it is difficult to draw any direct correlation from an enabling environment for innovation to improvements in health

Figure 1: A simple view of the current health innovation networks in Aotearoa New Zealand.



Key: CRIs Crown Research Institutes; NSCs National Science Challenges; CoREs Centres of Research Excellence; NIHI National Institute for Health Innovation; PHO Primary Health Organisation: R&D Research and Development: MTANZ Medical Technology Association of NZ; CMDT Consortium for Medical Device Technologies: NZHIT New Zealand Health IT; PDH Precision Driven Health; HINZ Health Informatics New Zealand; TTOs Tech Transfer Offices of Universities: i3 Institute for Innovation and Improvement; NZHIH New Zealand Health Innovation Hub.

outcomes and there are many other reasons for Waitematā DHB's relatively high standard of population health, mostly related to the socio-economic determinants of health. Measuring the benefits of an innovation enabling environment is challenging and is something that we need to continue to learn about and develop.

We hope that others around the country will add to the discussion with their experience of what has worked well in their contexts. There are lessons from across Aotearoa New Zealand about programmes and processes to take into the new healthcare system structure. It is our view that Te Whatu Ora (Health NZ) and the Te Aka Whai Ora (Māori Health Authority) should join up the existing exemplars of enabling innovation environments, their teams and their broader innovation networks (Figure 1), to optimise an innovation and improvement network that directly supports and works with the new structure. What has not worked well previously, in our opinion, is creating separate entities that sit outside the healthcare structure to "do" innovation for the healthcare system, and not integrating innovation, data and digital with quality improvement and clinical governance.

This proposal also appears to be supported by the recent move to re-integrate NHSX (driving digital transformation of the NHS) and NHS Digital back into NHS England. The recommendations from the recent independent review of data, digital and technology in the NHS by Laura Wade Gery,[26] accepted by the UK Government, include bringing together innovation and improvement, more closely linking data and digital to the business, building a pipeline of future talented leaders that combine clinical, managerial, digital and data experience, and building a transformation engine ["factory"]:

> *"To achieve the Long Term Plan aim, and respond to the rapid acceleration in digital adoption, NHSEI needs to 'transform the way it transforms' and improve how it supports innovation in the delivery of care. At the core, this involves the creation of a scalable capability that integrates clinical, operational and technological resources to transform patient pathways and service delivery.*
>
> *This capability builds real expertise in the art and science of transformation, learning continuously from experience. It needs to embed modern digital and transformation tools and techniques, and adopt a user, patient and citizen centred approach. It will use 'agile' change methodologies and operate through small, focused multi-disciplinary 'service' teams whose missions have longevity to build the right experience and continuity and technical solutions…The focus is relentless on delivering improvements in outcomes based on rapid deployment and continuous improvement rather than large scale traditional system programmes, although supported by underlying data and technology infrastructure."*[26]

Other international models may also be worth learning from, and others in the ecosystem are looking to exemplars, such as the Consortium for Medical Device Technologies (CMDT) developing an Australia New Zealand BioBridge with the Liverpool Innovation Precinct in Sydney.[27] We need to ensure learnings from international examples are adapted to our context: our position as a small country with a good health service, a strong and unique global pandemic response, a vibrant Indigenous culture of innovation currently with an upswing of Māori business R&D[6] and leading developments in important issues such as Indigenous data sovereignty, and a potential pendulum swing back to centralisation. It is time to bring all these elements together under our new national health system, making the most of this opportunity to remove the silos and perverse incentives that have hindered innovation and improvement implementation in the past.

In addition, the authors would like to add two further areas for development: a "thinktank" function providing continuous horizon scanning (including literature review and discussions with international networks) and ensuring the ongoing close relationship with regional and national direction for IT, data governance, and health service quality; and a Māori specific innovation pipeline at all levels—locally, regionally and nationally. This would be led by Māori for Māori, and would purposely develop and support Māori innovations to thrive. At Waitematā DHB this has been enabled by governance at the Iwi–DHB Partnership Board level, leadership and support at a management level from the Chief Advisor Tikanga and the Chief Executive, and investment in Māori researchers and research projects. This must reflect the principles of Te tiriti o Waitangi, reinforced in the findings to date of the Waitangi Tribunal Inquiry into Health Services and Out-

comes and in Whakamaua: Māori Health Action Plan 2020–2025—that is, the principles of tino rangatiratanga, equity, active protection, options, and partnership.[28,29]

Conclusions

"The Government should use its intended major health system reform to improve the mandate, funding and incentives for DHBs to participate in the healthtech innovation ecosystem. This change would be to the mutual benefit of the healthtech sector, and the efficiency, effectiveness and accessibility of New Zealand's health and disability system." – Productivity Commission [6]

A new national healthcare system structure will require an innovation and improvement focus in order to "do things differently" and produce different, and better, results than the current system. We need to reflect on what has worked well to date and what is happening internationally—embracing the potential to combine the best features with the new opportunities a "re-start" can bring.

"To create a future different from its past, health care needs leaders who understand innovation and how it spreads, who respect the diversity in change itself, and who, drawing on the best of social science for guidance, can nurture innovation in all its rich and many costumes." – Don Berwick, IHI [4]

COMPETING INTERESTS
Nil.

ACKNOWLEDGMENTS
We would like to acknowledge all those who have worked in the Institute for Innovation and Improvement, the Health Information Group, and on the Leapfrog Programme; in particular, Stuart Bloomfield, Andrew Cave, David Ryan, Delwyn Armstrong, Lara Hopley, Chris Southen, Sharon Puddle, without whom none of this would have been possible. We would like to acknowledge Karen Bartholomew and the team leading the Māori Health Pipeline and Workforce programmes. We also wish to acknowledge Dame Rangimārie Naida Glavish for her leadership and guidance on Māori tikanga, and the Waitematā DHB Board for their long-term support for this work.

AUTHOR INFORMATION
Robyn Whittaker: Associate Professor and Public Health Physician, i3, Waitematā DHB, Auckland, New Zealand. National Institute for Health Innovation, University of Auckland, Auckland, New Zealand.
Penny Andrew: Director, i3, Waitematā DHB, Auckland, New Zealand.
Rosie Dobson: Psychologist and Senior Research Fellow, National Institute for Health Innovation, University of Auckland, Auckland, New Zealand. i3, Waitematā DHB, Auckland, New Zealand.
Dale Bramley: Chief Executive Officer, Waitematā DHB, Auckland, New Zealand.

CORRESPONDING AUTHOR
Robyn Whittaker: i3, Waitematā DHB, Auckland, New Zealand. Private Bag 93-503, Takapuna, Auckland, 0740. 021 968029.
Robyn.whittaker@waitematadhb.govt.nz

URL
www.nzma.org.nz/journal-articles/innovation-in-aotearoa-new-zealands-healthcare-system-how-to-make-it-happen

REFERENCES
1. Lansisalmi H, Kivimaki M, Aalto P, Ruoranen R. Innovation in Healthcare: A Systematic Review of Recent Research. Nursing Science Quarterly 2006; 19 (1): 66-72.
2. Varkey P, Horne A, Bennet K. Innovation in Health Care: A Primer. Am J Med Qual 2008; 23: 382-8.
3. Arora A, Wright A, Cheng M, Khwaja Z, Seah M. Innovation Pathways in the NHS: An Introductory Review. Therapeutic Innovation & Regulatory Science 2021; 55: 1045-58.
4. Berwick D. Disseminating innovations in health care. JAMA 2003; 289(15): 1969-75.
5. Summary Outputs from a Transition Unit Innovation Workshop. 24th September 2021. Attended by author RW.
6. New Zealand Productivity Commission. 2021. New Zealand Firms: Reaching for the frontier. Final Report. 2021. ISBN 978-1-98-851961-6 (online). Available from: https://www.productivity.govt.nz/assets/Documents/Final-report-Frontier-firms.pdf
7. Jacobs S, Weiner B, Reeve B, Hofmann D, Christian M, Weinberger M. Determining the predictors of innovation implementation in healthcare: a quantitative analysis of implementation effectiveness. BMC Health Services Research 2015;15:6.
8. Omachonu, V.K. and Einspruch, N.G., 2010. Innovation in healthcare delivery systems: a conceptual framework. The Innovation Journal: The Public Sector Innovation Journal, 15(1), 1-20.
9. I3: Institute for Innovation and Improvement. Our Work. Accessed on 1/03/2022. Available from: https://i3.waitematadhb.govt.nz/our-work/
10. Glasgow R, Harden S, Gaglio B, Borsika R, Smith ML, Porter G, Ory M, Estabrooks P. RE-AIM Planning and Evaluation Framework: Adapting to new Science and Practice with a 20-year Review. Frontiers in Public Health 2019; 7: 00064 DOI=10.3389/fpubh.2019.00064
11. Chaudoir S, Dugan A, Barr C. Measuring factors affecting implementation of health innovations: a systematic review of structural, organisational, provider, patient and innovation level measures. Implementation Science 2013;8:22.
12. Helfrich C, Weiner B, McKinney M, Minasian L. Determinants of Implementation Effectiveness. Medical Care Research and Review 2007; 64(3):279-303.
13. Waitematā District Health Board. Board Reports – CEO Reports, Hospital Advisory Committee Quality Reports. Available from: www.waitematadhb.govt.nz/about-us/leadership/board-meetings/. For specific example, https://www.waitematadhb.govt.nz/assets/Documents/committees/2021/HAC-December-2021.pdf
14. Health Quality and Safety Committee. Choosing Wisely Recommendations and Resources. Available from: www.hqsc.govt.nz/resources/choosing-wisely/recommendations-and-resources/
15. Quarterly RMO (Resident Medical Officer) Run Feedback reports for the Auckland DHBs (not publicly available).
16. Waitemata DHB. Telehealth Trial Summary Report

2019. Available from: www.telehealth.org.nz/assets/Uploads/1907-Waitemata-Telehealth-Trial-Summary-Report-Final.pdf
17. Waitemata DHB. Waitemata DHB Annual Reports. Available from: www.waitematadhb.govt.nz/about-us/dhb-reporting/annual-reports/
18. Waitemata DHB Hospital Advisory Committee (HAC) (Board Committee) papers. Available from: www.waitematadhb.govt.nz/about-us/leadership/committee-meetings/
19. Health Quality and Safety Commission. Hopsital Acquired Complications Rates. Available here: www.hqsc.govt.nz/our-data/quality-and-safety-markers/ and www.hqsc.govt.nz/our-data/quality-dashboards/
20. Australia and New Zealand Hip Fracture Registry. Goldn Hip Award 2021. Available from: https://www.buzzsprout.com/1739857/9605400-secrets-to-success-waitemata-district-health-board?t=0 and https://www.waitematadhb.govt.nz/assets/Documents/board/2021/Board-150921.pdf
21. Waitemata DHB. Quality Accounts. Abdominal Aortic Aneurysm (AAA) Screening Pilot for Māori. Available from: http://www.qualityaccounts.health.nz/quality-initiatives/quality-initiatives/aaa-pilot-for-maori/
22. Waitemata DHB. Te Oranga Pukahukahu – Lung Health Check. Available from: https://www.waitematadhb.govt.nz/healthy-living/te-oranga-pukahukahu-lung-health-check/
23. BreastScreen Aotearoa. Information for Primary Care: 500 Maori Women Campaign – Breast Screening DataMatch Project. Available from: https://aucklandpho.co.nz/wp-content/uploads/2019/09/Information-to-primary-care.pdf
24. Ministry of Health. Maternity Clinical Indicator Trends in New Zealand. Available from: minhealthnz.shinyapps.io/maternity-clinical-indicator-trends/
25. Department of the Prime Minister and Cabinet. Our health and disability system. Building a stronger health and disability system that delivers for all New Zealanders April 2021. Available from: https://www.futureofhealth.govt.nz/assets/Uploads/Publications/health-reform-white-paper-apr21.pdf
26. Independent report. Putting data, digital and tech at the heart of transforming the NHS. Department of Health and Social Care, UK Government. Published 23 November 2021. Available at: https://www.gov.uk/government/publications/putting-data-digital-and-tech-at-the-heart-of-transforming-the-nhs
27. MedTech CMDT. BioBridge. Accessed on 1/03/2022. Available from https://www.cmdt.org.nz/biobridge
28. Waitangi Tribunal. Hauora: Report on Stage One of the Health Services and Outcomes Kaupapa Inquiry (Pre-publication version), Chapter 10 of Wai 2575 Waitangi Tribunal Report 2021. Accessed on 1/03/2022. Available from https://waitangitribunal.govt.nz/inquiries/kaupapa-inquiries/health-services-and-outcomes-inquiry/
29. Ministry of Health. 2020. Whakamaua: Māori Health Action Plan 2020-2025. Wellington: Ministry of Health. Available from: https://www.health.govt.nz/publication/whakamaua-maori-health-action-plan-2020-2025

Did new treatments contribute to a decrease in melanoma deaths?

Kylie Mason, Liam Kelly, Christopher Jackson, Deborah Read, Barry Borman

ABSTRACT

Melanoma is one of the most common cancers diagnosed in New Zealand, and New Zealand has one of the highest rates of melanoma incidence and mortality in the world. Monitoring by Environmental Health Intelligence NZ (EHINZ) has found a recent sharp decline in melanoma mortality rates in New Zealand. Since 2014 and 2015 (with 376 and 378 melanoma deaths, respectively), melanoma deaths have declined to 362 deaths in 2016, 308 deaths in 2017, and 296 deaths in 2018. We believe that two new PD-1 inhibitor drug treatments introduced in New Zealand in 2016—nivolumab (Opdivo, BMS) and pembrolizumab (Keytruda, MSD)—may have contributed to this decrease in melanoma mortality. Other factors are unlikely to have had such a major effect, with the drop unlikely due to random variation, and no major changes in melanoma registrations or melanoma thickness at diagnosis over the past decade. While our monitoring of the time trend is descriptive only, and cannot attribute causality, it does suggest a recent decrease in melanoma mortality rates at the population level. These national-level statistics reflect both what might be expected in the New Zealand situation with the introduction of PD-1 inhibitor treatments, based on clinical trials, and what oncologists are seeing at an individual level. Further studies could investigate this observational finding, to confirm whether PD-1 inhibitor drug treatments are having an impact on melanoma mortality and survival rates in New Zealand.

Melanoma is one of the most common cancers diagnosed in New Zealand, and New Zealand has one of the highest rates of melanoma incidence and mortality in the world.[1,2] These high rates are believed to be due to high UV levels, as well as a high proportion of New Zealanders being fair-skinned and at greater risk of skin damage from high UV exposure.[3] Given these high melanoma rates and the link to an environmental exposure, melanoma incidence and mortality are routinely monitored as part of the Environmental Health Intelligence NZ (EHINZ) surveillance programme, which provides information for action on environmental health issues in New Zealand. Decreasing the burden of melanoma in New Zealand would have a substantial impact on the health of many New Zealanders.

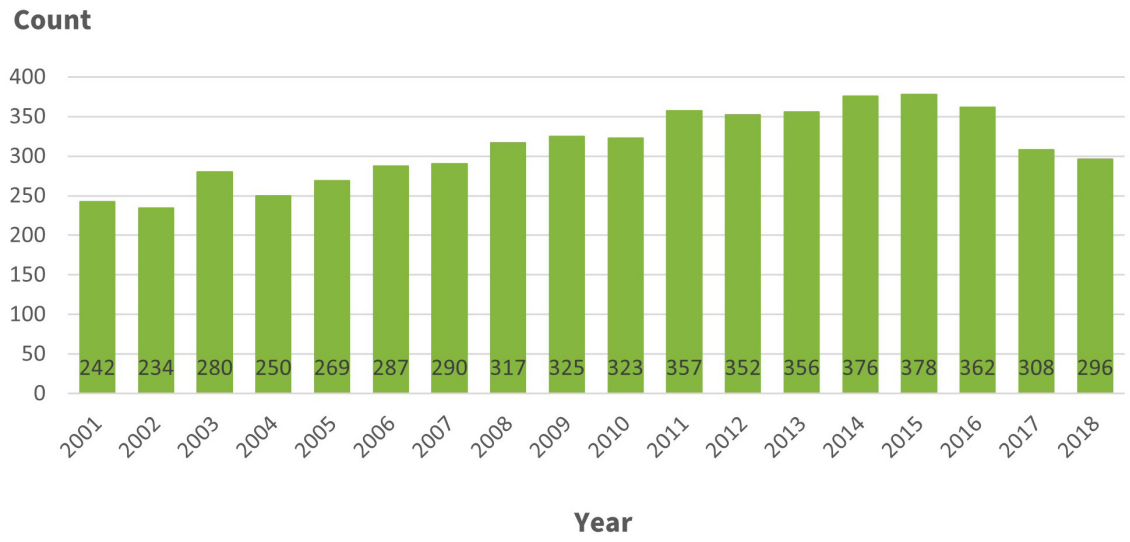
EHINZ's monitoring has recently found a sharp decline in melanoma mortality rates in New Zealand from 2016 onwards. From 2011 to 2015, at least 350 people died each year from melanoma, with 376 and 378 deaths in 2014 and 2015, respectively. Since 2015, deaths have declined, with 362 deaths in 2016, 308 deaths in 2017, and 296 deaths in 2018 (Figure 1). There has been a statistically significant decline in the age-standardised mortality rates over this time period, from 4.9 per 100,000 in 2015, to 3.3 per 100,000 in 2018 (Figure 2).

Additionally, preliminary mortality data for 2019, recently published on the Ministry of Health website, report 328 melanoma deaths in 2019, and an age-standardised rate of 3.6 per 100,000[4]—a slight increase from 2018, but a similar age-standardised rate to 2017 (3.7 per 100,000) and still lower than counts and rates from 2011 to 2015. Preliminary data are subject to change and need to be interpreted with caution; however, they suggest a potential continuation of lower counts and rates of melanoma deaths compared with previous years, which would need to be confirmed at a later date.

A potential explanation for the decline in melanoma mortality rates is the introduction of new treatments for advanced (metastatic) melanoma over this time period. Advanced melanoma has historically been associated with low survival rates.[5] In New Zealand, PHARMAC started funding the new treatments of (i) nivolumab (Opdivo, BMS) in July 2016, then (ii) pembrolizumab (Keytruda, MSD) in September 2016, for people with unresectable stage IIIC or stage IV disease (i.e., advanced melanoma unable to be treated with surgery).[6,7]

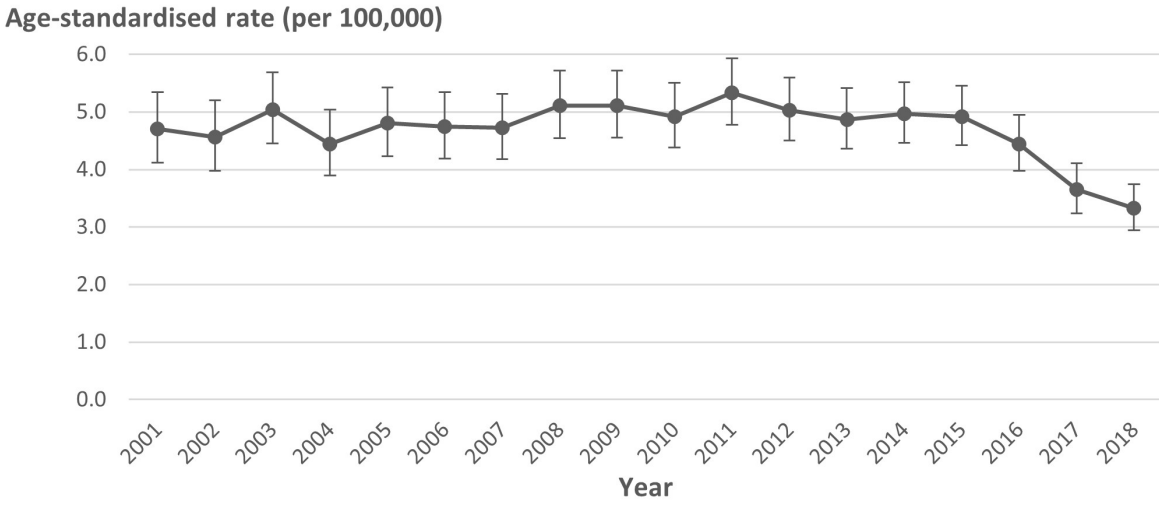
Prior to 2016, the only funded therapies in New Zealand for advanced melanoma were dacarbazine and interferon, neither of which had been shown to improve overall survival in clinical trials, and were associated with significant morbidity.[8] In 2010, ipilimumab, a CTLA-4 receptor monoclonal antibody, was the first therapy that demonstrated improved overall survival for met-

Figure 1: Number of melanoma deaths each year in New Zealand, 2001–2018.



Source: New Zealand Mortality Collection.

Figure 2: Age-standardised rate of melanoma mortality in New Zealand, 2001–2018.



Note: Age-standardised to the WHO world standard population. 95% confidence intervals are shown.
Source: New Zealand Mortality Collection.

astatic melanoma in any clinical study;[9] however, the list price was approximately $150,000 per course and it did not receive PHARMAC funding.

Subsequent studies demonstrated that nivolumab and pembrolizumab improved overall survival in phase 3 clinical trials. These drugs are PD-1 inhibitors, a novel class of monoclonal antibodies that bind to the programmed cell death receptor on T-lymphocytes, preventing inhibition of cytotoxic T-cells by the PD-L1 ligand on cancer cells, preventing immune escape.[10] The pivotal CHECKMATE-066 study demonstrated that compared to chemotherapy, nivolumab improved the rate of one-year overall survival from 42.1% to 72.9% (hazard ratio for death, 0.42; 99.79% CI, 0.25–0.73, p<0.001) in patients with metastatic cutaneous melanoma without an activating BRAF mutation.[11] Similarly, the KEYNOTE-006 study compared pembrolizumab at one of two dose schedules with ipilimumab. Patients were eligible irrespective of BRAF mutation status. Estimated one-year overall survival was improved from 58.2% with ipilimumab, to 68.4% and 74.1% with the three-weekly and two-weekly dose groups of pembrolizumab, respectively.[12] These results were durable at five years.[13,14] It is important to note that in both studies, eligibility was restricted to patients with good physical fitness (ECOG performance status 0 or 1) and with no evidence of brain metastases, which are discovered in a high proportion of patients with stage IV disease. This means it was not certain that clinical trial results would translate into a discernible improvement in population-level outcomes, if the benefit of the medicines were restricted to a small sub-group.

Starting in 2016, when nivolumab and pembrolizumab were introduced in New Zealand, we have observed a reduction in melanoma mortality rates, with further reductions in subsequent years. It is plausible that these new PD-1 inhibitor drug treatments have contributed to the decrease in melanoma deaths. The slight decrease in the melanoma mortality rate in 2016, followed by two years of sustained drops, suggests that something pivotal occurred in 2016 to impact mortality rates. The sustained reduction in mortality rates is also of note. Where a new drug improves disease control for a short period, it could be expected that there would be a displacement of deaths from one year to the following year(s). To date, we have observed a reduction in mortality rates from 2016 to 2018 (and a similarly low mortality rate in 2019 as in 2017, based on preliminary data). If the new treatments were indeed having an impact, we might expect a reduction in deaths, with two parts: a proportion of patients being cured, and a proportion having delayed death. We would see both as contributing in the early years, but in the following years we might see a slight attenuation due to delayed deaths (given an overall median survival time of about 2.75–3 years in clinical trials[13,14]).

Furthermore, the size of the reduction in deaths aligns with what could be expected from these new treatments. Although patient numbers and stage-specific information is not routinely available, approximately 300 people who die from melanoma each year in New Zealand could be considered eligible for treatment with these agents (subject to performance status and co-morbidity, and assuming 100% uptake). This is a reasonable estimate, given that (i) in 2016/17 there were a total of 367 new patients for PD-1 inhibitors (pembrolizumb or nivolumab) for first-line melanoma treatment, and (ii) in 2018/19, 316 new Special Authority initiations for pembrolizumab and nivolumab were approved for first-line melanoma treatment.[15] Phase 3 studies for patients with advanced melanoma suggest an objective response rate (absence of disease or decrease in extent of cancer after treatment) of 42–45% for these treatments, and a complete response rate (absence of disease after treatment) of 14% and 18% for pembrolizumab and nivolumab, respectively.[13,16] Based on clinical trials, and approximately 300 patients each year, 60–70 fewer deaths each year in New Zealand is within the range of what could be expected due to these new PD-1 inhibitor treatments.

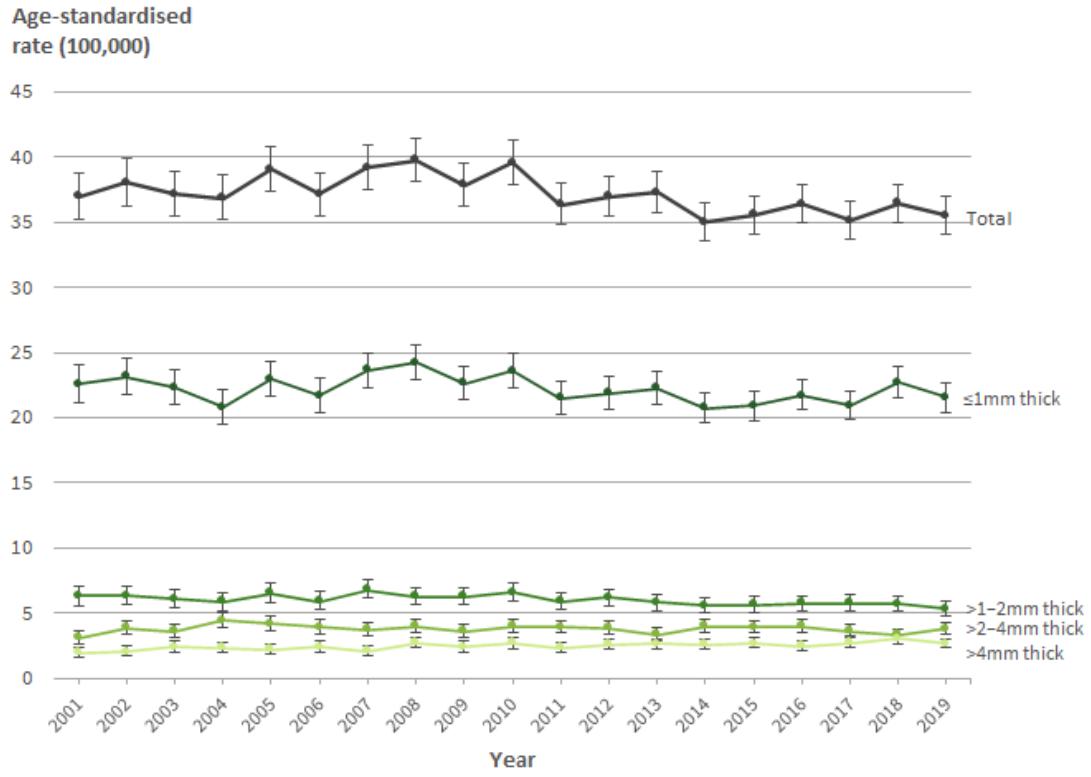
Other potential explanations are unlikely to account for the observed decrease in melanoma mortality rates. Firstly, random or stochastic variation is unlikely as the 95% confidence intervals do not overlap, and the decrease has been sustained over the three years 2016–2018. While the 2019 preliminary data shows a small increase in melanoma deaths to 328, the age-standardised mortality rate (3.6 per 100,000) is similar to that of 2017, and remains substantially lower than 5 per 100,000, the approximate level from 2008 to 2015. Secondly, our monitoring of melanoma registrations also shows no statistically significant change in melanoma registration (incidence) rates over this time period, with relatively stable rates from 2011 to 2020 (Figure 3).[17] Thirdly, there has been no statistically significant change in registration rates of thicker melanoma since 2011 (Figure 3),[17] suggesting that stage migration has not occurred. The thickness (measured

as the Breslow thickness) is a measure of severity, with thicker melanoma associated with a reduced survival rate.

This analysis has some limitations. Our monitoring of the time trend is descriptive only and cannot attribute causality. The analysis uses population-level data, rather than individual-level patient data, and therefore cannot definitively comment on whether the drug treatments have led to a lower mortality rate. Confirming these observational findings, for example through time-dependent survival analyses, would need information on number of patients treated, duration of treatment, and individual patient outcomes, which is not currently available in New Zealand. However, these data may become available in future years with the implementation of the national systemic therapies library known as the ACT-NOW (Anti-Cancer Therapy – Nationally Organised Workstreams) programme, implemented by Te Aho o Te Kahu – The Cancer Control Agency.

Nonetheless, our monitoring suggests a recent decrease in melanoma mortality at the population level. These national-level statistics reflect what might be expected in the New Zealand situation with the introduction of PD-1 inhibitors, based on clinical trials and what oncologists are seeing at an individual level. These results also suggest that the likely benefits attributed to nivolumab and pembrolizumab seen in the restricted population entered into registration trials may have been maintained when translated to a more heterogenous real world population. Future research could investigate whether these new PD-1 inhibitor treatments are indeed having an impact, and if so, whether this impact is maintained over time. This analysis has provided an example of the critical importance and necessity of ongoing regular monitoring of the national health data, and an inquisitive questioning of the potential reasons for unexpected changes.

Figure 3: Age-standardised rates of melanoma registrations in New Zealand, total registrations and by Breslow thickness, 2001–2019.



Note: Age-standardised to the WHO world standard population. 95% confidence intervals are shown.
Source: New Zealand Cancer Registry.

COMPETING INTERESTS
Nil.

ACKNOWLEDGEMENTS
We would like to thank Dr Jody Jordan for her comments on this paper, and the Ministry of Health for providing the data for these analyses, and for funding the Environmental Health Intelligence NZ (EHNIZ) programme.

AUTHOR INFORMATION
Kylie Mason: Principal Analyst, Environmental Health Intelligence New Zealand (EHINZ), Massey University, Wellington, New Zealand.
Liam Kelly: Analyst, Environmental Health Intelligence New Zealand (EHINZ), Massey University, Wellington, New Zealand.
Christopher G C A Jackson: Senior Lecturer in Medicine, Otago Medical School, Dunedin, New Zealand.
Deborah Read: Associate Professor, Environmental Health Intelligence New Zealand (EHINZ), Massey University, Wellington, New Zealand.
Barry Borman: Professor of Epidemiology, Environmental Health Intelligence New Zealand (EHINZ), Massey University, Wellington, New Zealand.

CORRESPONDING AUTHOR
Kylie Mason: Environmental Health Intelligence New Zealand (EHINZ), Massey University, PO Box 756, Wellington 6140. (04) 979 3124. k.mason@massey.ac.nz

URL
www.nzma.org.nz/journal-articles/did-new-treatments-contribute-to-a-decrease-in-melanoma-deaths

REFERENCES
1. Ferlay J, Ervik M, Lam F, et al. Global Cancer Observatory: Cancer Today [Internet]. Lyon, France: International Agency for Research on Cancer; 2020. Available from: https://gco.iarc.fr/today/home (accessed 11 August 2021).
2. Li Z, Fang Y, Chen H, Zhang T, Yin X, Man J, Yang X, Lu M. Spatiotemporal trends of the global burden of melanoma in 204 countries and territories from 1990 to 2019: Results from the 2019 global burden of disease study. Neoplasia. 2022 Jan;24(1):12-21.
3. McKenzie R. UV radiation in the melanoma capital of the world: What makes New Zealand so different? AIP Conference Proceedings. 2016;1810(1):20003.
4. Ministry of Health. *Mortality web tool.* Wellington: Ministry of Health; 2021. Available from: https://www.health.govt.nz/publication/mortality-web-tool (accessed 14 April 2022).
5. Bhatia S, Tykodi S S, Thompson J A. Treatment of metastatic melanoma: An overview. Oncology (Williston Park). 2009 May; 23(6):488-496.
6. PHARMAC. Decision to fund nivolumab (Opdivo) for advanced melanoma. Wellington: PHARMAC; 2016. Available from: https://pharmac.govt.nz/news-and-resources/consultations-and-decisions/decision-to-fund-nivolumab-opdivo-for-advanced-melanoma/ (accessed 24 September 2021).
7. PHARMAC. Decision regarding funding of pembrolizumab (Keytruda), nivolumab (Opdivo), posaconazole (Noxafil) and raltegravir (Isentress). Wellington: PHARMAC; 2016. Available from: https://pharmac.govt.nz/news-and-resources/consultations-and-decisions/decision-to-fund-nivolumab-opdivo-for-advanced-melanoma/ (accessed 8 November 2021).
8. Eggermont A M M, Kirkwood J M. Re-evaluating the role of dacarbazine in metastatic melanoma: what have we learned in 30 years? Eur J Cancer. 2004 Aug; 40(12): 1825-1836.
9. Hodi F S, O'Day S J, McDermott D F, et al. Improved Survival with Ipilimumab in Patients with Metastatic Melanoma. N Engl J Med. 2010 Aug; 363:711-723.
10. Syn N L, Teng M W L, Mok T S K, Soo R A. De-novo and acquired resistance to immune checkpoint targeting. Lancet Oncol. 2017 Dec;18(12): e731–41.
11. Robert C, Long G V, Brady B, et al. Nivolumab in Previously Untreated Melanoma without BRAF Mutation. N Engl J Med. 2015 Jan; 372:320-330.
12. Robert C, Schachter J, Long G V, et al. Pembrolizumab versus Ipilimumab in Advanced Melanoma. N Engl J Med. 2015 Jun 25;372(26):2521-32. doi: 10.1056/NEJMoa1503093. Epub 2015 Apr 19. PMID: 25891173.
13. Robert C, Ribas A, Schachter J, et al. Pembrolizumab versus ipilimumab in advanced melanoma (KEYNOTE-006): post-hoc 5-year results from an open-label, multicentre, randomised, controlled, phase 3 study. Lancet Oncol. 2019 Sep;20(9):1239-1251. https://doi.org/10.1016/S1470-2045(19)30388-2
14. Robert C, Long G V, Brady B, et al. Five-Year Outcomes With Nivolumab in Patients With Wild-Type BRAF Advanced Melanoma. J Clin Oncol. 2020 Sep; 38(33): 3937-3946.
15. PHARMAC. Pembrolizumab and nivolumab: Response to a request for information on funded PD-1 inhibitors (pembrolizumab and nivolumab). (25 November 2019). (Published response to Official Information Act 1982 request to PHARMAC). URL https://pharmac.govt.nz/news-and-resources/official-information-act/official-information-act-responses/pembrolizumab-and-nivolumab-2/

(accessed 7 March 2022).
16. Hodi F S, Chiarion-Sileni V, Gonzalez R, et al. Nivolumab plus ipilimumab or nivolumab alone versus ipilimumab alone in advanced melanoma (CheckMate 067): 4-year outcomes of a multicentre, randomised, phase 3 trial. Lancet Oncol. 2018 Nov;19(11):1480-1492. https://doi.org/10.1016/S1470-2045(18)30700-9
17. Environmental Health Intelligence NZ. Melanoma cancer registrations. [Factsheet]. Wellington: Environmental Health Intelligence NZ, Massey University; 2021. Available from: https://www.ehinz.ac.nz/assets/Factsheets/Melanoma-cancer-registrations_released_Jul_2021.pdf (accessed 8 November 2021).

Challenges in the treatment of a stingray injury: a rare case report in a rural New Zealand hospital

Benjamin J L Black, Monica J Londahl, Konrad K Richter

Though stingrays are commonly found in the vast Australasian waters, severe injuries are rare. Ray venom remains a poorly understood phenomenon, and the treatment of barb injuries can be challenging due to envenomation obscuring the clinical picture, as well as delayed presentations with bacterial infections.[1,2] There is a concern in New Zealand and other temperate climates that as climate change progresses, these injuries will become more common, as stingrays become a more familiar resident in our beaches.[3] Knowledge of the management of these injuries is therefore a useful addition to the armamentarium of frontline emergency and trauma staff. Here, we report a rare case of a thoracic penetrating stingray injury that required emergency treatment in our rural hospital.

Case presentation

A 48-year-old man was walking towards the shore at Ōreti Beach, near Invercargill in New Zealand, in water approximately 30cm deep, when he suffered severe pain in the right foot followed suddenly by a stab wound to the left chest.

There was a significant disturbance in the water to the right of him, and a large marine creature briefly surfaced which he caught a glimpse of. He managed to get out of the water unassisted, and an ambulance was called. The patient presented to our rural hospital with severe global chest pain, diaphoresis, dyspnoea and hypoxia (oxygen saturation of 90% while on 15L of oxygen via Hudson mask). He had a 4cm wound in the left chest with subcutaneous tissue visible (Figure 1); this was in the seventh intercostal space in the midaxillary line. He also had a 5mm puncture site on the plantar aspect of the right foot just proximal to the fifth digit (Figure 2). On chest examination, he had bilateral air entry with no clear lateralising signs. A small pneumothorax was suggested on chest X-ray (Figure 3), and an urgent intercostal drain was placed based on severe symptoms with no large release of air and no significant improvement to his oxygenation.

He was further investigated with extended Focused Assessment with Sonography in Trauma (e-FAST), which showed no free fluid in the abdomen, chest or pericardium. A CT scan of the chest (Figure 4) and abdomen was also performed which showed a small residual pneumothorax with no other significant injury seen in the chest or abdomen.

Treatment

The patient was treated with liberal IV opioids during his early presentation to ED; he received 250mcg of fentanyl, 8mg of morphine as well as 60mg of ketamine with little effect on his pain. His chest wound was explored in the emergency room with no obvious intrusion into the thoracic cavity found. After a washout and exploration of the wound with no debris found, the incision was primarily closed with non-absorbable sutures. The wound on his foot was inspected, washed out and left open. Local anesthesia, by way of infiltration during the exploration of the wound, as well as regional anesthesia (posterior tibial nerve block) was much more effective in improving his pain, significantly reducing his opioid requirement. Broad-spectrum IV antibiotics were used as well as a tetanus ADT™ booster. His pain was markedly improved the next day, and the intercostal drain was removed.

Outcome and follow-up

The patient made a good recovery from his injuries and was discharged from hospital after a two-night admission. He remained well six months following the injury with no major delayed complication becoming evident.

Figure 1: Stingray injury chest.

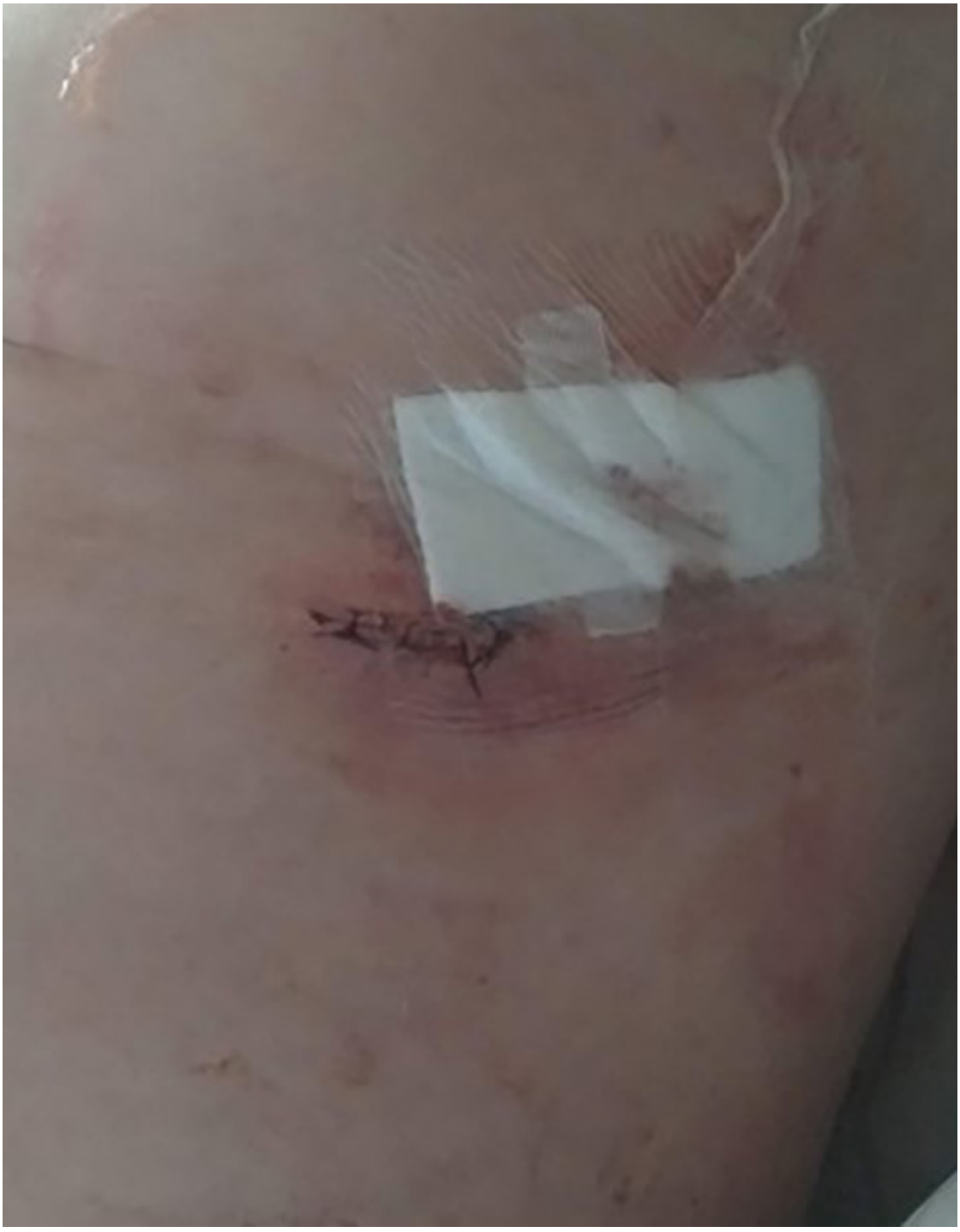


Figure 2: Stingray injury to the foot with oedema and erythema.

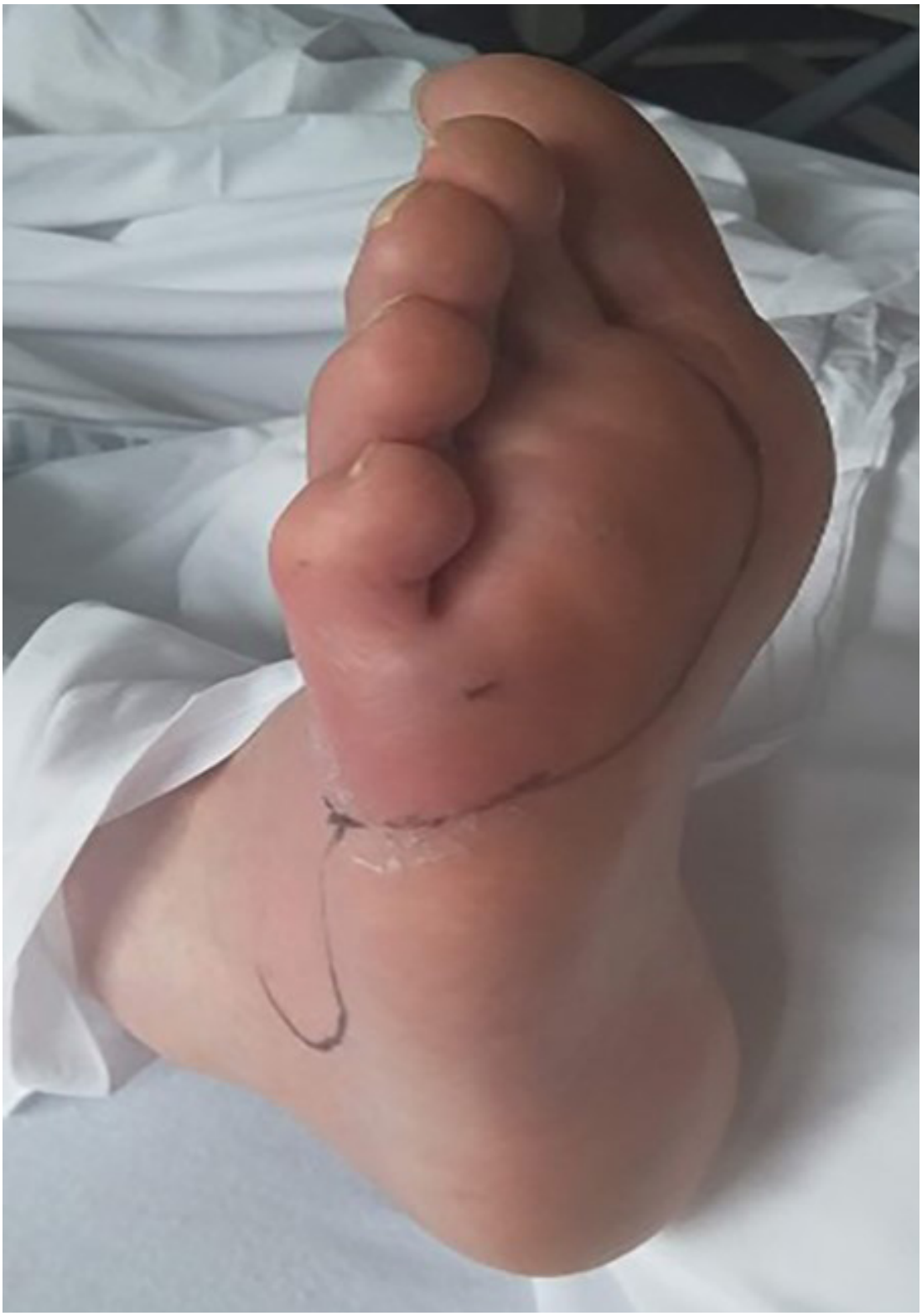


Figure 3: Stingray injury X-ray chest with pneumothorax.

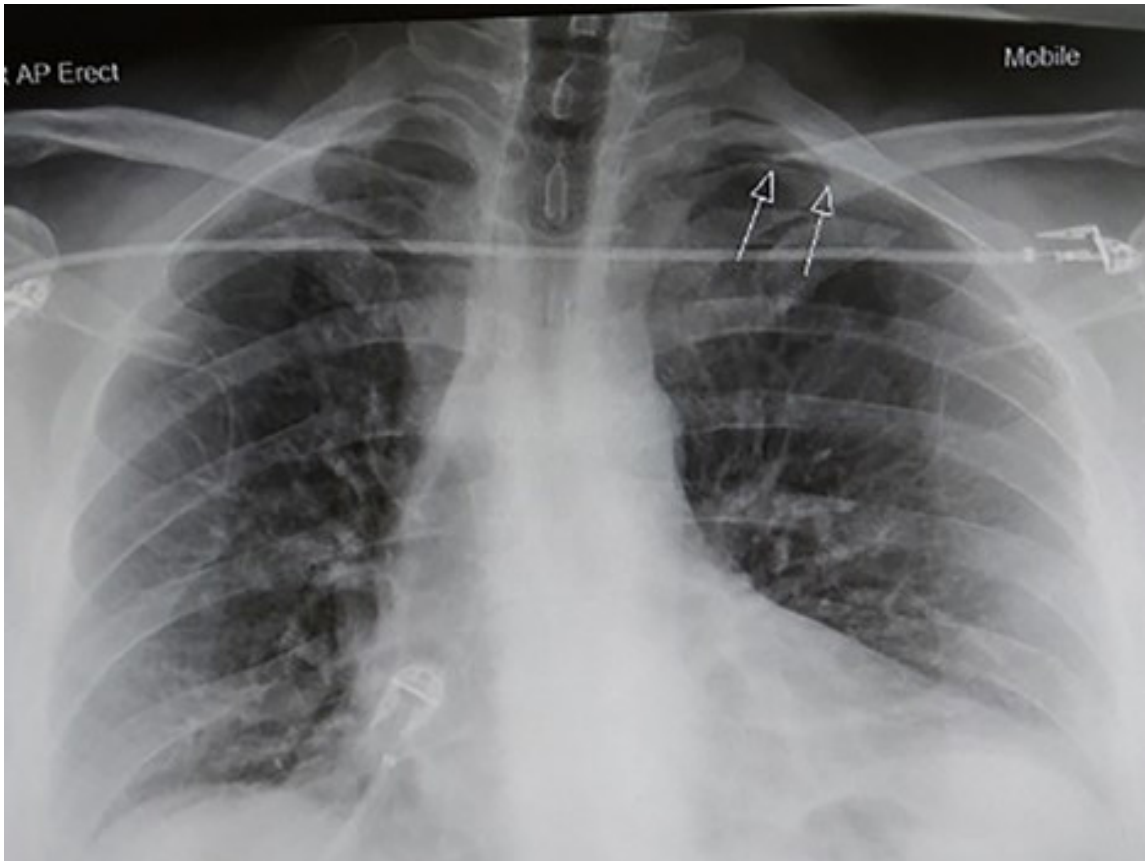
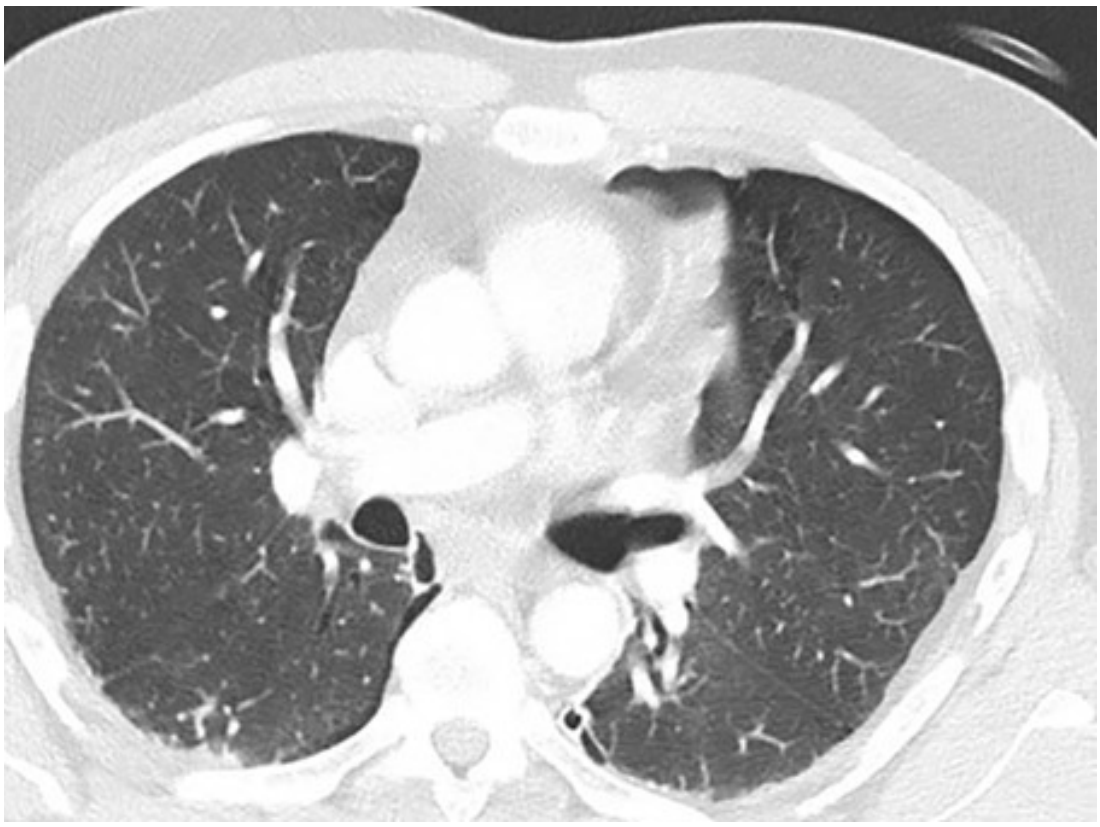


Figure 4: Chest CT with injury site.



Discussion

The pertinent factor, in this case, was that the patient's clinical signs were inconsistent with the underlying traumatic pathology. His presentation appeared to represent a more severe injury than what was discovered. The injury, instead, represented significant local and systemic envenomation from a stingray barb. Local anesthesia was the most effective in terms of analgesia for this patient, and indeed, this is in keeping with previously reported cases.[4] There is no anti-venom for stingray toxin, and management is primarily supportive care.[4] Systemic envenomation has a varied presentation, but commonly described symptoms include diaphoresis, syncope, nausea, diarrhea, and hypotension.[1,4] There have also been cases reported of cardiac arrhythmias following stingray envenomation, including supraventricular bigeminy.[5]

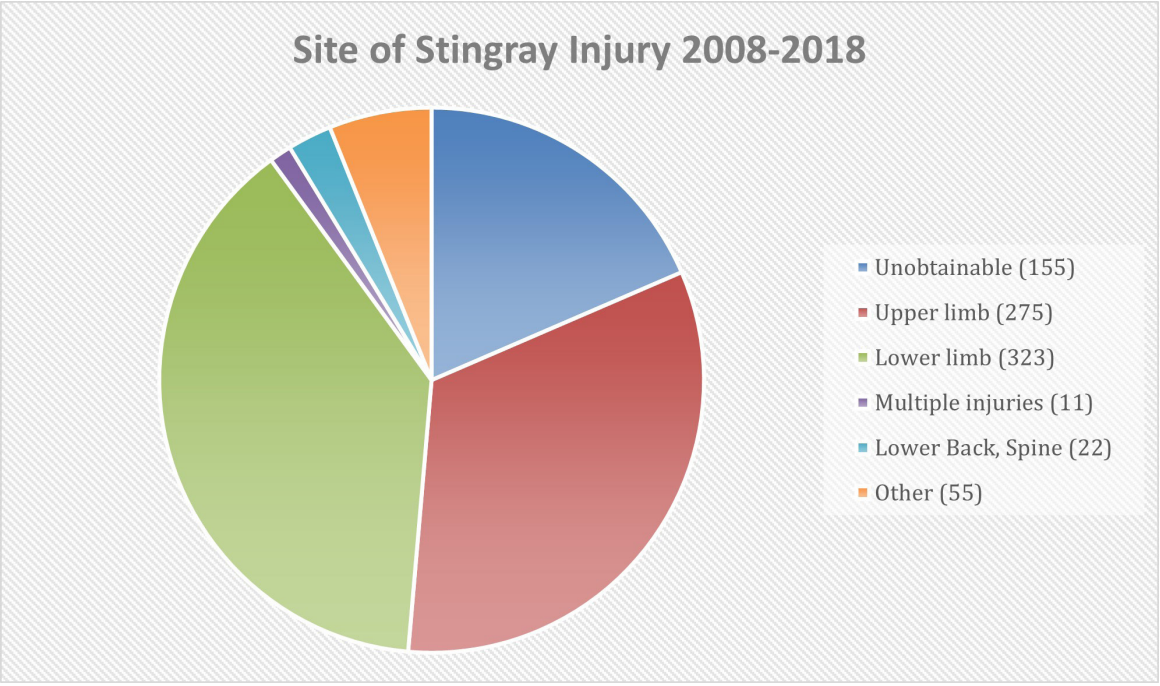
The mainstay of management of stingray penetrating trauma remains early explorative debridement, tetanus prophylaxis, and broad-spectrum antibiotics, which is common to most dirty penetrating wounds. Stingray toxin itself has been known to cause necrosis, and the injuries have been associated with necrotizing fasciitis and osteomyelitis, especially if they have sub-optimal initial wound management.[6] There have been previous necrotising soft tissue infections reported following stingray injuries involving vibrio subspecies similar to other marine organism related injuries.[5] Fluoroquinolones are often added to empiric antibiotic regimes to cover for this possibility.

Stingray venom is heat labile and can be denatured with hot water immersion of the affected areas.[1,2,4] The appropriate application of hot water would have been impractical for a penetrating thoracic wound like the one described, but it can be beneficial for more superficial wounds if the patient can tolerate this. Care must be taken to avoid thermal burns if using this technique; the toxin has to be exposed to temperatures of 45–50°C to denature, which will be intolerable to some patients. It is also an important consideration that a patient in such circumstances will typically be too distressed to accurately gauge the water's temperature, therefore ensuring someone other than the patient assesses the water temperature is necessary.

Although there is no randomised data, prospective studies indicate that this is an effective treatment for pain in many circumstances.[7] It also has been previously hypothesised that local anesthetic itself may have some direct counteraction to stingray toxin.[2]

There are only a handful of severe thoracic injuries from stingrays reported in Australasia, of which even fewer resulted in fatalities, with the most notable being Steve Irwin. The fatalities involved cases of direct mortal injuries from

Figure 5: Accident Compensation Data for New Zealand: 2008 to 2018.



trauma and delayed presentations secondary to necrosis and infection.[1,2] Traumatic pneumothoraxes are rare, but have been previously reported secondary to stingray injuries.[8] Most injuries from stingrays are to the upper and lower extremity when unlucky ocean goers encounter them when they are close to shore. This is confirmed by our national accident compensation data which shows 89% of the injuries with complete data related to stingrays in the last decade have been from extremity trauma (Figure 5). Usually docile creatures, stingrays tend to attack only if felt to be threatened.[4]

This case represents another addition to the literature of a severe penetrating thoracic trauma created by a stingray barb, and also another description of the significant regional and systemic effects of stingray toxin. The standard of care remains supportive care, generous local anesthesia, exploration, and debridement of a wound, which could include heated irrigation fluid as well as broad-spectrum antibiotics.

COMPETING INTERESTS
Nil.

AUTHOR INFORMATION
Benjamin J L Black MBChB: Surgical Registrar, Department of Surgery, Southland Hospital, Invercargill, New Zealand.
Monica J Londahl MPH: Research Fellow, University of Otago, School of Medicine, New Zealand.
Konrad K Richter MD, PHD: Consultant Surgeon, University of Otago, School of Medicine, New Zealand.

CORRESPONDING AUTHOR
Associate Professor Konrad Klaus Richter: Consultant General Surgeon, Surgical Oncologist, Colorectal Surgeon; Clinical Associate Professor Dunedin School of Medicine, Department of Surgery, Southland Hospital, Kew Road, Invercargill, New Zealand. 03 218 1949. konradklaus.richter@gmail.com

URL
www.nzma.org.nz/journal-articles/challenges-in-the-treatment-of-a-stingray-injury-a-rare-case-report-in-a-rural-new-zealand-hospital

REFERENCES
1. Evans R, Davies R. Stingray injury. Emerg Med J. 1996;13(3):224-225.
2. Fenner P, Williamson J, Skinner R. Fatal and non-fatal stingray envenomation. Med J Aust. 1989;151(11-12):621-625.
3. Needleman R, Neylan I, Erickson T. Environmental and Ecological Effects of Climate Change on Venomous Marine and Amphibious Species in the Wilderness. Wilderness Environ Med. 2018;29(3):343-356.
4. Slaughter R, Beasley D, Lambie B, Schep L. New Zealand's venomous creatures. N Z Med J. 2009;122:83-97.
5. Ikeda T. Supraventricular bigeminy following a stingray envenomation: a case report. Hawaii Med J. 1989;48(5):162-164
6. Ho PL, Tang W-M, Yuen K-S. Necrotizing fasciitis due to Vibrio alginolyticus Following an Injury Inflicted by a Stingray. Scand J Infect Dis. 1998;30(2):192-193.
7. Myatt T, Nguyen B J, Clark R F, et al. A prospective study of stingray injury and envenomation outcomes. J Emerg Med. 2018 Aug 1;55(2):213-7.
8. Suzuki T, Takada T, Fudoji J. Traumatic Pneumothorax Associated With Penetrating Neck Injury Caused by a Stingray: A Case Report. Wilderness Environ Med. 2017 Jun;28(2):119-121

Face masks and falls

John Hugh Thwaites, Julia Frances Thwaites

Over the past 20 months, many New Zealanders have been wearing face masks to reduce the transmission of COVID-19. Masks are thought to be beneficial in terms of reducing the chance of transmitting respiratory borne viruses including COVID-19.[1] Most people have been wearing standardised surgical masks, although many have opted for personalised cloth masks for comfort and fashion. However there have been reports on the difficulty of wearing masks due to adverse skin reactions,[2] and the challenges of communication for those with hearing loss.[3] Also of concern is the increased risk of falls and injuries due to obscuration of inferior peripheral vision caused by face masks and mask-related fogging of glasses.[4,5]

We present two patients admitted with significant injuries due to falls resulting from wearing masks.

Case reports

The first patient was a 91-year-old woman who fell down two steps while adjusting flowers on a church altar. She attributed her fall solely to her face mask impairing her inferior vision, as she was unable to view the steps. Her vision and cognition were normal, and she did not wear glasses except for reading. She had no other significant past medical history or disability. She mobilised independently and had no previous history of falls.

She sustained multiple facial fractures involving the maxillary sinuses, a displaced fracture of the floor of the left orbit, and a displaced fracture of the medial left pterygoid process. She also sustained fractures of her left distal radius and middle finger. She was assessed by the maxillofacial and orthopaedic teams as not requiring surgery, but rather a cast for her forearm. She was transferred to a rehabilitation hospital where she made a slow but uneventful recovery.

The second patient was a 74-year-old woman who tripped over a small concrete bollard whilst shopping. She attributed this entirely due to her inferior vision being obscured by her face mask, which had migrated proximally over her glasses with concomitant fogging of the lenses. Her glasses were standard single vision lenses. She sustained a right patella fracture and a left radial fracture, both requiring surgery. She had multiple underlying co-morbidities including rheumatoid arthritis, Sjögren's syndrome, and pulmonary amyloidosis and hemochromatosis; however, she was independently mobile and had no previous history of falls. She had a slow but uncomplicated recovery.

Discussion

Wearing face masks is important during the current COVID-19 pandemic, especially for those at higher risk of infection. Face masks, however, may increase the risk of falls and injuries through impairing inferior vision, which can be further exacerbated by mask-associated fogging of the lenses when wearing glasses.[4,5] In the two cases presented, both patients attributed their falls to impaired vision from their face masks, and in one case this was exacerbated by associated fogging of the lenses of her glasses.

People with impaired peripheral vision have an increased risk of falls and falls with injury.[6] This is concerning for older people already at increased risk of falls and injuries from falls.[7]

Vision and the ability to respond to visual cues are important factors that aid individuals in avoiding falls and falls with injury. Deficits in both central and peripheral vision can produce incorrect sensory inputs through misjudgments of distances and/or misinterpretations of spatial information.[6]

Multifocal lens glasses designed with progressive lenses, as opposed to two separate single lenses, can impair depth perception, and therefore cause impairment in detecting obstacles and are associated with increased risk of falls.[8] However this did not apply, as our one patient wearing glasses was wearing single lens glasses.

While falls in older people are commonly multifactorial, in these two cases both patients clearly attribute the falls to wearing face masks, and no other obvious, clinical cause for their falls was found.

Strategies to reduce the risks of falls with face masks include: advising older people of the poten-

tial risk of falls and injuries with face masks; ensuring a tight fit of the face mask to reduce any obstruction to vision and to reduce the likelihood of glasses fogging up;[4] if wearing glasses, washing the lenses in soapy water before using a mask to reduce mask-related fogging;[9] advising people to take their time before starting their walk, and to walk more slowly to allow more time to detect upcoming trip hazards and to plan a safe route.[4]

However, more research is required to explore and determine the risks of falls and injuries associated with face masks, particularly in older people during this pandemic, and to evaluate strategies to reduce such risk during these challenging times.

COMPETING INTERESTS
Nil.

AUTHOR INFORMATION
John Hugh Thwaites: Consultant Physician, Older Persons Health, Canterbury District Health Board, Christchurch.
Julia Frances Thwaites: University of Otago, Christchurch School of Medicine, Christchurch.

CORRESPONDING AUTHOR
John Hugh Thwaites: Consultant Physician, Older Persons Health, Canterbury District Health Board, Christchurch. john.thwaites@cdhb.health.nz

URL
www.nzma.org.nz/journal-articles/face-masks-and-falls

REFERENCES
1. Chu D K, Akl E A, Duda S, Solo K, Yaacoub S, Schunemann HJ, et al. Physical distancing, face masks, and eye protection to prevent person-to-person transmission of SARS-CoV-2 and COVID-19: a systematic review and meta-analysis. Lancet. 2020;395(10242):1973-87.
2. Techasatian L, Lebsing S, Uppala R, Thaowandee W, Chaiyarit J, Supakunpinyo C, et al. The Effects of the Face Mask on the Skin Underneath: A Prospective Survey During the COVID-19 Pandemic. J Prim Care Community Health. 2020;11:2150132720966167.
3. Chodosh J, Weinstein B E, Blustein J. Face masks can be devastating for people with hearing loss. BMJ. 2020;370:m2683.
4. Kal E C, Young W R, Ellmers T J. Face masks, vision, and risk of falls. BMJ. 2020;371:m4133.
5. Dankert J F, Virk M S. Mask-Related Glasses Fogging: A Predisposing Mechanism of Falls during the COVID-19 Pandemic. Case Rep Orthop. 2021;2021:5600216.
6. Patino C M, McKean-Cowdin R, Azen S P, Allison J C, Choudhury F, Varma R, et al. Central and peripheral visual impairment and the risk of falls and falls with injury. Ophthalmology. 2010;117(2):199-206 e1.
7. Abey-Nesbit R, Schluter P J, Wilkinson T, Thwaites J H, Berry S D, Jamieson H A. Risk factors for hip fracture in New Zealand older adults seeking home care services: a national population cross-sectional study. BMC Geriatr. 2019;19(1):93.
8. Lord S, Dayhew J, Sc B, Howland A. Multifocal Glasses Impair Edge-Contrast Sensitivity and Depth Perception and Increase the Risk of Falls in Older People. Journal of the American Geriatrics Society. 2002;50(11):1760-1766.
9. Malik S S, Malik S S. A simple method to prevent spectacle lenses misting up on wearing a face mask. Ann R Coll Surg Engl. 2011;93(2):168.

A case of macroenzyme aspartate aminotransferase (macro-AST) in a patient with seronegative rheumatoid arthritis

Bobby Li, James Falvey, Linda Pike, Christiaan Sies, Peter Chapman, Chris Florkowski

Aspartate aminotransferase (AST) is commonly measured as part of a liver function test panel. Although elevations in AST may indicate hepatic disease, AST elevations are not as liver specific as alanine aminotransferase (ALT) elevations, and they are also associated with myositis, rhabdomyolysis, acute myocardial infarction or haemolysis. Although not widely recognised by physicians, macroenzyme aspartate aminotransferase (macro-AST) caused by immunoglobulin binding to AST is also as an uncommon cause of AST elevation.

Case report

A 19-year-old female Caucasian patient with probable seronegative rheumatoid arthritis, with pain in her wrists, fingers and ankles and with associated stiffness, came to our attention following five weeks of consistently raised AST on three separate occasions (260–288 U/L (Reference Interval (RI): 0–50)). This was in the setting of otherwise normal liver function tests that were performed before commencing sulfasalazine. AST was measured using the Abbott ARCHITECT c16000. AST seven months previously was 28 U/L.

A number of investigations were performed to determine the cause of elevated AST, including measurement of creatine kinase (CK) and abdominal ultrasound, as well as a miscellaneous screen for causes of liver disease. AST recovery post polyethylene glycol (PEG) precipitation was determined to investigate for macro-AST. For this, 200 µL of 24% PEG 6,000 was added to 200 µL of patient sample, incubated at 20 minutes at 37°C and centrifuged at 3,000 rpm for five minutes. 200 µL of supernatant was diluted with 200 µL of 0.9% sodium chloride and vortexed before analysis for AST. The resulting AST was multiplied by four to account for dilution.

Results

The post-PEG recovery of AST was less than 4%, compared with 48% in a control patient, strongly suggestive of macro-AST (Table 1).

Normal CK (89 U/L (RI: 30–180)) suggested no substantial muscular source to explain elevated AST. Abdominal ultrasound demonstrated normal liver. Iron studies demonstrated iron deficiency rather than overload, with a transferrin saturation of 7% (RI: 16–45), and a ferritin of 49 µg/L (RI: 20–200) in context of a CRP of 11 mg/L (RI: <5). Caeruloplasmin was normal (0.47 g/L (RI: 0.15–0.60)). Alpha-1 antitrypsin had normal MM phenotype and level (2.9 g/L (RI: 1.0–2.0)). Alpha-fetoprotein was not elevated (<5 µg/L (RI: 0–16)). Hepatitis B and C serologies were negative. Anti-nuclear antibodies (ANA) were detected at 1:320 in a homogeneous, chromosome positive pattern (Table 2). Haemolysis was not considered likely, with a haemoglobin of 130 g/L and bilirubin of 5 µmol/L.

Due to analyser changeover in our laboratory, AST was subsequently found to be elevated on the Beckman Coulter AU5800. Interestingly, our patient's AST normalised nine months following the initial presentation (Figure 1).

Discussion

We describe a case of macro-AST in a patient with probable seronegative rheumatoid arthritis, supported by low post-PEG recovery of AST, and substantial exclusion of muscular or liver related causes of AST elevation.

Macro-AST is caused by immunoglobulin bound to AST, leading to decreased clearance of AST and elevated levels of AST in the plasma. Immunoglobulin G (IgG), immunoglobulin A (IgA) and immunoglobulin M (IgM) bound to AST have all been described.[1–8] Macro-AST is generally benign.

Table 1: Low post-PEG recovery of AST in case vs control sample indicative of macro-AST.

Sample	Pre-PEG AST (U/L)	Post-PEG AST (U/L)	% Recovery post-PEG
Current patient	291	<12	<4%
Control sample	233	112	48%

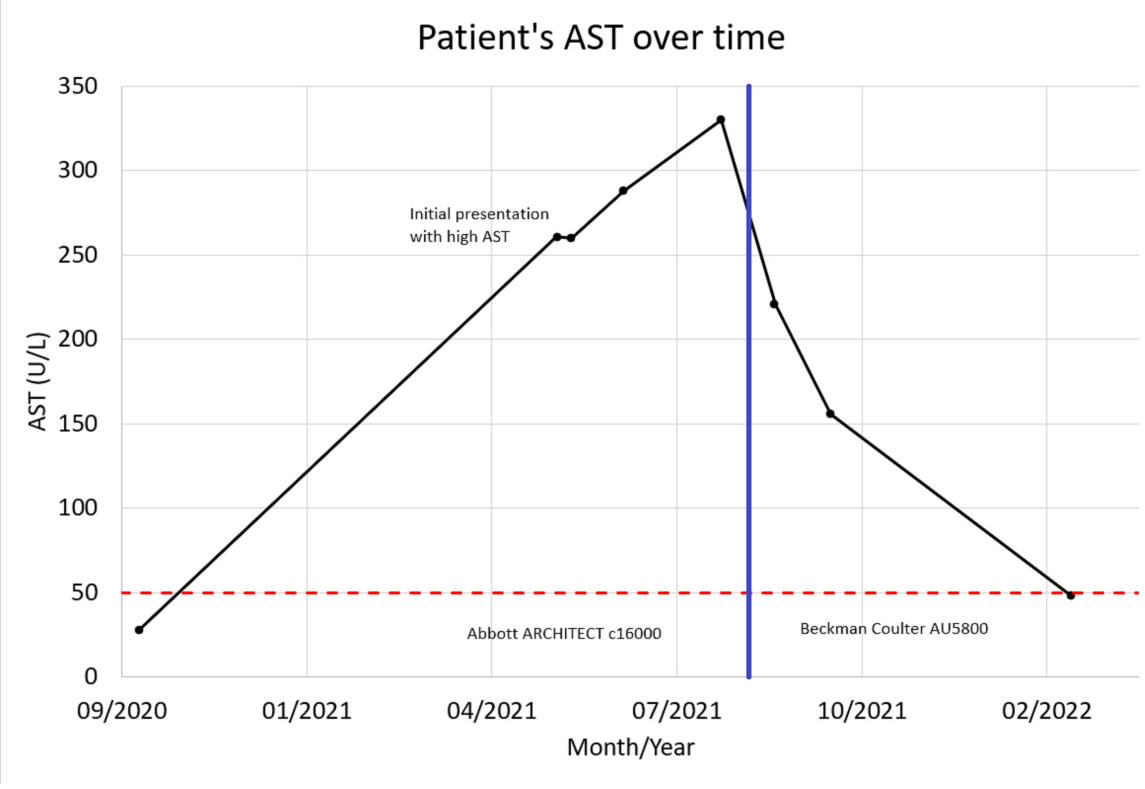
Table 2: Biochemistry of patient.

Biochemistry	Result	Reference Interval
Albumin	38 g/L	32–48
Bilirubin	5 µmol/L	2–20
Alkaline phosphatase (ALP)	76 U/L	30–150
Gamma-glutamyl transferase (GGT)	14 U/L	10–35
Aspartate aminotransferase (AST)	260 U/L	10–50
Alanine aminotransferase (ALT)	**24 U/L**	**0–30**
C-reactive protein (CRP)	11 mg/L	<5
Hepatitis C antibody	Negative	Negative
Hepatitis B surface antigen	Negative	Negative
Hepatitis B surface antibody	Negative	
Hepatitis B core antibody	Negative	Negative
Transferrin saturation	7%	16–45
Ferritin	49 µg/L	20–200
Creatine kinase	89 U/L	30–180
Glycated haemoglobin (HbA1c)	29 mmol/mol	20–40 mmol/mol
Copper	27.5 µmol/L	11.3–25.2
Caeruloplasmin	0.47 g/L	0.15–0.60
Alpha-1 antitrypsin level	2.9 g/L	1.0–2.0
Alpha-1 antitrypsin phenotype	MM	MM
Alpha-fetoprotein (AFP)	<5 µg/L	0–16
Immunoglobulin G (IgG)	14.5 g/L	7.0–14.0
Immunoglobulin A (IgA)	0.8 g/L	0.8–3.5
Immunoglobulin M (IgM)	0.5 g/L	0.5–2.0
Autoantibody screen		
Anti-nuclear antibody	1:320, homogeneous, chromosome positive	None detected
Smooth muscle	None detected	None detected
Mitochondrial antigens	None detected	None detected
Liver Kidney Microsomal	None detected	None detected

Although its pathogenesis is unclear, there have been other case reports of macro-AST in association with rheumatological conditions in the literature, hypothesised to be due to dysregulation of immune tolerance.[3,4] Prevalence is reported as 22–38.6% of paediatric patients with persistently isolated elevated AST, and 13.1% of adult patients with elevated AST and AST/ALT ratio.[5–7]

Macro-AST is an under recognised cause of AST elevation. In the appropriate clinical setting, an isolated elevation in AST should lead to correspondence with the laboratory to enable relevant studies to investigate the diagnosis of macro-AST. In some patients, macro-AST resolves spontaneously with time.[5] A percent precipitable activity ≥75% (i.e., post-PEG recovery ≤25%) was previously found to be the optimal threshold for determining macro-AST using 24% PEG 6,000.[5] Beyond PEG precipitation, other methods to prove macro-AST include gel filtration chromatography, ultrafiltration and Protein A or G immunodepletion (if it is an IgG macroenzyme).[5,8] Recognition of macro-AST as the cause of elevated AST is critical to avoid misattribution of elevated AST and avoid unnecessary invasive investigations.

Figure 1: Change in patient's AST over time. Upper reference limit indicated as the horizontal dashed line (50 U/L) and analyser changeover indicated by a solid vertical line.



COMPETING INTERESTS
Nil.

AUTHOR INFORMATION
Bobby Li: Chemical Pathology Registrar, Specialist Biochemistry, Canterbury Health Laboratories, Canterbury District Health Board, Christchurch.
James Falvey: Gastroenterologist, Canterbury District Health Board, Christchurch.
Linda Pike: Medical Laboratory Scientist, Specialist Biochemistry, Canterbury Health Laboratories, Canterbury District Health Board, Christchurch.
Christiaan Sies: Section Head of Specialist Biochemistry, Scientific Officer, Specialist Biochemistry, Canterbury Health Laboratories, Canterbury District Health Board, Christchurch.
Peter Chapman: Rheumatologist, Clinical Director of Department of Rheumatology, Immunology and Allergy, Canterbury District Health Board, Christchurch.
Chris Florkowski: Chemical Pathologist, Specialist Biochemistry, Canterbury Health Laboratories, Canterbury District Health Board, Christchurch.

CORRESPONDING AUTHOR
Dr Bobby Li, Chemical Pathology Registrar, Specialist Biochemistry, Canterbury Health Laboratories, Canterbury District Health Board, Christchurch.
Bobby.li@cdhb.health.nz

URL
www.nzma.org.nz/journal-articles/a-case-of-macroenzyme-aspartate-aminotransferase-macro-ast-in-a-patient-with-seronegative-rheumatoid-arthritis

REFERENCES
1. Tameda M, Shiraki K, Ooi K, et al. Aspartate aminotransferase-immunoglobulin complexes in patients with chronic liver disease. World J Gastroenterol. 2005;11(10):1529-1531.
2. Rubin A S, Sass D A, Stickle D F. Distribution of serum concentrations reported for macroenzyme aspartate aminotransferase (macro-AST). Pract Lab Med. 2017;8:65-69.
3. Mbagaya W, Foo J, Luvai A, et al. Persistently raised aspartate aminotransferase (AST) due to macro-AST in a rheumatology clinic. Diagnosis (Berl). 2015;2(2):137-140.
4. Rohani P, Imanzadeh F, Sayyari A, et al. Persistent elevation of aspartate aminotransferase in a child after incomplete Kawasaki disease: a case report and literature review. BMC Pediatr. 2020;20(1):73.
5. Caropreso M, Fortunato G, Lenta S, et al. Prevalence and long-term course of macro-aspartate aminotransferase in children. J Pediatr. 2009;154(5):744-748.
6. Magen-Rimon R, Tal G, Kaplan M, Shaoul R. The significance of isolated aspartate aminotransferase elevation in healthy paediatric patients. Acta Paediatr. 2022;111(3):675-679.
7. Moriyama T, Nobuoka M, Makino M. Incidence and properties of aspartate aminotransferase-immunoglobulin complexes in patients with a high serum aspartate to alanine aminotransferase ratio. Clin Chim Acta. 1990;190(1-2):47-56.
8. van Wijk X M R, Magee C A, Wu A H B, et al. A comparison of methods for evaluation of a case of suspected macro-aspartate aminotransferase. Clin Chim Acta. 2016;463:1-3.

Provision for Unmarried Maternity Cases

NZMJ, July 1922

URL: WWW.NZMA.ORG.NZ/JOURNAL-ARTICLES/PROVISION-FOR-UNMARRIED-MATERNITY-CASES

In the course of the interview which the representatives of the New Zealand Branch of the B.M.A. had with the Minister of Heath and the Minister of Justice on 24th March, the reference was made to the refusal of authorities to admit unmarried women to the state of maternity hospitals for confinement.

The members of deputation said it was considered by the Association that the Government's attitude should be not to make the difficulties of "the illegitimate" too great. The position at present was that women who had made the wrong step, but who were prepared to face the consequences rather than make a second blunder and risk their life by seeking abortion, had the doors of State maternity hospitals shut upon them and they were almost forced into the hands of the abortion-monger, or of the unscrupulous irregular midwife who took advantage of the patient's dire circumstances to fleece her. The only other possible way out was to enter one or other of the religious institutions provided for these people, but by so doing the stigma of illegitimacy was emphasised and generally there were conditions attached to entrance which could not always be complied with.

In every way, it was submitted, the condition of the "illegitimate" was made too hard, and that, however moralists might view the question, it was not for the State to penalise or victimise its members who had erred against social law in complying, perhaps with natural law.

In the Melbourne and Sydney State maternity hospitals married and single alike were admitted. There was absolutely no distinction to be made. A single girl could assume a married name and could be placed alongside a married woman who regarded her as married. As far as was known no complaint had been made against such admissions. In New Zealand when a single girl in trouble came to a doctor he could only advise her to go to the Salvation Army Home, or some such institution. If, for instance, she was advised to go to St. Mary's Home, in Auckland, she demurred because everyone knew that single girls went there. If she should be told to go to the St. Helen's or some other maternity hospital, and that no difference would be made because she was single, she would be easier in mind, and would get quickly over her trouble, and it would undoubtedly tend to diminish abortion. In the opinion of the deputation it would noy tend to an increase of illegitimacy.

Further, it was thought that some provision should be made for the care of illegitimate children who might eventually become very valuable citizens, as they often did. A girl who had to go to her daily occupation might not be able to pay a premium for the adoption of her child, and if a home could be established it would be of great service to the State. There was at least one such home in Melbourne.

The opportunity was also taken of directing the attention of both the Ministers to what the members of the deputation considered the inadequate punishment meted out to men found to be guilty of carnal knowledge with young girls of the age of 14, or even younger, and more especially to those scoundrels who at the same time infect them with venereal disease. It was pointed out that many of these criminals pleaded guilty, that no medical evidence was called to prove the great damage done to these children, and that they frequently got off with the absurd punishment of two years' imprisonment. The deputation strongly urged that in all such cases a report of medical examination be submitted, and that the widest powers be given to judges in dealing with this class of criminal.

After some discussion on the several questions raised, the Minster of Health promised to carefully consider the representations made by the deputation.