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The Influenza Epidemic
Utility of whole genome sequencing for multidrug resistant *Mycobacterium tuberculosis* isolates in a reference TB laboratory in New Zealand

Indira Basu, James E Bower, Sally A Roberts, Gillian Henderson, Htin Lin Aung, Gregory Cook, Odette Lowe, Sandie Newton

The emergence of multi-drug resistant tuberculosis (MDR-TB) has become a serious public health concern all across the globe. MDR-TB requires rapid detection to prevent further spread; often requiring alternate prolonged antibiotic treatment regimens with potent side-effects for the patient. New Zealand currently has a low burden of MDR-TB. But with increasing travel by New Zealanders overseas as well as increased immigration from high-risk countries, maintaining the status quo requires knowledge of state-of-the-art molecular technology like sequencing the whole genome of the *Mycobacterium tuberculosis*, the bacteria responsible for causing TB. This paper shows that in a reference TB laboratory like LabPLUS, adoption of this technology adds significant value when discrepancy arises between different testing methods employed to detect MDR-TB. This work lies at the frontier of research in this area and can make a big difference in recommending timely and appropriate antibiotic treatment and preventing the spread of this deadly disease.

Cutaneous squamous cell carcinoma: predictors of positive and close margins and outcomes of re-excision in Northland, New Zealand

Brodie M Elliott, Benjamin R Douglass, Daniel McConnell, Blair Johnson, Christopher Harmston

Non-melanoma skin cancer (NMSC) is the most commonly diagnosed and costly cancer in Australasia. Cutaneous squamous cell carcinoma (cSCC) accounts for approximately 25% of this disease and can be fatal. We evaluated all of the cSCC removed in Northland, New Zealand in 2015. We found that lesions of the head and neck, those removed in primary care and those with increased tumour thickness were more likely to have positive margins following surgical excision. Of the patients with a positive margin, only 52.6% went on to have a surgical re-excision and in this group 31.7% were found to have residual cutaneous squamous cell carcinoma. This is important as patients with a positive margin after surgery should be followed up and a reoperation considered.

Modelling the number of quitters needed to achieve New Zealand's Smokefree 2025 goal for Māori and non-Māori

Nick Wilson, Frederieke Sanne Petrović-van der Deen, Richard Edwards, Andrew Waa, Tony Blakely

In this modelling study we found that to achieve the New Zealand Government's Smokefree 2025 Goal (a below 5% smoking prevalence by 2025), there would need to be additional averages of 8,400 Māori long-term quitters per year (5.2 times the business-as-usual [BAU] level on average) and 8,800 extra non-Māori quitters per year during 2018 to 2025 (1.9 times the BAU level on average). Given these findings, it suggests that to achieve the Smokefree 2025 goal, the Government will need to massively increase investment in established interventions (smoking cessation support, mass media) while continuing with substantial tobacco tax increases, or else add substantive new strategies into the intervention mix.
Reliability of venous blood gas sodium, potassium and creatinine

Pourya Pouryahya, Zhiliang Caleb Lin, Lynn Tan, Alastair Meyer

A quick bedside (iSTAT/point of care blood test) electrolytes (sodium and potassium) and creatinine (a surrogate for kidney function) is as reliable as formal laboratory tests, which sometimes takes a while to be available.

Public support and sociodemographic correlates of public breastfeeding support in New Zealand

Yanshu Huang, Danny Osborne, Chris G Sibley

In 2016/17, the New Zealand Attitudes and Values Study, a large survey of New Zealander's social attitudes, assessed public attitudes toward women breastfeeding in public. We found that three quarters (75.3%) of New Zealanders support women breastfeeding in public. Only a small minority (5.2%) were opposed to women breastfeeding in public whereas a moderate proportion (19.5%) of New Zealanders were neutral on the issue. These results highlight that most New Zealanders hold relatively positive views of women breastfeeding in public. We recommend that future public health initiatives continue to work towards fostering support for women who choose to breastfeed in public.

New Zealand's experience of the 1918–19 influenza pandemic: a systematic review after 100 years

Jennifer A Summers, Michael G Baker, Nick Wilson

The 1918–1919 influenza pandemic has been New Zealand's most severe disaster event (around 9,000 deaths) and while it is a relatively well-studied disaster, there remain important research questions relating to this pandemic in New Zealand. This systematic review summarises all known published literature on the epidemiological, societal and transmission characteristics of the pandemic in New Zealand. Nevertheless, some research gaps remain, including the apparent marked reduction in birth rates in 1918–1919 and the reasons for no socioeconomic gradient despite other New Zealand evidence for occupational class variation in lifespan at this time. In the Centenary year of the 1918–19 Influenza Pandemic, now is the time for New Zealand to reflect on its impact and to ensure appropriate plans are in place to deal with future pandemics.

Sudden death in patients with serious mental illness

Erik Monasterio, Andrew McKean, Vimu Sinhalage Christopher Frampton, Roger Mulder

People who experience serious mental illnesses (SMI) are known to have poor health status and significantly premature mortality. National and international studies have shown that patients with serious mental illness have a 15- to 20-year gap in their life expectancy when compared to the general population. Of particular concern, studies also indicate that this gap in life expectancy is increasing. Our research studied the causes of sudden death for patients with SMI who received special mental health care in Canterbury between 2005 and 2009, with the aim of determining interventions to mitigate the risk of sudden death and premature mortality. This is particularly important given New Zealand's high suicide rate.
Reducing the impact of the impending myopia epidemic in New Zealand
Alex Petty, Graham Wilson

Myopia (short-sightedness) is an eye condition affecting children that is increasing around the world and is associated with a higher risk of other ocular disease later in life. Higher levels of myopia will have a profound social, economic and health burden in New Zealand. Fortunately, proven interventions to limit the onset and degree of myopia already exist. To limit the level of myopia in New Zealand we propose the creation of a multidisciplinary myopia action group (NZMAG) to serve as the guiding body for myopia related information and intervention in New Zealand. With prompt action now, the myopia epidemic seen in other countries can be reduced in New Zealand.

Guidelines for Gender Affirming Healthcare for Gender Diverse and Transgender Children, Young People and Adults in Aotearoa, New Zealand
Jeannie Oliphant, Jaimie Veale, Joe Macdonald, Richard Carroll, Rachel Johnson, Mo Harte, Cathy Stephenson, Jemima Bullock, David Cole, Patrick Manning

Health professionals and transgender advocates from around the country have created a new set of guidelines: Gender Affirming Healthcare for Gender Diverse and Transgender Children, Young People and Adults in Aotearoa New Zealand. The guidelines provide an approach to healthcare delivery which is uniquely Aotearoa/New Zealand, by utilising Māori models of health that recognise the importance of holistic care, while also referencing international standards. The new guidelines promote healthcare based on informed consent. This means that healthcare providers’ duty of care is to make sure that people seeking gender affirming care are empowered with all the information they need to make the best decisions for themselves. The guidelines make recommendations for district health boards. There is an urgent need for each DHB to develop a clear pathway for provision of gender affirming healthcare locally.

Public health and the radio frequency radiation emitted by cellphone technology, smart meters and WiFi
Susan Pockett

For many years there has existed good scientific evidence that radio frequency emissions like those put out by cellphones and their base stations, electricity smart meters and WiFi cause a number of biological effects likely to result in cancer, dementia and other diseases. However, the official narrative in New Zealand remains “causation not proven”, “more research needed”—and in the meantime, it’s fine for everyone to be involuntarily exposed to unmonitored levels of such emissions, more or less all the time. It is suggested that this narrative actually constitutes a giant experiment in its own right, an experiment which is (1) completely unethical (in that none of its subjects has given informed consent to participate) and (2) so badly designed that it actually makes ‘proving causation’ impossible, by preventing comparison of the health of an exposed group with that of a non-exposed group, because the latter no longer exists. Some recommendations for how to start implementing at least a weak version of the precautionary principle are offered.
Addressing the treatment gap in New Zealand with more therapists – is it practical and will it work?

Julia J Rucklidge, Kathryn A Darling, Roger T Mulder

The release of He Ara Oranga, the Report of the Government Inquiry into Mental Health and Addiction (https://mentalhealth.inquiry.govt.nz/assets/Summary-reports/He-Ara-Oranga.pdf) early this month, highlighted a mental health system that is struggling to cope with the escalating number of people with mental health issues. It is encouraging to see that the increasing morbidity associated with mental illness is being recognised and taken seriously in an effort to destigmatise psychiatric symptoms in our community. The Report should play a pivotal role in improving access and services for those struggling with mental health issues and ultimately lead to enhanced outcomes.

New Zealand data are clear that there is a rising number of people suffering from mental health problems; the New Zealand Health Survey identified that the number of adults with a mood disorder went up by 56% from 2006/2007 (10.8%) to 2016/2017 (16.8%). Rates of anxiety disorders went from 4.3% to 10.3%, an increase of 140%. These estimates come from using the K10 questionnaire. Based on these scores, 5% fell in the severe range, 9% moderate and 7% mild. Children are not immune to these problems, with an almost three-fold increase in that same time period in the number with emotional and behavioural problems, from 1.8% to 4.9% (www.health.govt.nz). Overall, these most recent data indicate that about one in five New Zealanders struggle with mental health problems in any given year, rates on par with international statistics; this equates to about 950,000 people based on a population of almost five million.

The most recent figures from Pharmac show that over that same decade of rising mental health problems (2007–2016), rates of prescriptions for antidepressants went up 48% and rates of prescriptions for antipsychotics went up 40% (www.pharmac.govt.nz). However, increasing access to psychiatric medications as well as increased spending has not resulted in improved mental health outcomes.1 The Report acknowledges that “we can't medicate or treat our way out of the epidemic of mental distress” (page 10).

The Report not only described the serious shortfalls of the current state of the New Zealand mental health system, it also outlined 40 recommendations, including “more options for talk therapies” (recommendation 12) and to increase access to psychotherapy beyond the most severe cases. The report outlined “The lack of available services, especially talk therapies, was blamed for much of the perceived ineffectiveness and inefficiency of the current system” (page 56).

Overseas initiatives, such as the Improving Access to Psychological Therapies programme in the UK and the Medicare-funded scheme for Better Access to Mental Health Care in Australia, that have focused on increasing the number of health professionals available to offer psychological treatments, were cited as evidence that offering talk therapies was a viable and cost-effective way forward.2 However, before investing in more resources, is it realistic to substantially increase the pool of psychologists/therapists in New Zealand sufficiently to meet the growing demand?

There are currently 3,713 psychologists (that number includes clinical, counselling, neuropsychologist, educational psychologists and general scope) on the New Zealand psyche. It is encouraging to see that the increasing morbidity associated with mental illness is being recognised and taken seriously in an effort to destigmatise psychiatric symptoms in our community. The Report should play a pivotal role in improving access and services for those struggling with mental health issues and ultimately lead to enhanced outcomes.

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There are currently 3,713 psychologists (that number includes clinical, counselling, neuropsychologist, educational psychologists and general scope) on the New Zealand psyche.
Zealand Psychologists Board’s Register but only 3,005 hold a 2018–2019 Annual Practicing Certificate. Of these 3,005, 1,639 are actively registered under the Clinical Scope of practice, the scope of practice usually identified as those professionals who can treat the most severe cases. The number of psychologists to the number of people who could benefit from psychological treatments is 1:312 or one clinical psychologist for every 145 individuals with severe mental health problems (5% of the population).

Assuming a full-time psychologist can see about 80 patients a year (based on a work load of 20 patients a week and 10 sessions per patient), alongside the acknowledgement that a substantial number of psychologists only work part-time, our current workforce of psychologists realistically might see about 200,000 patients/year. These estimates may be optimistic as based on 2016 figures, 169,454 New Zealanders used specialist mental health services.

There are other professionals who can offer evidence-based psychotherapies, such as counsellors and social workers. Indeed, there are 3,000 counsellors registered with the New Zealand Association of Counsellors (about the same as psychologists; however, they typically treat the mild end of the spectrum and are not trained to treat those with serious mental health problems) and about 6,500 registered social workers (most of whom do not work in a therapeutic capacity treating people with psychiatric disorders). Together, they could possibly see another 200,000 individuals/year.

These estimates leave about 550,000 individuals struggling with mental health problems unable to access “talk therapies”. Alan Kazdin calls this unseen group the treatment gap, that is “the discrepancy in the proportion of the population in need of services and the proportion that actually receive them”. Most people (the Report estimates it is between 30–50%) with mental health problems do not receive any help at all.

The challenge is that the treatments that predominate in psychological services are intensive, one-to-one, in person and often provided in a specialised clinic setting. To meet the suggestions of the Report to allow for greater access to psychological services beyond the top 3% to all those in need, we realistically need to triple the workforce. Is this an achievable goal?

Consider clinical psychology as an example. New Zealand training programmes graduate around 60 clinical psychologists per year (about 10–12 per training programme). Even if we were able to double the number of clinical psychologists trained each year to meet the needs of the most severe cases (which would be resource intense requiring many more supervisors and teachers, as well as cause substantial logistical challenges for universities and internship placements), it will be over a decade before we can increase the workforce enough to meet the current need of specialists to help with the most severe cases. Further, these calculations assume that all clinical psychologists work full-time in clinical practice, stay in New Zealand, are effective with all patients, and that the population does not grow over that time period. Immigration could potentially assist with a faster growth of the workforce; however, there is a worldwide shortage of clinical psychologists. Similar challenges would be faced with attempts to substantially increase other disciplines.

In addition, even if we trained an adequate pool of therapists to refer patients to, UK data identify that only half of patients referred for talking therapies actually enter into treatment, with the rest either declining or dropping out. Māori and Pacific people, those who live rurally, and those in poverty struggle to access individualised therapies. Even if people are seen by a therapist, at best 50% of them recover. There is substantial room for diversifying treatment options offered to patients.

It is therefore unrealistic to think we can address the escalating mental health crisis by simply training more mental health professionals. This is not to say we should stop efforts to increase the workforce—more professionals offering psychological therapies are definitely required. Rather, we identify that increasing the workforce on its own is unachievable within current resources. Other innovative therapies (that can reach more people with fewer resources) and preventative methods need to be seriously prioritised and implemented. The Report showed less emphasis and recommendations targeted at prevention initiatives and therapies beyond talk therapies.
What are other ways forward? There is robust data showing that the more deprived one is, the greater the prevalence of psychological distress. Addressing the poverty gap is a necessary long-term solution for improving the mental health of the community. Alongside improving deprivation should be developing novel delivery of health services to have better reach within communities. As identified in the Report, e-therapies have broader reach than traditional therapies at a lower cost. Researchers at the University of Auckland developed a uniquely New Zealand intervention: a therapeutic computer game for young people (SPARX). It also guides users to apply skills learned in the game to real-life situations. It incorporates Māori cultural elements, and research has found it is effective and enjoyable. Programs like this could be a way to reach those with mild-moderate mental health difficulties and those who don't access psychological treatments for other reasons.

Kazdin suggests a number of other avenues of novel delivery including using social media, nudging therapies, interventions in unconventional settings (like hairdressers), lifestyle changes (controlling diet, exercising, meditating), task shifting (expanding the workforce by using more lay individuals), and best-buy interventions (simple interventions that are cheap but can have broad effects such as increasing taxes or reducing access to spaces where one can smoke in order to reduce cigarette consumption). Focus on prevention would also be an aspiring long-term solution, including reducing exposure to adverse childhood experiences. With any intervention, it is essential that evaluation is incorporated into implementation.

The evidence is clear that maternal wellbeing during pregnancy, child-parent attachment, and early childhood experiences create the blueprint for our mental health later in life. Nutrition, physical activity, sleep quality, and stress management contribute in an ongoing way to wellbeing throughout life. Nutritional interventions, in the form of dietary manipulation, focused treatments on the microbiome, and supplementation with additional nutrients, have gained substantial traction in the last decade with research identifying that nutrition plays an integral role in prevention and treatment of mental health problems. The focus in the Report on increasing talk therapies shadows the opportunities afforded by many of these other innovative and preventative approaches.
REFERENCES:


Why the new ‘living’ Australian Stroke Guidelines matter to New Zealand

Karim Mahawish, P Alan Barber, Anna McRae, Julia Slark, Annemarei Ranta


The guideline covers the most critical topics of stroke care from pre-hospital to post-discharge care, as well as the management of transient ischaemic attack (TIA). It is intended to aid the development of locally appropriate clinical pathways, and help to guide clinical judgement.

One novel feature of this guideline, a world-first, is the ability for realtime updates. Given the rate at which new evidence has been emerging in recent years, this is a major advantage. The new guideline, now exclusively existing as an online document, facilitates the real-time incorporation of new recommendations.

A few changes from past recommendations are worth noting for New Zealand practice. One such feature is the recommendation for general practitioners to use the New Zealand-developed Best Practice Advocacy Centre (BPAC) TIA/Stroke electronic decision-support tool, as it was found to significantly reduce 90-day vascular event rates (73% reduction) in practices that accessed this tool during a recent randomised controlled trial from New Zealand.1

The most revolutionary research to emerge in stroke treatment, and which is given a strong recommendation in the guideline, is endovascular thrombectomy (stroke clot retrieval) for patients with ischaemic stroke caused by a large vessel occlusion in the internal carotid artery middle cerebral artery (M1 segment) or basilar artery.2 The recent DAWN3 and DEFUSE 34 studies used computed tomography cerebral perfusion imaging to identify patients with a significant ischaemic penumbra and thus be most likely to benefit from endovascular thrombectomy. These studies showed that the therapeutic window could be expanded up to 24 hours in such patients with significant improvements in outcome. The challenge for New Zealand will be to set up round-the-clock access for all New Zealanders to advanced imaging and interventional neuroradiology services using a coordinated air and road transport.

The Ministry of Health has recently approved a National Stroke Clot Retrieval Service Improvement Programme to help address current gaps.

Other changes include a more aggressive blood pressure lowering target in intracerebral haemorrhage. The INTERACT 25 trial has resulted in a weak recommendation for acute lowering of blood pressure to a target systolic of around 140mmHg in patients with intracerebral haemorrhage. In INTERACT 2, this target had to be achieved within an hour of randomisation and maintained for seven days. This will be a challenge to achieve in many New Zealand hospitals outside a high-dependency setting.

The guideline issues a weak recommendation for dual antiplatelet therapy (DAPT) with aspirin and clopidogrel for three weeks in patients with TIA or minor stroke based on the CHANCE trial,6 which included patients with ABCD2 ≥ 4 or NIHSS ≤ 3 scores. The POINT trial,7 yet to be included in the guideline, used DAPT for 90 days.
and demonstrated a significant reduction in stroke recurrence at the expense of also an increase in the risk of haemorrhage. The benefit mainly accrued in the first few weeks of therapy, while the bleeding risk was more sustained. This suggests that a shorter duration of DAPT, for around 30 days, is probably safe and still effective; although this time frame was not part of the primary outcome of the trial so a degree of caution has to be applied.

The guideline offers a strong recommendation to use direct oral anticoagulants (DOACs) in preference to warfarin for patients with non-valvular atrial fibrillation. A recent systematic review showed reduced mortality and lower rates of intracranial haemorrhage in patients taking DOACs compared with warfarin. Idarucizumab, the reversal agent for the direct thrombin inhibitor Dabigatran, provides additional reassurance for its use. The once daily anti-Xa inhibitor Rivaroxaban has now been funded by PHARMAC for use as stroke prevention in patients with non-valvular atrial fibrillation, but a reversal agent is not yet available.

The Australian Guideline does not include information to provide New Zealand culturally specific guidance, and clinicians are advised to continue to refer to the 2010 New Zealand Stroke Guidelines on these matters. However, more needs to be done in this area. Population-based data taken from the Auckland Regional Community Stroke Studies (ARCOS) have demonstrated a gradual decline in overall stroke incidence since 1981; yet between 2002 and 2011, there has been a two-fold increase in first stroke in those aged 16–49 among Māori and Pacific peoples. Further, ethnic inequalities in stroke survival have also increased significantly in the last 10 years. This may be due to differences in severity at presentation or in access and utilisation of increasingly effective acute stroke interventions. Māori and Pacific groups continue to experience stroke at a significantly younger age (mean age of first stroke is 60 and 62 years, respectively) compared with New Zealand Europeans (mean age 75 years). Māori and Pacific non-valvular atrial fibrillation patients are diagnosed 10 years earlier than non-Māori/Pacific patients. The currently ongoing HRC funded REGIONS Care project aims to add additional substantial evidence on how to improve clinical stroke management for these patient groups.

The guideline provides the latest evidence-based guidance for the management of stroke patients in New Zealand and must be adopted in New Zealand to improve stroke outcomes for all. Interested readers are encouraged to look through the guidelines in the new look and easy to use online format. Key priorities for the optimisation of outcomes following stroke include improved access to acute organised stroke care, including reperfusion and endovascular thrombectomy, and organised stroke rehabilitation services. The work of the National and Regional Stroke Networks as well as individual DHBs and health providers and engaged consumers with support from the Ministry of Health and the Stroke Foundation have achieved much over the past 10 years, but ongoing efforts are needed.

Competing interests: Nil.

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Utility of whole genome sequencing for multidrug resistant Mycobacterium tuberculosis isolates in a reference TB laboratory in New Zealand

Indira Basu, James E Bower, Sally A Roberts, Gillian Henderson, Htin Lin Aung, Gregory Cook, Odette Lowe, Sandie Newton

ABSTRACT

New Zealand has a low burden of multi-drug resistant TB (MDR-TB), but with increased mobility within the population, rapid detection and treatment of MDR-TB is a priority from the public health point of view. Mycobacterium Reference Laboratory in LabPLUS, Auckland City Hospital receives referred Mycobacterium tuberculosis complex (MTBC) isolates from all over New Zealand for second-line drug susceptibility testing (DST) and 24-loci MIRU VNTR genotyping. Between 2002 and 2013, 38 multidrug resistant Mycobacterium tuberculosis (MDR-TB) isolates were recorded by culture-based DST. A retrospective study revealed that in 12 of these 38 MDR-TB isolates (28%) there was a discrepancy between the genotypic and the phenotypic results. In order to address this, whole genome sequencing (WGS) was performed on the discrepant MDR-TB isolates. Reported here are the additional information on the drug resistant markers from WGS, which shed light on the discordance between results from the culture-based DST and the molecular diagnostic tests. These results underscore the utility of WGS in a reference mycobacterium laboratory in New Zealand to supplement other molecular tests and to assist in a rapid but accurate diagnosis and appropriate management of MDR-TB.

Mycobacterium tuberculosis (Mtbc), the causative agent of tuberculosis (TB) kills 1.4 million people annually according to WHO.¹ Increase in multi-drug resistant TB (MDR-TB) defined by resistance to the first line anti-tuberculous agents, rifampicin (RIF) and isoniazid (INH), has added to the global concern with increased travel and globalisation. New Zealand has a low burden of MDR-TB at <7.0 cases per 100,000 population. However, a significant proportion of cases, 76%, are born outside of New Zealand, or are currently residing with, or have recently resided with a person born outside of New Zealand.² In 2014, cases born in the Southern and Central Asia region had the highest notification rates followed by South-East Asia. A number of countries from these regions, such as India, China, Philippines and Indonesia are considered to be high TB burden countries.³ Of concern is the emergence of multi-drug resistance TB with China, India and the Russian Federation accounting for 47% of all MDR-TB cases globally.³ Treatment for MDR-TB is longer, and requires more expensive and more toxic drugs.

For these reasons it is important to be able to rapidly identify cases infected with MDR-TB strains to ensure that the case is treated appropriately and that the risk of further transmission to others is minimised.

The timely diagnosis and administration of the appropriate anti-tuberculous drug...
The sensitivity and the specificity of these rapid commercial molecular diagnostic tests for RIF and INH resistance are not 100%. Hence there is a risk if treatment of the patients is commenced with second-line drugs based on RIF-resistant and INH-resistant results from these rapid molecular diagnostic tests alone. Such a situation might permit further spread of drug-resistant strains and also promote the selection of strains with even greater resistance. Thus any discrepancy in result between molecular resistance testing and phenotypic testing is of importance to clinicians treating a patient.

More recently these limitations in the commercial molecular diagnostic tests are being overcome by shifting from targeting of individual genes for resistance mutation towards sequencing the entire bacterial genome allowing for the detection of mutations in multiple genes all at once. The technology is widely known as the whole genome sequencing, which is performed on next-generation sequencing platforms, the Illumina Mi-Seq (Illumina, Inc., Hayward, CA) being one of them. But this technology needs highly skilled scientists.7

In response to an expected increase in the number of cases of MDR-TB in New Zealand we sought to increase our capability to diagnose rapidly and accurately cases of MDR-TB. We report here our experience with whole genome sequencing of selected New Zealand MDR-TB isolates from 2002 till 2013.

**Method**

The Mycobacterium Reference Laboratory in the Microbiology Department, LabPLUS, Auckland City Hospital performs first-line DST for all Mtb isolates from cases in the Northern District Health Board (DHB) Region as well as the second-line anti-tuberculous drug susceptibility testing for MDR-TB isolates for all of New Zealand. Molecular Microbiology section routinely performs different molecular tests for genotypic drug resistance profile to provide faster result on suspected MDR-TB isolates as well as mycobacterial interspersed repeat unit-variable number of tandem repeat (MIRU-VNTR) 24-loci genotyping of all New Zealand Mtb isolates to assist the Public Health in an outbreak investigation and for epidemiological purposes.8 The results of MIRU-VNTR 24-loci genotyping for MDR-TB isolates in this study are mostly unique strains of Mtb (Table 1).8

**Selection of isolates for the study**

From 2002 till 2013, 38 MDR-TB were isolated in New Zealand (Figure 1). Cepheid Xpert® MTB/RIF assay (Cepheid, Sunnyvale, CA, US), and Genotype MTBDRplus test
(Hains Lifescience, Nehren, GmbH) were used for routine clinical diagnostics from 2010. About 44% of these MDR-TB cultures were isolated and cultured prior to introduction of these molecular tests and hence were retrospectively tested on these two platforms. Results showed discordance in interpretation of the resistance to first-line drugs between the phenotypic culture-based DST and genotypic molecular results for 12 MDR-TB isolates. These 12 isolates were selected for whole genome sequencing. The discrepancies are documented in Table 1 and explained in detail later in the Results and Discussion section.

Phenotypic drug susceptibility testing

Culture-based DST is performed routinely on all MTBC isolates using the MGIT as described previously. Critical concentrations of antibiotics were in accordance with World Health Organization guidelines for MGIT™ BACTEC™ 960. Using culture-based DST result, 38 laboratory confirmed cases of MDR-TB isolates were recorded in the time period spanning 2002 till 2013. (Figure 1).

Molecular tests

Cepheid Xpert® MTB/RIF test (Cepheid, Sunnyvale, CA, US) and Genotype MTBDRplus (Hains Lifescience, Nehren, GmbH) commercial tests for MDR-TB are used routinely on clinical specimens when they fit the pre-test probability criteria as described earlier. Briefly, the criteria used to determine whether the cultured isolate had a high pre-test probability of being MDR-TB are as follows: the specimen was from a patient from an area of high TB incidence, or from a contact of a confirmed TB patient or from a relapsed or a treatment failure case.

Rifampicin (RIF) resistance when detected by Cepheid Xpert® MTB/RIF test and/or Genotype MTBDRplus was further confirmed by in-house rpoB gene sequencing of the rifampicin-resistance determining region (RRDR) of rpoB gene as previously described. This confirmation of mutation in the rpoB gene by sequencing was routinely performed after an earlier study from our laboratory revealed the possibility of false positive RIF-resistance result from Cepheid Xpert® MTB/RIF test.

Whole genome sequencing

The genomic DNA extraction of these 12 MDR-TB isolates chosen for whole genome sequencing (WGS) were performed on pure Mtb grown in the BACTEC Mycobacterial Growth Indicator Tube (MGIT) 960 system (Becton Dickinson, Sparks, MD, US). Briefly, 1.5ml of MGIT broth was vortexed with glass beads for 30s in a 2ml sterile microcentrifuge tube, and centrifuged at 13,000Xg for 10 min. The supernatant was discarded and 300μl of Tris buffer was added to the pellet. After further vortexing for 30s, the
A microcentrifuge tube was heated at 95°C for 15 min in a heating block. The isolates were then treated with lysozyme and proteinase K/RNase A for lysis of the cells and removal of protein/RNA, respectively. MagNA Pure LC semi-automated extraction platform (Roche Molecular Diagnostics, Branchburg, NJ, US) was used for extraction of genomic DNA following the manufacturer’s protocol. Nextera XT kit (Illumina, Inc., Hayward, CA) was used for library preparation for WGS. Nanodrop and Qubit instruments (Thermo Fisher Scientific) were used for the quantification of the library. Sequencing was performed on the Illumina MiSeq (Illumina, Inc., Hayward, CA) using paired-end 250-bp reads. After sequencing, for analysis of the data, the reads were mapped against the *Mycobacterium tuberculosis* H37RV reference sequence (NC_000962.3) using Burrows-Wheeler transform (BWA) software. Single-nucleotide polymorphism (SNP) analysis was performed using Genome Analysis Toolkit (GATK) pipeline to identify mutations associated with resistance and the effects of the SNP were predicted using a program for annotating and predicting the effects of single nucleotide polymorphisms called SNPeff. The accession number for these isolates are SAMN06472852, SAMN06472853, SAMN06472854, SAMN06472855, SAMN06472856, SAMN06472857, SAMN06472858, SAMN06472859, SAMN06472860, SAMN06472861, SAMN06472862, SAMN06472863 in the GeneBank.

## Results and discussion

Retrospective testing of the NZ MDR-TB isolates with Cepheid Xpert® MTB/RIF test (Cepheid, Sunnyvale, CA, US) and Genotype MTBDRplus (Hains Lifescience, Nehren, GmbH) failed to identify 12 of the isolates as MDR-TB (28%) as documented in Table 1. The darker cells in each row of Table 1 highlight the phenotypic and genotypic discrepancy.

### Table 1: Discrepancy between the phenotypic and the genotypic drug resistance profiles of the 12 multi-drug resistant *M. tuberculosis* culture isolates, New Zealand, 2003–2013.

<table>
<thead>
<tr>
<th>Isolate number</th>
<th>Year of isolation</th>
<th>Site of infection</th>
<th>MIRU-VNTR 24-loci typing result</th>
<th>Phenotypic resistance to RIF</th>
<th>Genotypic resistance to RIF: <em>rpoB</em> gene mutation</th>
<th>Phenotypic resistance to INH</th>
<th>Genotypic resistance to INH: <em>inhA</em> gene mutation</th>
<th>Genotypic resistance to INH: <em>katG</em> gene mutation</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>2005</td>
<td>Sputum</td>
<td>Clustered</td>
<td>resistant</td>
<td>NMD</td>
<td>High level</td>
<td>WT</td>
<td>S315T</td>
</tr>
<tr>
<td>2</td>
<td>2006</td>
<td>Sputum</td>
<td>Clustered</td>
<td>resistant</td>
<td>NMD</td>
<td>High level</td>
<td>WT</td>
<td>S315T</td>
</tr>
<tr>
<td>3</td>
<td>2013</td>
<td>Sputum</td>
<td>Unique</td>
<td>resistant</td>
<td>NMD</td>
<td>High level</td>
<td>WT</td>
<td>S315T</td>
</tr>
<tr>
<td>4</td>
<td>2013</td>
<td>Pelvic aspirate</td>
<td>Unique</td>
<td>resistant</td>
<td>S531L</td>
<td>High level</td>
<td>C-15T</td>
<td>WT</td>
</tr>
<tr>
<td>5</td>
<td>2012</td>
<td>Sputum</td>
<td>Unique</td>
<td>resistant</td>
<td>S531L</td>
<td>High level</td>
<td>C-15T</td>
<td>WT</td>
</tr>
<tr>
<td>6</td>
<td>2010</td>
<td>Bronchial Washings</td>
<td>Unique</td>
<td>resistant</td>
<td>S531L</td>
<td>High level</td>
<td>C-15T</td>
<td>WT</td>
</tr>
<tr>
<td>7</td>
<td>2009</td>
<td>Right Cervical LN</td>
<td>Unique</td>
<td>resistant</td>
<td>S531L</td>
<td>High level</td>
<td>C-15T</td>
<td>WT</td>
</tr>
<tr>
<td>8</td>
<td>2009</td>
<td>Sputum</td>
<td>Clustered</td>
<td>resistant</td>
<td>D516Y</td>
<td>High level</td>
<td>C-15T</td>
<td>WT</td>
</tr>
<tr>
<td>9</td>
<td>2010</td>
<td>Sputum</td>
<td>Unique</td>
<td>resistant</td>
<td>H526Y</td>
<td>High level</td>
<td>NMD</td>
<td>S315L</td>
</tr>
<tr>
<td>10</td>
<td>2009</td>
<td>Sputum</td>
<td>Unique</td>
<td>resistant</td>
<td>S531L</td>
<td>High level</td>
<td>NMD</td>
<td>S315L</td>
</tr>
<tr>
<td>11</td>
<td>2007</td>
<td>Sputum</td>
<td>Clustered</td>
<td>resistant</td>
<td>S531L</td>
<td>High level</td>
<td>NMD</td>
<td>S315L</td>
</tr>
<tr>
<td>12</td>
<td>2005</td>
<td>Sputum</td>
<td>Unique</td>
<td>resistant</td>
<td>S531L</td>
<td>High level</td>
<td>NMD</td>
<td>S315L</td>
</tr>
</tbody>
</table>

*The cells with phenotypic and genotypic discrepancies are in darker shades.

*Result from Xpert® MTB/RIF and Genotype MTBDRplus with confirmation by RRDR *rpoB* sequencing.

*Result from Genotype MTBDRplus test.

*NMD—No mutation detected.

*WT—wild-type referring to no mutation in the gene conferring resistance.
Rifampicin resistance

The first 3 isolates (Table 1; isolate numbers 1, 2 and 3) did not show any RIF-resistance using Cepheid Xpert® MTB/RIF test (Cepheid, Sunnyvale, CA, US) and Genotype MTBDRplus (Hains Lifescience, Nehren, GmbH). As mentioned in the introduction, these tests target the mutations located in the 81bp rifampicin-resistance determining region (RRDR) of the \(rpoB\) gene, which can be found in 96% of RIF-resistant \(M.\) \(tuberculosis\) strains worldwide. As these two molecular diagnostic tests only interrogate the most frequent mutations responsible for RIF resistance, they have their limitations.

WGS revealed that these three phenotypically and genotypically discrepant MDR-TB isolates (Table 2; isolate number 1, 2 and 3 from 2005, 2006 and 2013 respectively) showed a mutation at position G508T (\(M.\) \(tuberculosis\) numbering) of the \(rpoB\) gene resulting in amino acid change, V170F (Table 2). This mutation has been previously described in the literature to be associated with rifampicin resistant strains. Presence of this uncommon mutation outside the 81bp \(rpoB\) gene RRDR explains why Cepheid Xpert® MTB/RIF and Genotype MTBDRplus did not detect these \(rpoB\) gene mutations. Hence these tests with their limitations have the potential to give a rapid yet false negative result when used prospectively.

Isoniazid resistance

The next five discrepant MDR-TB isolates (Table 1; isolate numbers 4–8) were resistant to isoniazid (INH) both at a concentration of 0.1ug/ml (low-level) and 0.4ug/ml (high-level). Resistance to INH at a concentration of 0.1ug/ml (low-level) has been shown to be conferred by a mutation in the promoter region of the \(inhA\) gene at -C15T while resistance to INH at 0.4ug/ml (high-level) is conferred by mutation in the \(katG\) gene. Both these mutations can be detected by the Genotype MTBDRplus test. Even though these five discrepant MDR-TB isolates (Table 1; isolate numbers 4–8) were phenotypically resistant to isoniazid (INH) both at a concentration of 0.1ug/ml (low-level) and 0.4ug/ml (high-level), they only exhibited mutation at C-15T, which has been shown to correspond to low-level INH resistance at 0.1ug/ml.

Table 2: Results from whole genome sequencing addressing the discrepancy between phenotypic and genotypic drug resistance results for first line drugs—rifampicin (RIF) and isoniazid (INH).

<table>
<thead>
<tr>
<th>Isolate number</th>
<th>Year of isolation</th>
<th>Site of infection</th>
<th>(rpoB) mutation</th>
<th>(katG) mutation</th>
<th>(inhA) mutation</th>
<th>Other genes for INH resistance (mutation)*</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>2005</td>
<td>sputum</td>
<td>V170F*</td>
<td>S315T*</td>
<td>WT</td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>2006</td>
<td>sputum</td>
<td>V170F*</td>
<td>S315T*</td>
<td>WT</td>
<td></td>
</tr>
<tr>
<td>3</td>
<td>2013</td>
<td>sputum</td>
<td>V170F*</td>
<td>S315T*</td>
<td>WT</td>
<td></td>
</tr>
<tr>
<td>4</td>
<td>2013</td>
<td>pelvic aspirate</td>
<td>S531L; A286V</td>
<td>NMD</td>
<td>C-15T; I21V</td>
<td></td>
</tr>
<tr>
<td>5</td>
<td>2012</td>
<td>sputum</td>
<td>S531L</td>
<td>NMD</td>
<td>C-15T; I194T</td>
<td></td>
</tr>
<tr>
<td>6</td>
<td>2010</td>
<td>BW</td>
<td>S531L</td>
<td>NMD</td>
<td>C-15T; I21V</td>
<td></td>
</tr>
<tr>
<td>7</td>
<td>2009</td>
<td>R. cervical LN</td>
<td>S531L; I491V</td>
<td>NMD</td>
<td>C-15T; I21V</td>
<td></td>
</tr>
<tr>
<td>8</td>
<td>2009</td>
<td>sputum</td>
<td>D516Y</td>
<td>D419Y</td>
<td>C-15T</td>
<td></td>
</tr>
<tr>
<td>9</td>
<td>2010</td>
<td>sputum</td>
<td>H526Y</td>
<td>NMD</td>
<td>NMD</td>
<td>(accD6) (D229G)</td>
</tr>
<tr>
<td>10</td>
<td>2009</td>
<td>sputum</td>
<td>S531L; T347A</td>
<td>NMD</td>
<td>NMD</td>
<td>(accD6) (D229G)</td>
</tr>
<tr>
<td>11</td>
<td>2007</td>
<td>sputum</td>
<td>S531L</td>
<td>NMD</td>
<td>NMD</td>
<td>(ndh) (V18A)</td>
</tr>
<tr>
<td>12</td>
<td>2005</td>
<td>sputum</td>
<td>S531L; T52P</td>
<td>NMD</td>
<td>NMD</td>
<td>(accD6) (D229G)</td>
</tr>
</tbody>
</table>

*Result obtained from WGS data are in bold.

*Result obtained from Genotype MTBDRplus tests.

*Result obtained from Xpert MTB/RIF and Genotype MTBDRplus tests confirmed by RRDR \(rpoB\) sequencing.

NMD—No mutation detected.
WGS showed additional mutations in \textit{inhA} gene at I21V for three of these discrepant isolates (Table 2; isolate numbers 4, 6 and 7). This mutation has been previously reported to correspond to a high-level INH resistance at 0.4ug/ml where they have been present in addition to C-15T.\textsuperscript{17} For the isolate 5, WGS showed a different mutation, I194T in the \textit{inhA} gene, which also has been associated previously with high-level INH resistance in MDR-TB isolate from Portugal in addition to the C-15T.\textsuperscript{18} Isolate 8 had a mutation in D419Y of the \textit{katG} gene which has been linked to high-level INH resistance in Brazilian isolates.\textsuperscript{19} These additional mutations in \textit{inhA} gene and \textit{katG} gene explain the high-level phenotypic resistance to INH for these five discrepant MDR-TB isolates (numbers 4–8), but these additional uncommon mutations were not detected by Genotype MTBDR\textsuperscript{plus} test.

The last four discrepant MDR-TB isolates (Table 1; isolates 9–12) were phenotypically resistant to INH using culture-based DST but did not show any mutation in \textit{inhA} or \textit{katG} genes, which are commonly implicated in most of INH-resistance\textsuperscript{5} and hence are not detected by Genotype MTBDR\textsuperscript{plus}.

WGS also did not detect any mutation in the \textit{inhA} gene or the \textit{katG} gene that has been associated with INH resistance for these four discrepant MDR-TB isolates (Table 1; isolates 9–12). Further interrogation of the WGS data for other putative genes implicated in INH resistance showed a mutation in the acetyl-CoA carboxylase gene, \textit{accD6} in isolates 9, 10 and 12 (Table 2). This mutation in \textit{accD6} gene at D229G has been reported in literature to be to be associated with INH-resistance and present in MDR-TB strains.\textsuperscript{20} Isolate 11 had a mutation in NADH dehydrogenase gene, \textit{ndh} resulting in the amino acid change V18A that has been reported to be associated with an isoniazid-resistant Mtb isolate from Brazil.\textsuperscript{21}

This is a rapidly changing area; over the last 10 years rapid molecular assays designed to detect Mtb, resistance to rifampicin as well as resistance to other first- and second-line anti-tuberculous medications directly from clinical specimens or cultures have become available. For the majority of Mtb cases in New Zealand, this capability is not required. However, with an increasing MDR-TB burden globally it is important that, despite being a low TB burden country, we can rapidly diagnose such cases. WGS provide useful information over and above that obtained from the current widely used commercial molecular diagnostic tests and help address the discrepancy between phenotypic and genotypic results. It will benefit clinical decision-making by supporting the choice of an appropriate and accurate drug regime for MDR-TB cases in a timely manner. With decreasing cost of WGS and the increasing ease of data handling with newer pipelines, WGS results hold the potential to be available ahead of the culture-based DST.\textsuperscript{22}

Not only can WGS provide information about drug susceptibility but it will replace the current molecular typing method since it has been shown that result from WGS is superior to MIRU-VNTR 24-loci typing for assisting Public Health in contact tracing.\textsuperscript{22} WGS provides a higher level of discrimination between isolates than this method because it looks at the entire genome and not just a standard set of ‘housekeeping’ genes. This has the potential to reduce unnecessary public health contact traces from occurring. Currently cases may belong to the same MIRU-VNTR but have no epidemiological links. These cases in the MIRU-VNTR cluster may be found to be unrelated by WGS reducing the need for contact tracing.

Other high income countries are moving away from culture-based TB diagnostics and shifting to WGS for identification of \textit{Mycobacterium} species, identification of drug resistance and molecular strain typing.\textsuperscript{22} New Zealand is in a position to be able to follow this approach. The DHB diagnostic laboratories have well-established referral pathways that would support the establishment of a single provider for TB molecular diagnostics.

Hence, WGS promises to increase the sensitivity of the molecular diagnostic result for timely and effective management of MDR-TB and would eventually help develop an algorithm that would reduce the potential for misdiagnosis of MDR-TB prospectively when used in combination with the currently used molecular methods. This study underscores the utility of WGS to supplement the current molecular tests in a reference Mycobacteriology laboratory setting in New Zealand.
Competing interests:
Nil.

Acknowledgements:
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URL:

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Cutaneous squamous cell carcinoma: predictors of positive and close margins and outcomes of re-excision in Northland, New Zealand

Brodie M Elliott, Benjamin R Douglass, Daniel McConnell, Blair Johnson, Christopher Harmston

ARTICLE

ABSTRACT

BACKGROUND: Non-melanoma skin cancer (NMSC) is the most commonly diagnosed and costly cancer in Australasia. Cutaneous squamous cell carcinoma (cSCC) accounts for approximately 25% of NMSC. A better understanding of predictors of close and positive margins following surgical excision will help guide treatment.

METHODS: A retrospective study was carried out of all primary cSCC histologically diagnosed in Northland, New Zealand in 2015. The cohort was identified by searching the regional pathology database. The primary outcome of interest was positive and close (≤1mm) margin rate following surgical excision and factors influencing them. Secondary outcomes of interest were outcomes of re-excisions.

RESULTS: A total of 1,040 cSCC were identified in 890 unique patients and 825 lesions were surgically excised. Increased odds of positive margin on surgical excision was found with increased tumour thickness (OR 1.56, 95% CI 1.24–1.96), tumours from the head and neck (OR 2.78, 95% CI 1.33–5.80) and those excised in primary care (OR 2.20, 95% CI 1.07–4.52). Increased odds of close margins was found in females (OR 2.01, 95% CI 1.3–3.2) and excision in primary care (OR 2.44 95% CI 1.5–3.98). Residual tumour was present in 13 (31.7%) patients with positive margins and 0 patients with close margins.

CONCLUSIONS: Lesions of the head and neck, those removed in primary care and with increased tumour thickness were more likely to have positive margins following surgical excision. Close margins were associated with excision in primary care and female gender. The value of re-excising tumours with close margins remains uncertain.
Many series have reported rates of positive margins, including factors associated with positive margins. Most commonly size, thickness and anatomical location are implicated. However, a majority of studies are limited by not considering compounding factors through use of multivariate analysis. The pathological outcomes in re-excisions of these lesions have also been reported but no previous studies have examined rates and factors leading to close margin rates. Greater understanding of the factors influencing close margin rates and outcomes of re-excisions is critical in improving treatment in patients with cSCC. This knowledge will aid effective decision making in both primary and secondary care with the intent to increase success of surgical excision to avoid costly reoperations, which can increase patient morbidity.

We have previously reported the basic demographics and outcomes in our large cohort of patients from both primary and secondary care. The aim of this study was to define the rate of positive and close margins following primary excision of cSCC, examine outcomes of re-excisions and investigate predictive factors for inadequate excision using multivariate analysis.

Methods

A 12-month retrospective study was carried out of all primary cSCC diagnosed in Northland for one year commencing 1 January 2015. Patients undergoing primary surgical excision were identified and these formed the primary cohort for this study.

Cases were identified by searching the Northland District Health Board pathology database and a database of outsourced pathological specimens using key terms. Together these databases contain all histological specimens processed in Northland; both public and private from primary and secondary care. The 15,719 pathology reports obtained from this search were manually screened to identify all cSCC that were excised by primary surgical excision. Demographic data was obtained from the district health board data warehouse, lesion characteristics and anatomical location data was extracted from the pathology report, and if excised in secondary care, this data was further supplemented by operation notes obtained from the hospital results reporting system CONCERTO. These variables were entered into a Microsoft Excel spreadsheet.

A positive margin was defined as tumour being present at the histological resection margin and a close margin was defined as tumour being present within one millimetre of the resection margin. Inadequate excision included both positive and close margins. Resection margin distances were defined as the shortest distance between resection margin and tumour cells.

The primary area of interest was the rate of positive and close margins as well as predictive factors on multivariate analysis, secondary area of interest was pathological outcomes following re-excision in those with positive and close margins.

Descriptive statistics were used to describe basic demographics and distributions were assessed for normality. Paired t-tests were used to ascertain differences between continuous data assumed to be normally distributed, Wilcoxon-Mann-Whitney was used as a non-parametric analog and Chi-squared test was used for categorical variables. Univariate analysis was used to determine statistically significant variables. If variables were clinically justifiable and exhibited significance at P of <0.10 in explanatory analysis it was entered into a multivariate logistic regression model. Statistical analyses were carried out using SPSS version 25.0 (SPSS Inc., Chicago, IL, USA). All tests were two-sided and P values less than 0.05 were considered statistically significant.

The data used in this study was collected as part of a service evaluation of patients referred with suspicions skin lesions to Northland District Health Board and was approved by locality assessment. Data collection was discussed with the Health and Disability Ethics Committee and an "out of scope letter" obtained on 29 March 2016.

Results

The patients and lesion characteristics of this patient cohort have been previously described in detail.

Patient characteristics/demographics

A total of 1,040 cSCC were identified in 890 patients. During this time period, 825 lesions were surgically excised in 701 patients. The
The median enrolment age was 75.1 years old (SD 10.2). The cohort was made up of 432 men and 269 women.

**Lesion characteristics**

The median lesion diameter at study diagnosis was 6.1mm (IQR 4.0–9.5mm). The median histologic thickness was 2.4mm (IQR 1.7–3.5mm). In regards to anatomical location, 385 lesions (47%) were excised from the head and neck, 22% from the upper limb, 22% from the lower limb and 9% from the trunk.

**Surgical characteristics**

Surgical excision in primary care occurred for 54% of lesions. In secondary care, 38% of excisions were performed by an hospital contracted Medical Officer Special Scale (MOSS) or General Practitioner with Special Interest (GPwSI), the remaining lesions were excised by a consultant surgeon (25.5%), private specialist (19.5%) or surgical registrar (16.6%). Tumour size and thickness was recorded within pathology reports of 581 (70.9%) of excised specimens.

**Surgical outcomes and predicting positive and close margins**

On histologic examination following surgical excision, 78 of the 825 (9%) lesions were found to have a positive margin (Table 1). Of those, 53 had a positive deep margin, 42 had a positive radial margin and 14 lesions were positive in both deep and radial margins. When defined as having tumour cells within 1mm of excision margins, 139 (17%) lesions had close margins (Table 2). Combining these groups revealed that 26% of total excisions had tumour cells at or within 1mm of excision margins.

**Table 1:** Comparison of patient and tumour characteristics in lesions found to have positive and close (<1mm) compared to distant margins on surgical excision.

<table>
<thead>
<tr>
<th></th>
<th>Positive margins n=78</th>
<th>Close margins n=139</th>
<th>Distant margins n=608</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Age, years</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean ± SD</td>
<td>76.4 ± 10.4</td>
<td>74.72 ± 10.2</td>
<td>75.0 ± 10.2</td>
</tr>
<tr>
<td><strong>Sex, n (%)</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>49 (62.8)</td>
<td>77 (55.4)</td>
<td>449 (60.1)</td>
</tr>
<tr>
<td>Female</td>
<td>29 (37.2)</td>
<td>62 (44.6)*</td>
<td>295 (39.5)</td>
</tr>
<tr>
<td><strong>Surgical characteristics, n (%)</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Excised in primary care</td>
<td>45 (57.7)</td>
<td>89 (64.0)**</td>
<td>399 (53.4)</td>
</tr>
<tr>
<td><strong>Histologic characteristics, median (IQR)</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Tumour diameter</td>
<td>6.1 (5.0–11.0)**</td>
<td>5.6 (3.5–8.1)</td>
<td>5.6 (3.9–9.0)</td>
</tr>
<tr>
<td>Tumour thickness</td>
<td>2.9 (2.0–5.0)*****</td>
<td>2.5 (1.8–3.5)</td>
<td>2.3 (1.6–3.2)</td>
</tr>
<tr>
<td><strong>Tumour characteristics, n (%)</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Metastases</td>
<td>4 (5.1)**</td>
<td>0 (0)</td>
<td>7 (0.9)</td>
</tr>
<tr>
<td>Perineural invasion</td>
<td>4 (5.1)**</td>
<td>5 (3.6)**</td>
<td>7 (0.9)</td>
</tr>
<tr>
<td>Lymphovascular invasion</td>
<td>1 (1.3)</td>
<td>1 (0.7)</td>
<td>3 (0.4)</td>
</tr>
<tr>
<td><strong>Anatomical location, n (%)</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Head and neck</td>
<td>48 (61.5)**</td>
<td>77 (55.4)**</td>
<td>337 (45.1)</td>
</tr>
<tr>
<td>Trunk</td>
<td>2 (2.6)*</td>
<td>12 (8.6)</td>
<td>71 (9.5)</td>
</tr>
<tr>
<td>Upper limb</td>
<td>16 (20.5)</td>
<td>35 (25.2)</td>
<td>166 (22.2)</td>
</tr>
<tr>
<td>Lower limb</td>
<td>12 (15.4)</td>
<td>14 (10.1)**</td>
<td>16.8 (22.5)</td>
</tr>
</tbody>
</table>

*P≤0.05; **P≤0.01; ***P≤0.001; SD, standard deviation; n, number; IQR, interquartile range.

**Note:** Distant margin is defined as absence of tumour cells within 1mm of surgical margins.
Table 2: Multivariate binary logistic regression analysis demonstrating significant predictors of positive and close margins.

<table>
<thead>
<tr>
<th></th>
<th>Positive margins</th>
<th>Close margins</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>OR (95% CI)</td>
<td>P Value</td>
</tr>
<tr>
<td>Age, years</td>
<td>1.00 (0.9–1.1)</td>
<td>0.588</td>
</tr>
<tr>
<td>Female sex</td>
<td>0.89 (0.4–1.9)</td>
<td>0.771</td>
</tr>
<tr>
<td>Histologic tumour diameter, mm</td>
<td>0.92 (0.83–1.02)</td>
<td>0.128</td>
</tr>
<tr>
<td>Histologic tumour thickness, mm</td>
<td>1.56 (1.24–1.96)</td>
<td>&lt;0.001***</td>
</tr>
<tr>
<td>Excised from head and neck</td>
<td>2.78 (1.33–5.80)</td>
<td>0.007**</td>
</tr>
<tr>
<td>Excised in primary care</td>
<td>2.20 (1.07–4.52)</td>
<td>0.033*</td>
</tr>
</tbody>
</table>

*P≤0.05; **P≤0.01; ***P≤0.001; OR, Odds Ratio; CI, Confidence interval.

Table 2 describes the findings of multivariate analysis. Odds of positive margin on surgical excision was significantly increased with deeper tumours (OR 1.56, 95% CI 1.24–1.96), tumours from the head and neck (OR 2.78, 95% CI 1.33–5.80) and those excised in primary care (OR 2.20, 95% CI 1.07–4.52). On separate multivariate analysis, the odds of close margin on surgical excision was significantly increased in lesions excised in primary care (OR 2.44, 95% CI 1.5–3.98) as well as lesions on females (OR 2.01, 95% CI: 1.3–3.2).

Outcomes of re-excisions

In patients with positive margins, 52.6% went on to have a surgical re-excision and in patients with close margins, 13.6% were re-excised. Residual tumour was present in 31.7% (13) patients with positive margins and no patients with close margins (Table 3).

Discussion

This study has demonstrated a high close margin rate despite an acceptable positive margin rate in a large cohort of patients undergoing primary excision of cSCC. Tumours of the head and neck, increased tumour thickness and surgical excision in primary care are significantly correlative with positive margin rate on multivariate analysis. Primary care excision and female sex were significantly associated with close margin rates. The rate of residual tumour in those with positive margins is similar to previous studies.

The burden of non-melanoma skin cancer in Australasia is significant, with Australia and New Zealand having the highest rates of cSCC in the world.15–17 Despite effective methods to prevent cSCC, the incidence has been shown to continue to increase worldwide. Adequate treatment of patients with cSCC is imperative to improve outcomes, avoid unnecessary repeat procedures and reduce costs. Incomplete excisions are however likely to be inevitable as the decision between larger excisions needing greater expertise and possibly more reconstruction have to be balanced with the local resources constraints and consideration of cosmesis.

In contrast to other healthcare systems, the high rate of lesions in Australasia has led to NMSC being commonly treated in both primary as well as secondary care.18,19 Surgical excision is usually curative, but adequate pathological margins are important for management. The intent is

Table 3: Surgical outcomes and residual cancer rate in lesions with positive and close margins.

<table>
<thead>
<tr>
<th>Margin status, n (%)</th>
<th>Re-excised, n (%)</th>
<th>Tumour cells in re-excision</th>
</tr>
</thead>
<tbody>
<tr>
<td>Positive margin</td>
<td>78 (9.5%)</td>
<td>41 (52.6%)</td>
</tr>
</tbody>
</table>
| Close margin (<1mm)  | 139 (16.8%)      | 19 (13.7%)                | 0 (0%)
twofold; to ensure complete excision of the primary tumour and to remove in-transit micro-metastases around the tumour. There are several guidelines available worldwide. But in general, most advise surgical margins of 4–6mm depending on lesions characteristics, and margins of up to 10mm are recommended for high risk tumours. Re-excision of tumours with positive margins is considered standard, but recommendations in patients with close margins are less clear. Current Australian guidelines advise consideration of re-excision or radiotherapy, and one previous study has recommended re-excision in this group. The surgical literature has previously concentrated on positive margin rate in cSCC and several papers have investigated factors associated with positive margins in squamous cell carcinoma, including two studies from New Zealand and one in Australia. A large recent systematic review has calculated a pooled incomplete excision rate of 8.8% with simple surgical excision. The majority of studies in this review considered an incomplete excision as one where tumour was present at the excised margin. Only one study included tumour cells up to 1mm from the margin and reported an incomplete excision rate of 16%. These findings are in keeping with our data where we report a 9% positive margin rate and a 17% close margin rate. This gives a potential incomplete excision rate of 26%, despite an acceptable positive margin rate. In studies that have assessed factors that can predict positive margins, the results have varied. In broad terms, tumours of the head and neck and larger tumours are more consistently associated with positive margins. Two studies have examined outcomes in primary and secondary care with variable results. These previous studies are however limited, due to failure to take account of complicating variables through use of multivariate analysis. Our data has instigated anatomical location, tumour depth and excision in primary care being associated with a higher positive margin rate through these means. It is interesting to note that in our data tumour diameter was not a significant factor once multivariate analysis had taken place.

Close margin rates were also associated with excision in primary care and female gender. Secondary care physicians should continue to be encouraged to support primary care by facilitating local courses and opportunities to upskill. In addition, we recommend consideration of referring tumours of the head and neck as well as tumours that appear thicker to more specialist clinicians. It is unclear exactly why female gender affects close margin rates. It is known that there is variance in anatomic distribution of cSCC between genders, a phenomenon which has also been demonstrated in our study. In addition, it has been suggested that cSCC of the lower limb represents a pathologically distinct lesion from cSCC elsewhere. It is possible that this, together with other complicating factors such as a higher consideration of cosmesis, account for our observations.

Re-excision in patients with positive margins was associated with a 31% residual cancer rate, similar to that reported by Bovill et al. Follow up from this UK study has shown that a positive re-excision was associated with higher rates of loco-regional recurrence and therefore extended follow-up was recommended. Bovill et al also demonstrated a 13% positive re-excision rate in patients with close margins and recommended re-excision in this group. This is in contrast to our data where no re-excisions in this small group of patients contained residual tumour. It is likely that larger studies are needed to determine the significance of a close surgical margin but in the interim, reporting of close margins and consideration of further treatment should be a minimum requirement for clinicians excising cSCC.

Despite its retrospective nature, this study has analysed a high number of consecutive cSCC excisions across primary and secondary care. All pathological reports were individually reviewed by the study team, and it is the first large study to consider patients with close margins. There was however, inconsistency in regional pathological reporting especially with regards to lesion size and thickness. It is also possible that a subgroup of patients went to another region to have a lesion re-excised, but it is likely that this number of patients is low.

In conclusion, this is the first study to report rates, predicting variables and outcomes of surgical excision in patients...
with both positive and close margins following surgical excision for cSCC. It is recommended that referring tumours of the head and neck and those with increased clinical thickness to more specialist clinicians is considered. The need for re-excision in patients with close margins remains uncertain and larger studies are needed.

Competing interests:
Nil.

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URL:

REFERENCES:
14. Elliott BM, Douglass BR, McConnell D, Johnson B, Harmston C. Incidence,


Modelling the number of quitters needed to achieve New Zealand’s Smokefree 2025 goal for Māori and non-Māori

Nick Wilson, Frederieke Sanne Petrović-van der Deen, Richard Edwards, Andrew Waa, Tony Blakely

ABSTRACT

AIM: To estimate the numbers of people required to quit smoking in New Zealand to achieve the Smokefree 2025 goal and to compare these with current levels of quitting.

METHODS: We used the established BODE tobacco forecasting model to project smoking prevalence separately for Māori and non-Māori to 2025 under a business-as-usual (BAU) scenario. We then determined by what factor current annual cessation rates would have to increase to achieve an adult smoking prevalence of under 5% by the year 2025, while annual smoking uptake rates continued to follow BAU patterns. Comparisons were also made in terms of estimated current long-term quitters arising from official reports of smoking cessation service use (Quitline and face-to-face support services).

RESULTS: To achieve a below 5% smoking prevalence by 2025, there would need to be additional averages of 8,400 Māori long-term quitters per year (5.2 times the BAU level on average) and 8,800 extra non-Māori quitters per year during 2018 to 2025 (1.9 times the BAU level on average). We estimated that the Quitline and funded face-to-face smoking cessation services are generating 2,000 Māori and 6,100 non-Māori long-term quitters per year. But this represents only 19% of Māori and only 34% of the non-Māori quitters required.

CONCLUSIONS: This modelling work suggests that to achieve the Smokefree 2025 goal, there would need to be very major increases in quit rates. To achieve this goal the New Zealand Government will need to massively increase investment in established interventions (smoking cessation support, mass media) while continuing with substantial tobacco tax increases, or else add substantive new strategies into the intervention mix.

Projections of future smoking prevalence suggest that a continuation of current policies and services will be insufficient to achieve the New Zealand Government’s Smokefree 2025 goal (generally considered to be <5% adult daily smoking prevalence). In particular, this modelling work has suggested that the under 5% target would be missed for non-Māori and by a very wide margin for Māori, a particular concern given the importance of addressing ethnic inequalities in health in this country.

Despite the urgent need for more progress, no New Zealand Government has published a plan setting out how the Smokefree 2025 goal will be achieved (although in 2018 the goal of developing an action plan was announced by the Associate Minister of Health). Furthermore, current tobacco control funding by central government is mainly allocated to the provision of individual-level smoking cessation services (eg, the Quitline) and pharmacotherapy (largely funded by Pharmac). Given this background, we aimed to inform planning to achieve the Smokefree 2025 goal by estimating the numbers of people required to quit smoking to achieve the goal and to compare these with current levels of quitting.
Methods

We used the established BODE<sup>1</sup> tobacco forecasting model<sup>1–3,6,7</sup> to project smoking prevalence separately for Māori and non-Māori to 2025 under a business-as-usual (BAU) scenario. This BAU scenario assumed a continuation of current annual trends in smoking uptake and cessation rates (established between the 2006 and 2013 Censuses) with the added impact of the scheduled 10% annual tobacco tax increases until the last one in January 2020 (for details see van der Deen et al<sup>3</sup>). We projected the total daily smoker population each year, as well as the net number of successful quitters. The latter was the difference in the total of daily smokers between the current and the previous year, after excluding reductions due to daily smokers who had died during the year and additional young people estimated to have been prevented from taking up smoking compared to the previous year.

We then determined by what factor current annual cessation rates would have to increase to achieve adult smoking prevalence of under 5% by the year 2025, while annual smoking uptake rates continued to follow BAU patterns (ie, remained unchanged). In this way it was possible to estimate the additional number of successful quitters needed among Māori and non-Māori smoker populations each year to achieve the Smokefree 2025 goal.

Finally, we estimated the number of long-term quitters generated by the Quitline and Ministry of Health-funded face-to-face smoking cessation services. We used data provided by the Ministry for the last three quarterly reporting periods of 2017 and the first quarter of 2018.<sup>8</sup> For estimating the long-term quit rate for these service users, we used the estimate of 13.4% from a published New Zealand study of the Quitline<sup>9</sup> (which considered data from four published trials involving this Quitline<sup>10–13</sup>). Of note however, is that we had to apply this 13.4% figure (derived from studies of the telephone-delivered part of the Quitline Service) to all Quitline Service users (including those using the text-messaging service and email conversation service) and to face-to-face cessation services. This was owing to a lack of data on quit success rates for these other types of service delivery.

Results

Under the BAU trends in smoking cessation and uptake, the projected smoking prevalences in 2025 were 17.4% for Māori and 7.2% for non-Māori (see Table 1 and Table 2 respectively). Under these projections, there will still be around nearly 90,000 Māori smokers and 220,000 non-Māori smokers in the year 2025, around 64,000 and 67,000 more respectively than would be still smoking if a prevalence of 4.99% for both population groups was achieved.

From 2018–2025, an average of around 2,000 Māori and 9,200 non-Māori smokers were estimated to quit successfully under BAU conditions each year (see Tables), with greater numbers quitting in the earlier years. To achieve a below 5% smoking prevalence by 2025, there will need to be additional averages of an extra 8,400 Māori long-term quitters per year (5.2 times the BAU level) and 8,800 extra non-Māori quitters per year (1.9 times the BAU level on average). However, assuming a constant rate of quitting over time (as seems most sensible, and is embedded in our forecasting model), these numbers are much higher in the early years. For example, around 20,200 Māori and 14,800 non-Māori additional quitters would be required in 2018, and an average of around 15,000 Māori and 12,400 non-Māori additional quitters from 2018–2020 for this initial period (see Tables).

We estimated that the Quitline and funded face-to-face smoking cessation services are currently generating around 8,100 long-term quitters per year (6,000 and 2,100 respectively), including 2,000 Māori and 6,100 non-Māori quitters. This represents around 29% of the around 28,000 required quitters per year during the 2018–2025 period overall, only 19% for Māori and 34% for non-Māori. Figures 1 and 2 show these number of quitters relative to the total number of quitters required to achieve the Smokefree goal by the year 2025.
Discussion

This analysis suggests that there will have to be a very substantial increase in numbers of smokers enrolling with, and quitting through, the Quitline and face-to-face smoking cessation services to achieve the numbers of quitters to be on track to achieve the Smokefree 2025 goal. In particular, the increase required in service provision and supported quitting through the services for Māori to achieve the goal (over five times the BAU level) seems unrealistic.

It is possible that our results have over-estimated the difficulty of achieving the Smokefree 2025 goal. For example, increasing use of e-cigarettes\textsuperscript{14} and new types of non-combusted nicotine-delivery products appearing on the market (eg, ‘JUUL’\textsuperscript{15}) may possibly result in increased quit rates of tobacco cigarettes. We also did not take into account the likely beneficial impact of plain (standardised) packaging introduced in New Zealand in 2018. Conversely, we may have slightly overestimated the beneficial impact of tobacco tax increases due to tobacco industry strategies such as increasing the number of budget brands available and not fully passing through the tax into higher prices for these products.\textsuperscript{16} Furthermore, we may have underestimated smoker numbers and the numbers of quitters required because we used census estimates for smoking prevalence in our model. Smoking prevalence estimates from the census tend to be lower.

Table 1: Projected smoking prevalence and number of Māori smokers by year into the future under business-as-usual (BAU) annual trends in smoking uptake and cessation rates and under increased cessation rates that would be needed to achieve <5% adult daily smoking prevalence by 2025.

<table>
<thead>
<tr>
<th>Year</th>
<th>Projected adult smoking prevalence (crude) assuming BAU (includes current plans of tobacco tax increases until 2020)*</th>
<th>Projected number of smokers assuming BAU</th>
<th>Projected number of successful quitters each year under BAU (difference in the number of smokers each year minus smokers who died and averted initiators)**</th>
<th>Projected smoking prevalence under sufficiently high cessation rates to achieve &lt;5% smoking prevalence by 2025 (ie, baseline cessation rates were increased to achieve the target)</th>
<th>Hypothetical total smoker population on track to reach the &lt;5% target</th>
<th>Number of smokers that would need to quit successfully each year to achieve &lt;5% smoking prevalence by 2025*</th>
<th>Additional number of successful quitters (relative to BAU) needed each year to achieve &lt;5% smoking prevalence by 2025</th>
</tr>
</thead>
<tbody>
<tr>
<td>2018</td>
<td>24.0%</td>
<td>108,000</td>
<td>2,740</td>
<td>19.6%</td>
<td>87,600</td>
<td>22,900</td>
<td>20,200</td>
</tr>
<tr>
<td>2019</td>
<td>22.7%</td>
<td>104,000</td>
<td>2,760</td>
<td>15.3%</td>
<td>69,800</td>
<td>17,200</td>
<td>14,400</td>
</tr>
<tr>
<td>2020</td>
<td>21.5%</td>
<td>101,000</td>
<td>2,900</td>
<td>12.1%</td>
<td>56,400</td>
<td>13,100</td>
<td>10,200</td>
</tr>
<tr>
<td>2021</td>
<td>20.6%</td>
<td>98,000</td>
<td>1,440***</td>
<td>9.8%</td>
<td>47,000</td>
<td>9,190</td>
<td>7,750</td>
</tr>
<tr>
<td>2022</td>
<td>19.7%</td>
<td>96,000</td>
<td>1,430</td>
<td>8.1%</td>
<td>39,500</td>
<td>7,060</td>
<td>5,620</td>
</tr>
<tr>
<td>2023</td>
<td>18.9%</td>
<td>94,000</td>
<td>1,620</td>
<td>6.8%</td>
<td>33,700</td>
<td>5,610</td>
<td>3,990</td>
</tr>
<tr>
<td>2024</td>
<td>18.1%</td>
<td>92,000</td>
<td>1,580</td>
<td>5.8%</td>
<td>29,300</td>
<td>3,320</td>
<td>2,760</td>
</tr>
<tr>
<td>2025</td>
<td>17.4%</td>
<td>90,000</td>
<td>1,480</td>
<td>4.99% (on target)</td>
<td>25,900</td>
<td>3,200</td>
<td>1,850</td>
</tr>
</tbody>
</table>

*For long-term projections under BAU (out to the year 2060), see Figure 1 in the previous publication using the same model: van der Deen et al 2016\textsuperscript{3}).

**This column represents the projected number of successful quitters between this and the previous year under baseline trends in smoking uptake and cessation, and excludes those who died or were prevented from taking up smoking (as a result of existing tobacco control strategies—including tobacco tax increases through to January 2020). It is as such, not the exact difference between the number of smokers in this and the previous year in the column on the left.

***This lower number of quitters in this year is due to the end of the current series of annual tobacco tax increases (see Methods).

All values are rounded to three meaningful digits.
Table 2: Projected smoking prevalence and number of non-Māori smokers by year into the future under business-as-usual (BAU) annual trends in smoking uptake and cessation rates and under increased cessation rates that would be needed to achieve <5% adult daily smoking prevalence by 2025.

<table>
<thead>
<tr>
<th>Year</th>
<th>Projected adult smoking prevalence (crude) assuming BAU (includes current plans of tobacco tax increases until 2020)*</th>
<th>Projected number of smokers assuming BAU</th>
<th>Projected number of successful quitters each year under BAU (difference in the number of smokers each year minus smokers who died and averted initiators)*</th>
<th>Projected smoking prevalence under sufficiently high cessation rates to achieve &lt;5% smoking prevalence by 2025 (i.e., baseline cessation rates were increased to achieve the target)</th>
<th>Hypothetical total smoker population on track to reach the &lt;5% target</th>
<th>Number of smokers that would need to quit successfully each year to achieve &lt;5% smoking prevalence by 2025*</th>
<th>Additional number of successful quitters (relative to BAU) needed each year to achieve &lt;5% smoking prevalence by 2025</th>
</tr>
</thead>
<tbody>
<tr>
<td>2018</td>
<td>9.9%</td>
<td>295,000</td>
<td>11,900</td>
<td>9.4%</td>
<td>280,000</td>
<td>26,700</td>
<td>14,800</td>
</tr>
<tr>
<td>2019</td>
<td>9.4%</td>
<td>281,000</td>
<td>11,600</td>
<td>8.5%</td>
<td>254,000</td>
<td>23,900</td>
<td>12,300</td>
</tr>
<tr>
<td>2020</td>
<td>8.9%</td>
<td>268,000</td>
<td>11,300</td>
<td>7.7%</td>
<td>231,000</td>
<td>21,600</td>
<td>10,300</td>
</tr>
<tr>
<td>2021</td>
<td>8.5%</td>
<td>257,000</td>
<td>8,250</td>
<td>7.0%</td>
<td>212,000</td>
<td>17,200</td>
<td>8,990</td>
</tr>
<tr>
<td>2022</td>
<td>8.2%</td>
<td>247,000</td>
<td>8,100</td>
<td>6.4%</td>
<td>195,000</td>
<td>15,700</td>
<td>7,610</td>
</tr>
<tr>
<td>2023</td>
<td>7.8%</td>
<td>238,000</td>
<td>7,940</td>
<td>5.9%</td>
<td>179,000</td>
<td>14,300</td>
<td>6,380</td>
</tr>
<tr>
<td>2024</td>
<td>7.5%</td>
<td>229,000</td>
<td>7,600</td>
<td>5.4%</td>
<td>166,000</td>
<td>12,900</td>
<td>5,310</td>
</tr>
<tr>
<td>2025</td>
<td>7.2%</td>
<td>220,000</td>
<td>7,160</td>
<td>4.99% (on target)</td>
<td>153,000</td>
<td>11,500</td>
<td>4,380</td>
</tr>
</tbody>
</table>

*See the footnotes for Table 1.

Figure 1: Projected annual number of Māori quitters required to achieve <5% adult daily smoking prevalence by 2025, including the estimated number of quitters achieved via current Ministry of Health funded smoking cessation services.
than the estimates in the New Zealand Health Survey (especially for Māori), as we have detailed elsewhere, albeit somewhat less different for the most recent New Zealand Health Survey data. Our estimates of long-term quit rates achieved by the Quitline may also be overestimated, given our assumption that the 13.4% quit rate from users of the telephone-delivered approach of Quitline Service also applied to those using the text-messaging service, the email conversation service and face-to-face smoking cessation services.

Despite these limitations, it is unlikely that they would substantially change the key finding of this current work, which is that an unrealistically large increase in the usage of cessation services on its own would be required to meet the Smokefree 2025 goal. We note that others have also described the role of assisted quitting through health service provision as modest (in terms of achieving population smoking prevalence reductions). For example, unassisted quitting dominates in Australia with 54% to 69% of ex-smokers having quit unassisted according to a recent systematic review of Australian studies.

So if the Government is to achieve its Smokefree 2025 goal we see two main options for moving forward as detailed below.

1. **Greatly enhanced investment in established tobacco control measures:** This option would involve massively increased investment in cessation services (eg, the Quitline) and associated mass media campaigns, and other approaches to increase the uptake. Together this package has been shown to be very cost-effective, as per our modelling work on the New Zealand Quitline. New Zealand appears to have under-invested in mass media campaigns historically, even though some of these campaigns have shown to assist with advancing tobacco control for Māori (eg, the successful “Its About Whanau” campaign). Continuing to raise tobacco taxes would need to be part of this mix, albeit with using some of the tax revenue to assist smokers with quitting. Furthermore, to reduce the risk of financial hardship for smokers who can’t readily quit, some of the tobacco tax revenue could be used to support smokers quitting with, or shifting to longer-term use of e-cigarettes, which are much cheaper than tobacco and are probably less harmful to health.
2. Adding substantive novel interventions into the tobacco control intervention mix: To maximise confidence in achieving the goal, the Government could consider adding to the established intervention mix in the above Option One, one or more novel endgame strategies. These include: a sinking lid on tobacco supply, substantial tobacco retail outlet reduction, adopting a “tobacco-free generation” policy or restricting the sale of tobacco to very-low-nicotine content tobacco products. The latter approach is being explored by the US Food and Drug Administration (FDA). All except the sinking lid option are included in a comprehensive action plan prepared by New Zealand health sector groups. Including any of these substantive interventions would require law changes—which we recognise has political risks. However, relative to the above Option One, these substantive novel strategies are likely to greatly increase the health gain achieved and achieve much larger cost-savings from reduced disease treatment costs (as per modelling work which considered 16 tobacco-related diseases).

Conclusions
This modelling work suggests that to achieve a below 5% smoking prevalence by 2025 for both non-Māori and Māori, there will need to be very major increases in quit rates (ie, 1.9 and 5.2 times the projected BAU levels respectively). To achieve this goal the New Zealand Government will need to massively increase investment in established interventions (smoking cessation support, mass media) while continuing with substantial tobacco tax increases, or else add substantive new strategies into the intervention mix.
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Reliability of venous blood gas sodium, potassium and creatinine

Pourya Pouryahya, Zhiliang Caleb Lin, Lynn Tan, Alastair Meyer

ABSTRACT

OBJECTIVE: To determine the level of correlation between sodium, potassium and creatinine readings between point-of-care venous blood gas (VBG) and laboratory biochemistry measurements (LBM).

METHODS: Data was obtained from three Monash Health (one of the largest health networks in metropolitan Melbourne) emergency departments. 16,527 VBGs were matched with LBM for sodium, 16,437 for potassium and 8,597 for creatinine. Pearson correlation and further subgroup analyses were carried out to explore if acid-base imbalance affected sodium, potassium or creatinine reliability in VBG.

RESULTS: The range of VBG values showed more variation in comparison to LBM. There was good correlation ($r>0.8$, $p<0.001$) between measured values with the exception of potassium in acidaemia, however, there was consistent and statistically significant difference in measured values.

CONCLUSIONS: The small mean differences across all three parameters observed although statistically significant are unlikely to be clinically significant. With minor calibrations, this would be an easily corrected problem. As such, we recommend that sodium, potassium and creatinine measurements can be used interchangeably between the VBG and LBM, with the exception of potassium levels in acidaemia. Potassium levels in acidaemia should be used with caution due to lower correlation.

Due to the nature of acute presentations in emergency departments (ED), point-of-care venous blood gas is widely used and becoming increasingly popular.1 Quick turnover of patients or necessity to institute time-critical management in critically unwell patients such as diabetic ketoacidosis (DKA) or electrolyte imbalance regardless of cause and for ease of re-evaluation2 are two main reasons of this popularity. A number of parameters are measured on a venous blood gas (VBG).

Multiple researches since 2001 have supported the use of VBGs secondary to being less invasive with sufficient agreement and correlation when acid base status, electrolytes or even haemoglobin are of concern. However, it’s not a substitute for arterial blood gases (ABG) when assessing ventilation and oxygenation. VBG applicability is yet to be ascertained in shock states or mixed acid-base disturbances.3 Furthermore, VBGs have not been validated with laboratory methods (LBM) using a large sample size. If validated, swifter investigations, referrals and diagnoses can be reached with resulting cost-effectiveness. For instance, semi-urgent contrast CT scans that are reliant on renal function could be performed without delay with a VBG creatinine reading.

Some previous publications have compared electrolyte measurements in VBG and LBM, but none of them included creatinine in their studies,4-10 and there hasn’t been any clear agreement when comparing these parameters. In addition, the largest published study cited less than 1,000 samples.10 Utilising a larger sample size will reduce the chance of random error and may give light to a more definitive answer as to the correlation between the two measurement methods. Using the power of a larger sample size, this paper will explore the potential of using VBG readings interchangeably with the LBM. In particular, we
will explore the correlation of electrolytes sodium and potassium, as well as creatinine.

Methods

Data was obtained from Monash Health emergency department presentations. Monash Health is one of the major health networks in Melbourne, with an annual ED census of approximately 200,000 presentations across three hospitals: Monash Medical Centre (tertiary), Dandenong and Casey (district) hospitals. This study was approved by Monash Health and the Monash University Human Research and Ethics Committee.

21,770 individualised VBG readings were matched against LBM samples, received by the laboratory within five minutes (ensuring the same samples). These samples were matched by a hospital identification number, and duplicate readings from the same patient (eg, across a few days) were excluded. These readings were obtained for the period when records for both VBGs and LBM were accessible electronically. 16,527 records were matched for sodium, 16,437 for potassium and 8,597 for creatinine through patient identification numbers and registered sample time. Error readings were excluded, resulting in 16,514 samples for sodium, 16,509 samples for potassium and 8,597 samples for creatinine (Figure 1).

Statistical analysis was carried out using Microsoft Office Excel 2011, and further subgroup analysis including Pearson correlation coefficient was carried out to explore the effect of acid-base disturbances on the reliability of the sodium and potassium readings.

Pearson correlation coefficient (PCC) also referred to as Pearson’s r, is a measure of the linear correlation between two variables (the covariance of the two variables divided by the product of their standard deviations. It has a value between +1 and −1, where 1 is total positive linear correlation, 0 is no linear correlation and −1 is total negative linear correlation.

Results

Sodium and potassium

Both acidaemia and alkalaemia were recorded, with the mean pH (7.37) within the human physiological range (7.35–7.45). For both electrolytes, the VBG returned a wider range of results than the LBM, however, mean and standard deviations (SD) of the values were similar (Table 1). Mean differences for both electrolytes across all pH states were significant (p<0.001). Sodium levels across all pH states were marginally over-estimated by the VBG. Despite the over-estimation, there was high correlation (r=0.84–0.85) between the VBG and LBM.

**Figure 1:** Study design diagram, including excluded results due to error.

*Readings excluded were due to "error" readings on instrument.
Potassium levels were marginally underestimated across all pH states. Apart from a medium strength correlation \( r=0.58 \) for potassium in acidaemia, results were highly correlated \( r=0.85-0.89 \) in the other pH states and overall (Table 2).

**Creatinine**

With regards to creatinine, we noticed a slight increased variation comparing VBG with LBM (SD 123 vs 118) despite similar minimum and maximum values (Table 3).

A significant mean difference of 2.55 was observed with a high correlation between the samples \( r=0.99 \) (Table 4).

All mean differences recorded were statistically significant \( p<0.001 \), with good correlation \( r>0.8 \). However, in the subgroup analyses, potassium in an acidaemic sample demonstrated a lower correlation comparing VBG and LBM.

**Discussion**

The LBM utilises indirect whereas the VBG measures direct ion-sensing electrodes to determine serum electrolytes. The differing methods give a good case for further investigation to understand their comparability and interchangeable utility in clinical practice.

In direct method (VBG), the electrolytes are measured on an undiluted sample with a turn over time of between 2–3 minutes.

---

**Table 1: VBG parameters.**

<table>
<thead>
<tr>
<th>Value</th>
<th>Range</th>
<th>Unit</th>
</tr>
</thead>
<tbody>
<tr>
<td>pH</td>
<td>7.35–7.45</td>
<td></td>
</tr>
<tr>
<td>( \text{PvCO}_2 )</td>
<td>35–35 mmHg</td>
<td></td>
</tr>
<tr>
<td>Bicarbonate ( (\text{HCO}_3^-) )</td>
<td>20–24 mmol/L</td>
<td></td>
</tr>
<tr>
<td>Base Excess ( (\text{BE}) )</td>
<td>-3 to +3 mmol/L</td>
<td></td>
</tr>
<tr>
<td>Sodium ( (\text{Na}^+) )</td>
<td>135–145 mmol/L</td>
<td></td>
</tr>
<tr>
<td>Potassium ( (\text{K}^+) )</td>
<td>3.5–5 mmol/L</td>
<td></td>
</tr>
<tr>
<td>Chloride ( (\text{Cl}^-) )</td>
<td>95–107 mmol/L</td>
<td></td>
</tr>
<tr>
<td>Blood sugar level ( (\text{BSL}) )</td>
<td>4–12 mmol/L</td>
<td></td>
</tr>
<tr>
<td>Lactate ( (\text{Lact}) )</td>
<td>less than 2 mmol/L</td>
<td></td>
</tr>
<tr>
<td>Creatinine</td>
<td>60–110 umol/L</td>
<td></td>
</tr>
<tr>
<td>Haemoglobin</td>
<td>130–180 g/L</td>
<td></td>
</tr>
</tbody>
</table>

---

**Table 2: Potassium and sodium values in VBG and LBM.**

<table>
<thead>
<tr>
<th>Analysis</th>
<th>Minimum</th>
<th>Maximum</th>
<th>Mean</th>
<th>SD</th>
</tr>
</thead>
<tbody>
<tr>
<td>pH (VBG)</td>
<td>6.36</td>
<td>7.74</td>
<td>7.37</td>
<td>0.082</td>
</tr>
<tr>
<td>Na ( (n:16,514) )</td>
<td>120</td>
<td>166</td>
<td>138</td>
<td>4.07</td>
</tr>
<tr>
<td>LBM</td>
<td>121</td>
<td>154</td>
<td>137</td>
<td>3.71</td>
</tr>
<tr>
<td>K ( (n:16,509) )</td>
<td>2.5</td>
<td>7.6</td>
<td>4.043</td>
<td>0.565</td>
</tr>
<tr>
<td>LBM</td>
<td>2.9</td>
<td>7.5</td>
<td>4.169</td>
<td>0.546</td>
</tr>
</tbody>
</table>

---

**Table 3: Analysis of differences between sodium and potassium values by metabolic state in VBG and LBM.**

<table>
<thead>
<tr>
<th>Comparison</th>
<th>Mean difference</th>
<th>SD</th>
<th>95% CI</th>
<th>R</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Na</td>
<td>Overall</td>
<td>1.1</td>
<td>2.21</td>
<td>1.07; 1.14</td>
<td>0.84</td>
</tr>
<tr>
<td></td>
<td>Aklalaemia</td>
<td>0.777</td>
<td>2.17</td>
<td>0.67; 0.89</td>
<td>0.85</td>
</tr>
<tr>
<td></td>
<td>Acidaemia</td>
<td>1.26</td>
<td>2.42</td>
<td>1.20; 1.33</td>
<td>0.84</td>
</tr>
<tr>
<td></td>
<td>Normal pH</td>
<td>1.07</td>
<td>2.11</td>
<td>1.03; 1.11</td>
<td>0.84</td>
</tr>
<tr>
<td>K</td>
<td>Overall</td>
<td>-0.127</td>
<td>0.256</td>
<td>-0.131; -0.123</td>
<td>0.89</td>
</tr>
<tr>
<td></td>
<td>Aklalaemia</td>
<td>-0.146</td>
<td>0.258</td>
<td>-0.159; -0.133</td>
<td>0.85</td>
</tr>
<tr>
<td></td>
<td>Acidaemia</td>
<td>-0.0617</td>
<td>0.821</td>
<td>-0.0843; -0.0391</td>
<td>0.58</td>
</tr>
<tr>
<td></td>
<td>Normal pH</td>
<td>-0.128</td>
<td>0.237</td>
<td>-0.132; -0.123</td>
<td>0.88</td>
</tr>
</tbody>
</table>
whereas in indirect method (LBM), the plasma sample is diluted then analysed, with the process time being at least 30 minutes, as such to be able to reliably utilise the VBG results in assessment and management of a critically unwell patient, VBG would be optimal.

Sodium and potassium haemeostasis occur in slightly different but related ways. Sodium is closely related to fluid balance through baroreceptors, aldosterone and ADH, and potassium is mainly intracellular and largely maintained by renal mechanisms as part of the body's buffering system. As a result, changes in pH might affect their concentrations, hence the rationale for studying electrolyte changes generally as well as various pH states. Apart from potassium in the acidaemia, the rest of the correlation coefficients (r) by pH states and in general, were demonstrating high correlation. The fact that potassium is generally underestimated by VBG and acidosis can maintain hyperkalaemia, the VBG might be more sensitive to higher potassium levels, resulting in a lowered mean difference. It is interesting that even though the mean difference is the least out of all four pH states, the correlation should be only moderate (r=0.58).

From clinical perspective and its potential life-threatening nature, hyperkalaemia is crucial to be recognised imminently either clinically or biochemically, therefore a further specific subgroup analysis was performed. Reviewing all the LMB with potassium level of more than 5mmol/L revealed just one discrepancy where an LBM reading of 6mmol/L was reported as 5.4mmol/L on the VBG samples with no major clinical significance, confirming a strong correlation again as demonstrated.

Correlation of the hyperkalaemia in VBG with ECG findings was out of the scope of this study. However, we believe any abnormal ECG findings suggestive of hyperkalaemia in a clinically unstable patient requires urgent intervention regardless. Consequently, we believe that the VBG is clinically useful in the acute setting to identify hyperkalaemia.

According to Menchine et al, VBG electrolyte results were 100% specific and 97.8% sensitive in DKA. The authors, with a sample of 342 patients, demonstrated that correlation coefficients of 0.9 for sodium. This is in agreement with our finding that sodium levels highly correlates between VBG and LBM. The study also showed good correlations between other parameters like chloride (r=0.73), bicarbonate (r=0.94) and the anion gap (r=0.81), which is beyond the scope of our study but are additional preliminary findings in support of the utility of the VBG especially in an emergency situation like DKA.

Multiple other studies with limited samples, purported that biochemistry and glucose results were comparable but had relatively few samples. In one study, 59 paired samples from the paediatric intensive care unit were underestimated and statistically significant. King and Campbell found good agreement between VBG and formal UECs however concluded that the results should be used with caution because of wide limits of agreement. In a Turkish study, the authors found an underestimation of potassium levels with the VBG. Finally, another study found a significant difference in potassium levels in the normal pH range; the conclusion was that potassium levels are not reliable on the VBG.

Table 4: Range of creatinine values in VBG and LBM.

<table>
<thead>
<tr>
<th>Creatinine (µmol/L)</th>
<th>Minimum (µmol/L)</th>
<th>Maximum (µmol/L)</th>
<th>Mean (µmol/L)</th>
<th>SD</th>
</tr>
</thead>
<tbody>
<tr>
<td>VBG</td>
<td>10.5</td>
<td>1,655</td>
<td>110</td>
<td>123</td>
</tr>
<tr>
<td>LBM</td>
<td>9</td>
<td>1,585</td>
<td>108</td>
<td>118</td>
</tr>
</tbody>
</table>

Table 5: Analysis of differences of creatinine values recorded on VBG and LBM.

<table>
<thead>
<tr>
<th>Creatinine comparison</th>
<th>MD</th>
<th>SD</th>
<th>95% CI</th>
<th>R</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>2.55</td>
<td>18.0</td>
<td>2.17 ; 2.94</td>
<td>0.99</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>
A potential limitation to the study is lack of ability to control for the sampling of the blood gases. As this was a retrospective study and as large a sample size as possible was desired, there was no control for site or method of collection including tourniquet placement. This is possibly relevant in that tissue metabolism and ischemia varies with these variable changes and can contribute to differences in blood gas readings.\textsuperscript{13-14} Secondly, we excluded extreme results which were obviously in error (refer to methods), but there might have been some less extreme readings that were retained for comparison which were not clinically correlated and would have been discarded or the test re-run. Finally, our results might vary with others depending on calibration of machine and possibly brand and model.

**Conclusions**

Limited researches with conflicting findings are available on this topic and studies thus far have had relatively small sample sizes. Our study demonstrated good positive correlation between venous blood gas and laboratory biochemistry measurements of sodium, potassium and creatinine, with the exception of potassium in the acidemia. Minor adjustments in VBG assay could be made to potentially reduce the mean difference, however, the small mean differences might not significantly affect clinical decision making in management, especially with a slight difference of 2.55 for creatinine. Based on our study, sodium, potassium and creatinine measurements can be used interchangeably between the techniques with mild correction, and in acidemia potassium levels should be used with caution in lieu of a lower observed correlation.

**Take home message**

Overall there is a good clinical positive correlation between venous blood gas and laboratory biochemistry measurements of sodium, potassium and creatinine.
REFERENCES:


Public support and sociodemographic correlates of public breastfeeding support in New Zealand

Yanshu Huang, Danny Osborne, Chris G Sibley

ABSTRACT

AIMS: The present study examined levels of support for public breastfeeding and sociodemographic correlates of public breastfeeding attitudes in New Zealand.

METHOD: Data (N=19,598) were from the 2016/17 New Zealand Attitudes and Values Study, a nationwide longitudinal panel study of the social attitudes of New Zealand adults aged 18 and older. The survey included an item measuring support for women breastfeeding in public alongside relevant sociodemographic variables.

RESULTS: Most New Zealanders (75.3%) supported breastfeeding in public, whereas a small minority (5.2%) were opposed (a further 19.5% were neutral on the issue). In terms of sociodemographic correlates of public breastfeeding support, men (relative to women), being older, identifying with a religion and being of Asian ethnicity (relative to European/Pākehā) were associated with lower support. Conversely, being a parent, having more children (given birth to, fathered or adopted), being in a serious romantic relationship, having attained higher education and being of Māori ethnicity (relative to European/Pākehā) were associated with greater support for public breastfeeding.

CONCLUSIONS: New Zealanders expressed high levels of support for public breastfeeding. Reliable sociodemographic correlates of public breastfeeding support were also identified. These results provide the first comprehensive overview of New Zealanders’ support towards breastfeeding in public.

Breastfeeding provides various health benefits for infants, including increased protection against childhood infectious diseases and improvements to early childhood cognitive development, as well as a lower likelihood of developing ovarian or breast cancer for women who breastfeed. Accordingly, the World Health Organization recommends that infants be breastfed exclusively for at least the first six months of life. In New Zealand, although the right to breastfeed is technically protected by legislation against gender-based discrimination, breastfeeding in public is not specifically protected by the law. This subtle legal distinction has important implications, as policies that protect the right to breastfeed in public increases breastfeeding rates.

In 2017, approximately 77% of all newborn infants were exclusively or fully breastfed at two weeks of age, 72% were breastfed exclusively at six weeks, before dropping to 58% at three months. Although there are many factors that may contribute to the reduction in breastfeeding rates (eg, personal factors), social attitudes towards breastfeeding may be a critical barrier to breastfeeding in public. However, few studies have been conducted in New Zealand that directly examine levels of public support for breastfeeding in public. We address this oversight by investigating attitudes towards public breastfeeding using a large, national sample of New Zealand adults.
Two factors that might contribute to the decrease in breastfeeding rates are the lack of legislation and the lack of facilities supporting breastfeeding in public spaces. For instance, mothers may feel discomfort and embarrassment with the idea of breastfeeding in public. Hyper-awareness of public scrutiny and the perceived unacceptability of public breastfeeding may lead to feelings of awkwardness and unwanted exposure. Due to these fears, mothers may avoid breastfeeding in public or withdraw from breastfeeding earlier than they would otherwise. Additionally, people may perceive breastfeeding inside the home as more acceptable than breastfeeding in public spaces. Taken together, both the perceived acceptability of breastfeeding by mothers, as well as the public's attitude in general, may constrain women's breastfeeding options.

Research on support for breastfeeding in public has yielded inconsistent results, suggesting that there is considerable cross-cultural variability in attitudes and norms. In a community survey conducted in rural Newfoundland and Labrador, 51.9% of respondents indicated that they would be uncomfortable around a woman breastfeeding in public. Similarly, a survey of New York City residents found that 50.4% of respondents were unsupportive of public breastfeeding. Yet other studies identify high levels of support for breastfeeding in public. A study conducted in Tennessee, US, found that people's comfort with being around a breastfeeding mother in a public space increased from 58.4% in 2004 to 66.5% in 2008. Comparatively, positive attitudes were observed in a study of Canadian adults in Ottawa, where 75% of respondents thought it was acceptable for women to breastfeed in restaurants and shopping malls. Similarly, a study of Western Australian adults found relatively high support between 1995 and 2009, with around 70% of participants believing it was acceptable to breastfeed across a range of public settings (eg, public transport, shopping malls).

The present study

Attitudes towards breastfeeding in public in New Zealand has been largely overlooked in recent years. As such, a review of decade-old research is warranted. Echoing themes from the international literature, qualitative research reveals that New Zealand mothers experience various social barriers, including public scrutiny when negotiating the decision to breastfeed in public. Similarly, a quantitative study in New Zealand showed that many mothers felt embarrassed when breastfeeding in public and, as a result, reduced the duration of their breastfeeding. Finally, a study of Māori women’s and whānau experiences with breastfeeding indicated that almost half of participants perceived that breastfeeding in public was seen as unacceptable by the general public. However, societal attitudes towards public breastfeeding has yet to be investigated in New Zealand.

The aim of this study was to address this oversight by examining attitudes towards public breastfeeding in New Zealand using a national sample of adults. First, we examined rates of public support for breastfeeding in public. Second, we explored sociodemographic factors associated with public breastfeeding support. In doing so, we address a notable gap in the literature by assessing how sociodemographic characteristics are associated with public breastfeeding support. In doing so, we address a notable gap in the literature by assessing how sociodemographic characteristics are associated with public breastfeeding support. In doing so, we address a notable gap in the literature by assessing how sociodemographic characteristics are associated with public breastfeeding support. In doing so, we address a notable gap in the literature by assessing how sociodemographic characteristics are associated with public breastfeeding support. In doing so, we address a notable gap in the literature by assessing how sociodemographic characteristics are associated with public breastfeeding support. In doing so, we address a notable gap in the literature by assessing how sociodemographic characteristics are associated with public breastfeeding support. In doing so, we address a notable gap in the literature by assessing how sociodemographic characteristics are associated with public breastfeeding support. In doing so, we address a notable gap in the literature by assessing how sociodemographic characteristics are associated with public breastfeeding support. In doing so, we address a notable gap in the literature by assessing how sociodemographic characteristics are associated with public breastfeeding support.
the option to participate in the study. In following waves, booster sampling of adults aged 18–65 was conducted to increase the sample size and address sample attrition. Specifically, random samples were drawn from the 2012, 2014 and 2017 New Zealand Electoral Rolls and then incorporated into the study at Time 4 (2011/12), Time 5 (2013/14) and Time 8 (2016/17), respectively. Additional participants were recruited from an unrelated survey featured on a New Zealand news website at Time 3 (2011).

Measures

Opposition to breastfeeding in public

Time 8 (2016/17) of the NZAVS included a measure of opposition towards breastfeeding in public. Participants were asked to rate their agreement to the following item, “Women should avoid breastfeeding in public”, using a 7-point Likert scale with anchors at 1 (Strongly Disagree) and 7 (Strongly Agree).

Sociodemographics

A variety of sociodemographic variables were also measured. These included gender, age, ethnicity (European/Pākehā, Māori, Pacific Nations descent, Asian descent), religious affiliation, parental status, the number of children the participant had given birth to, fathered or adopted, relationship status (serious romantic relationship), employment status, education (11-unit ordinal rank of qualifications according to New Zealand Qualifications Standards), population density (urban vs rural), birthplace (being born in New Zealand or outside of New Zealand) and a measure of area-level socioeconomic deprivation (New Zealand Deprivation Index 2013).

Table 1: Unweighted and weighted demographic characteristics of the sample (N=19,598; Time 8 (2016/17) of the NZAVS).

<table>
<thead>
<tr>
<th>Characteristic (n)</th>
<th>% (unweighted)</th>
<th>% (weighted)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Gender</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Women (12,351)</td>
<td>63.0</td>
<td>54.3</td>
</tr>
<tr>
<td>Men (7,247)</td>
<td>37.0</td>
<td>45.7</td>
</tr>
<tr>
<td><strong>Age (years)</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>18–29 (2,061)</td>
<td>10.5</td>
<td>11.5</td>
</tr>
<tr>
<td>30–44 (4,534)</td>
<td>23.1</td>
<td>24.0</td>
</tr>
<tr>
<td>45–64 (10,697)</td>
<td>54.6</td>
<td>53.3</td>
</tr>
<tr>
<td>65+ (2,306)</td>
<td>11.8</td>
<td>11.2</td>
</tr>
<tr>
<td><strong>Religious affiliation</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes (7,460)</td>
<td>38.1</td>
<td>41.2</td>
</tr>
<tr>
<td>No (12,138)</td>
<td>61.9</td>
<td>58.8</td>
</tr>
<tr>
<td><strong>Parental status</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes (14,450)</td>
<td>73.7</td>
<td>72.5</td>
</tr>
<tr>
<td>No (5,148)</td>
<td>26.3</td>
<td>27.5</td>
</tr>
<tr>
<td><strong>Relationship status (serious romantic relationship)</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes (14,851)</td>
<td>75.8</td>
<td>75.4</td>
</tr>
<tr>
<td>No (4,747)</td>
<td>24.2</td>
<td>24.6</td>
</tr>
<tr>
<td><strong>Employment status</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes (15,416)</td>
<td>78.7</td>
<td>78.8</td>
</tr>
<tr>
<td>No (4,182)</td>
<td>21.3</td>
<td>21.2</td>
</tr>
</tbody>
</table>
Table 1: Unweighted and weighted demographic characteristics of the sample (N=19,598; Time 8 (2016/17) of the NZAVS) (continued).

<table>
<thead>
<tr>
<th><strong>Population density</strong></th>
<th>Unweighted</th>
<th>Weighted</th>
</tr>
</thead>
<tbody>
<tr>
<td>Urban (12,830)</td>
<td>65.5</td>
<td>69.0</td>
</tr>
<tr>
<td>Rural (6,768)</td>
<td>34.5</td>
<td>31.0</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th><strong>Born in New Zealand</strong></th>
<th>Unweighted</th>
<th>Weighted</th>
</tr>
</thead>
<tbody>
<tr>
<td>Yes (15,509)</td>
<td>79.1</td>
<td>73.1</td>
</tr>
<tr>
<td>No (4,089)</td>
<td>20.9</td>
<td>26.9</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th><strong>Number of children</strong></th>
<th>Unweighted</th>
<th>Weighted</th>
</tr>
</thead>
<tbody>
<tr>
<td>No children (5,148)</td>
<td>26.3</td>
<td>27.5</td>
</tr>
<tr>
<td>One child (2,376)</td>
<td>12.1</td>
<td>12.4</td>
</tr>
<tr>
<td>Two to three children (10,011)</td>
<td>51.2</td>
<td>49.7</td>
</tr>
<tr>
<td>Four or more children (2,036)</td>
<td>10.4</td>
<td>10.4</td>
</tr>
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<table>
<thead>
<tr>
<th><strong>Education</strong></th>
<th>Unweighted</th>
<th>Weighted</th>
</tr>
</thead>
<tbody>
<tr>
<td>No qualifications (562)</td>
<td>2.9</td>
<td>3.1</td>
</tr>
<tr>
<td>Partial/full secondary school (5,647)</td>
<td>28.8</td>
<td>27.8</td>
</tr>
<tr>
<td>Non-undergraduate tertiary qualifications (3,861)</td>
<td>19.7</td>
<td>19.5</td>
</tr>
<tr>
<td>Undergraduate qualification (5,193)</td>
<td>26.5</td>
<td>27.7</td>
</tr>
<tr>
<td>Postgraduate qualification (4,335)</td>
<td>22.1</td>
<td>21.8</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th><strong>Ethnicity</strong></th>
<th>Unweighted</th>
<th>Weighted</th>
</tr>
</thead>
<tbody>
<tr>
<td>European/Pākehā (17,757)</td>
<td>90.6</td>
<td>79.1</td>
</tr>
<tr>
<td>Māori (2,155)</td>
<td>11.0</td>
<td>11.5</td>
</tr>
<tr>
<td>Pacific Nations descent (495)</td>
<td>2.5</td>
<td>6.4</td>
</tr>
<tr>
<td>Asian descent (902)</td>
<td>4.6</td>
<td>14.0</td>
</tr>
</tbody>
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<table>
<thead>
<tr>
<th><strong>Area-level socioeconomic deprivation</strong></th>
<th>Unweighted</th>
<th>Weighted</th>
</tr>
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<tbody>
<tr>
<td>1–5 (Low deprivation; 12,359)</td>
<td>63.1</td>
<td>61.0</td>
</tr>
<tr>
<td>6–10 (High deprivation; 7,239)</td>
<td>36.9</td>
<td>39.0</td>
</tr>
</tbody>
</table>

1Children ever given birth to, fathered or adopted.
2Participants may identify with more than one ethnicity.

Analysis procedure
Regression analyses were conducted in **Mplus**. Descriptive statistics and bivariate correlations of all measures were examined in SPSS. Post-stratification sample weighting was applied to all analyses to adjust for sample biases in gender, ethnicity and region. Due to the large sample size, statistical significance was defined as **p<.005**.

Results
Overall support for breastfeeding in public
Overall, most participants strongly supported public breastfeeding, as indicated by low agreement with the statement “Women should avoid breastfeeding in public” ($M=2.02$, $SD=1.52$). Based on weighted sample estimates, 75.3% of partici-
pants supported public breastfeeding (rating their agreement to the statement as 1 or 2), whereas only 5.2% of the sample were opposed to public breastfeeding (ratings of 6 or 7). A further 19.5% of participants expressed neutral views towards public breastfeeding (ratings of 3 to 5). Post-stratification sample weighted means, standard deviations and bivariate correlations across all measures are summarised in Table 2.

**Sociodemographic correlates**

A multiple linear regression was conducted to examine sociodemographic correlates of opposition to public breastfeeding. All variables were entered into the model simultaneously. Ethnicity was dummy-coded, with European/Pākehā assigned as the reference category. Table 3 displays the results of these analyses. To these ends, men, relative to women, ($B=0.19$), being older ($B=0.02$) and identifying with a religion ($B=0.27$) correlated positively with opposition to breastfeeding in public. In contrast, being a parent ($B=-0.28$), having more children ($B=-0.06$), being in a relationship ($B=-0.14$) and education ($B=-0.06$) correlated negatively with opposition to women breastfeeding in public.

As for ethnic group differences, Māori (vs European/Pākehā) expressed less opposition towards public breastfeeding ($B=-0.13$), whereas Asian peoples were more opposed to breastfeeding in public ($B=0.48$). Conversely, there was no difference in attitudes towards public breastfeeding between participants of Pacific Nations descent and European/Pākehā ($p=0.41$). Likewise, employment status, population density, birthplace and area-level socioeconomic deprivation were unassociated with attitudes towards public breastfeeding ($p$s>.005).

**Table 2: Descriptive statistics and bivariate correlations across sociodemographic factors and attitudes towards public breastfeeding.**

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<tbody>
<tr>
<td>---</td>
<td>.11**</td>
<td>.04**</td>
<td>-.04**</td>
<td>-.03**</td>
<td>-.05**</td>
<td>.01</td>
<td>.04**</td>
<td>.07**</td>
<td>.07**</td>
<td>.06**</td>
<td>-.02</td>
<td>.01</td>
<td>-.02</td>
<td>.03</td>
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<tr>
<td>---</td>
<td>.11**</td>
<td>.04**</td>
<td>-.04**</td>
<td>-.03**</td>
<td>-.05**</td>
<td>.01</td>
<td>.04**</td>
<td>.07**</td>
<td>.07**</td>
<td>.06**</td>
<td>-.02</td>
<td>.01</td>
<td>-.02</td>
<td>.03</td>
</tr>
<tr>
<td>M</td>
<td>.46</td>
<td>.49</td>
<td>.32</td>
<td>.24</td>
<td>.35</td>
<td>.49</td>
<td>.45</td>
<td>.154</td>
<td>.43</td>
<td>.41</td>
<td>.27</td>
<td>.72</td>
<td>.46</td>
<td>.44</td>
</tr>
<tr>
<td>SD</td>
<td>.50</td>
<td>.49</td>
<td>.32</td>
<td>.24</td>
<td>.35</td>
<td>.49</td>
<td>.45</td>
<td>.154</td>
<td>.43</td>
<td>.41</td>
<td>.27</td>
<td>.72</td>
<td>.46</td>
<td>.44</td>
</tr>
</tbody>
</table>

* $p<.001$, ** $p<.005$  
Weighted correlation coefficients, means, and standard deviations.  
*0 = women, 1 = men.  
*Dummy-coded; 0 = no Māori identification, 1 = Māori identification.  
*Dummy-coded; 0 = no Pacific identification, 1 = Pacific identification.  
*Dummy-coded; 0 = no Asian identification, 1 = Asian identification.  
*0 = yes, 1 = no.  
*11-unit ordinal rank of qualifications, 0 = no qualifications, 1–3 = partial/full secondary school, 4–6 = non-graduate tertiary qualifications, 7 = undergraduate degree, 8–10 = post-graduate qualifications.  
*0 = rural, 1 = urban.  
*Area-level socioeconomic deprivation; 0 = least deprived, 10 = most deprived.  
*1 = Strongly Disagree, 7 = Strongly Agree.
Discussion

The present study examined support for breastfeeding in public in New Zealand. Most participants (75.3%) agreed that women should be able to breastfeed in public, whereas 5.2% were unsupportive of breastfeeding in public (19.5% of our sample were neutral on the issue). These results are optimistic compared to past research in New Zealand which suggested that mothers perceived public breastfeeding as being embarrassing and unaccepted by society.16–18 Additionally, these results are comparable to levels of support in similar Western nations. Russell and Ali found that a majority (78.2–80.9%) of people from Ottawa, Canada thought that breastfeeding in a restaurant and/or a shopping mall was acceptable.13 Similarly, a study from Western Australia found that around 70% of people thought that it was acceptable to breastfeed across a range of public areas (eg, restaurants and public transport).14 Nevertheless, we found higher levels of support for breastfeeding in public than comparable surveys from the US, where just over half of participants were supportive of public breastfeeding.10,11

We found that men expressed greater opposition to public breastfeeding relative to women. This finding is notable, as past research has revealed inconsistent gender differences in support for public breastfeeding. For example, in Western Australia and Canada, men expressed greater support for public breastfeeding than did women.13,14 Conversely, Mulready-Ward and Hackett found no gender differences in support for

Table 3: Multiple linear regression of sociodemographic correlates of opposition to breastfeeding in public.

<table>
<thead>
<tr>
<th></th>
<th>$B$</th>
<th>95% CI</th>
<th>$SE$</th>
<th>$\beta$</th>
<th>$z$</th>
</tr>
</thead>
<tbody>
<tr>
<td>Intercept</td>
<td>1.52</td>
<td>[1.35, 1.69]</td>
<td>0.09</td>
<td>1.01</td>
<td>17.48**</td>
</tr>
<tr>
<td>Gender*</td>
<td>0.19</td>
<td>[0.13, 0.24]</td>
<td>0.03</td>
<td>.06</td>
<td>6.94**</td>
</tr>
<tr>
<td>Age</td>
<td>0.02</td>
<td>[0.02, 0.02]</td>
<td>0.001</td>
<td>.21</td>
<td>19.48**</td>
</tr>
<tr>
<td>Māori$^b$</td>
<td>-0.13</td>
<td>[-0.21, -0.05]</td>
<td>0.04</td>
<td>-.03</td>
<td>-3.08'</td>
</tr>
<tr>
<td>Pacific nations$^c$</td>
<td>-0.08</td>
<td>[-0.26, 0.11]</td>
<td>0.09</td>
<td>-.01</td>
<td>-0.82</td>
</tr>
<tr>
<td>Asian$^d$</td>
<td>0.48</td>
<td>[0.35, 0.61]</td>
<td>0.07</td>
<td>.11</td>
<td>7.11**</td>
</tr>
<tr>
<td>Religious affiliation$^e$</td>
<td>0.27</td>
<td>[0.22, 0.32]</td>
<td>0.03</td>
<td>.09</td>
<td>9.93**</td>
</tr>
<tr>
<td>Parental status$^a$</td>
<td>-0.28</td>
<td>[-0.38, -0.19]</td>
<td>0.05</td>
<td>-.08</td>
<td>-5.83*</td>
</tr>
<tr>
<td>Number of children</td>
<td>-0.06</td>
<td>[-0.10, -0.03]</td>
<td>0.02</td>
<td>-.06</td>
<td>-3.93**</td>
</tr>
<tr>
<td>Relationship status$^a$</td>
<td>-0.14</td>
<td>[-0.21, -0.08]</td>
<td>0.04</td>
<td>-.04</td>
<td>-4.12**</td>
</tr>
<tr>
<td>Employment status$^a$</td>
<td>-0.07</td>
<td>[-0.14, -0.01]</td>
<td>0.03</td>
<td>-.02</td>
<td>-2.09</td>
</tr>
<tr>
<td>Education$^f$</td>
<td>-0.06</td>
<td>[-0.07, -0.05]</td>
<td>0.01</td>
<td>-.10</td>
<td>-11.49**</td>
</tr>
<tr>
<td>Urban vs Rural$^g$</td>
<td>0.01</td>
<td>[-0.04, 0.06]</td>
<td>0.03</td>
<td>.003</td>
<td>0.45</td>
</tr>
<tr>
<td>Born in NZ$^c$</td>
<td>-0.07</td>
<td>[-0.15, -0.002]</td>
<td>0.04</td>
<td>-.02</td>
<td>-2.01</td>
</tr>
<tr>
<td>NZ Deprivation$^h$</td>
<td>-0.001</td>
<td>[-0.01, 0.01]</td>
<td>0.01</td>
<td>-.001</td>
<td>-0.13</td>
</tr>
</tbody>
</table>

* $p<.005$, ** $p<.001$. 
R$^2$ = .078, $p<.001$. 
Weighted regression coefficients. 
Opposition to breastfeeding in public; 1 = Strongly Disagree, 7 Strongly Agree. 
$^a$ 0 = women, 1 = men. 
$^b$ Dummy-coded; 0 = no Māori identification, 1 = Māori identification. 
$^c$ Dummy-coded; 0 = no Pacific identification, 1 = Pacific identification. 
$^d$ Dummy-coded; 0 = no Asian identification, 1 = Asian identification. 
$^e$ 0 = yes, 1 = no. 
$^f$ 11-unit ordinal rank of New Zealand qualifications; 0 = no qualifications, 1–3 = partial/full secondary school, 4–6 = non-undergraduate tertiary qualifications, 7 = undergraduate degree, 8–10 = post-graduate qualifications. 
$^g$ 0 = rural, 1 = urban. 
$^h$ Area-level socioeconomic deprivation; 1 = least deprived, 10 = most deprived.
breastfeeding in public in New York City,\textsuperscript{11} whereas another US-based study found that women were more comfortable than men with the idea of breastfeeding in public.\textsuperscript{22}

Age was also correlated positively with opposition to public breastfeeding, which is consistent with past work which revealed that people over 44 years old in Western Australia and people older than 65 in New York City were more unaccepting of public breastfeeding relative to younger age groups.\textsuperscript{11,14} Yet our results conflict with research from Tennessee which showed that older age groups (25–65+) were more comfortable with women breastfeeding in public than the youngest age group (18–24).\textsuperscript{12}

Explaining the apparent cross-cultural discrepancies in public support for breastfeeding would be an important direction for future research.

Although past research has largely overlooked the association between religious affiliation and public breastfeeding support, our results reveal that participants who identified with a religion were more opposed to public breastfeeding than were their non-religious counterparts. These results appear consistent with past research showing that maternal religious affiliation and engagement negatively correlates with breastfeeding initiation and duration.\textsuperscript{23} The circumstances under which breastfeeding occur may, however, influence perceptions of its acceptability. Specifically, breastfeeding within the home is generally more accepted than breastfeeding in public.\textsuperscript{9} As such, although religious affiliation may be related to support for breastfeeding in general, the perceived acceptability may be qualified by where the breastfeeding occurs. Given these findings, primary and community care providers should consider families’ religious beliefs when providing consultation about breastfeeding and breastfeeding locations.

Perhaps unsurprisingly, we also found that both being a parent and the number of children participants had correlated positively with support for public breastfeeding. This is consistent with research showing that having more children at home was linked to greater perceived acceptability of public breastfeeding.\textsuperscript{13} However, Mulready-Ward and Hackett did not find a relationship between having children younger than 12 years old in the home and comfort with being around a woman breastfeeding in public.\textsuperscript{11}

Additionally, being in a relationship was associated with greater support for public breastfeeding. This finding is consistent with a study from Tennessee, which showed that participants in a relationship were more likely to feel comfortable with women breastfeeding in public.\textsuperscript{12} We also found that there was no difference in support for public breastfeeding between those who were employed or those who were unemployed (including those who are retired). These results might contradict past research which found that retired people (relative to full-time employed individuals) and unemployed people were more opposed to public breastfeeding.\textsuperscript{13,24}

Our results also demonstrated that education correlated positively with support for breastfeeding in public. This finding is consistent with international research, which found that higher education was linked to greater support for public breastfeeding in Western Australia,\textsuperscript{14} the US\textsuperscript{11,12} and Canada.\textsuperscript{13}

Past research has also found that birthplace affects attitudes towards breastfeeding in public. Russell and Ali found that participants born in Canada were less supportive of public breastfeeding, although those whose native language was neither English nor French were particularly opposed to breastfeeding in public.\textsuperscript{13} Conversely, another study found that participants born outside of Australia were less accepting of public breastfeeding.\textsuperscript{14} Yet a survey from New York City found that birthplace had no effect on support for breastfeeding in public.\textsuperscript{11} Our results further complicate these findings by showing that being born in New Zealand (relative to being born outside of New Zealand) was unrelated to attitudes towards public breastfeeding. Collectively, these findings demonstrate the need to attend to cross-cultural norms to understand the influence birthplace has on support for public breastfeeding, as there appears to be cross-country variability in attitudes towards public breastfeeding. Although our results suggest that birthplace is unrelated to public breastfeeding attitudes, breastfeeding support tailored for mothers born outside of New Zealand remains important.
to address. Primary care providers could help by increasing awareness of societal support of public breastfeeding in New Zealand.

Finally, our results suggested that, relative to European/Pākehā, Māori were more supportive, whereas Asian peoples were less supportive, of public breastfeeding. Our findings echo results from New York City which revealed that Asian peoples were less supportive of public breastfeeding than their Caucasian counterparts. Likewise, our finding that Māori participants were more supportive of public breastfeeding complements a previous qualitative study by Glover and colleagues on Māori mothers and their whānau, which suggested that they perceived society as unaccepting of public breastfeeding. Considering the high levels of support found in the current study, the perceived norms around public breastfeeding may have changed in the decade since the Glover study.

Implications

Many women who breastfeed perceive society to be unaccepting of breastfeeding in public—a perception that may lead them to avoid public breastfeeding or stop breastfeeding altogether. However, fostering community support for breastfeeding may counteract these restrictive trends. Indeed, co-worker support of breastfeeding in workplaces predicts greater self-efficacy to continue breastfeeding. As such, the high levels of support observed in the current study may help to counteract the fear and embarrassment some women may feel when deciding whether or not to breastfeed in public. Consistent with this perspective, community acceptance of breastfeeding in general correlates positively with the perceived ease of breastfeeding.

Thus, our findings could benefit clinical practice and public health initiatives aimed at fostering breastfeeding. Given that past research shows that Māori communities may perceive society as being unaccepting of public breastfeeding, primary and community care providers could utilise our findings to assuage fears of public judgement associated with public breastfeeding. In turn, these targeted campaigns could increase breastfeeding rates in communities with traditionally lower rates of breastfeeding (eg, Māori and deprived communities). Furthermore, as our findings suggest that Asian peoples express the least amount of support for public breastfeeding, public health campaigns could specifically target this population when trying to bolster support for breastfeeding in public.

Limitations

Although our study makes a number of important contributions to the literature, it is worth noting some of its limitations. Due to the omnibus format of the NZAVS survey, there was only enough space for a single-item measure of support for breastfeeding in public. As such, we were unable to assess the perceived acceptability of breastfeeding across a range of locations. Yet research demonstrates that there may be key differences in support depending on location. For example, breastfeeding is seen as more acceptable in shopping malls than in restaurants. Similarly, the perceived importance of discretion or the effort on the part of the mother to “cover-up” when breastfeeding was not assessed. This is an oft-noted factor when people consider the acceptability of breastfeeding in public. As such, future work in New Zealand should examine situational variability in support for breastfeeding in public. Such research could help to inform public health initiatives aimed at reducing the stigma associated with public breastfeeding, as well as to increase the number of facilities available for women who breastfeed in public spaces.

Finally, we were unable to assess people’s (dis)comfort with being around someone breastfeeding in public. To these ends, past research reveals differences in support depending on the perceived acceptability and comfortability with breastfeeding in public. Specifically, people report being more comfortable in the presence of a breastfeeding mother than they rate the acceptability of breastfeeding in public. These critical contradictions suggest that attitudes towards public breastfeeding are multifaceted and that a multitude of factors (including one’s affective responses to, and the location of, breastfeeding) should be considered when assessing support for breastfeeding in public.
Concluding comments

The present study provided the first comprehensive overview of support for public breastfeeding in New Zealand. To these ends, our findings provide an optimistic outlook on societal attitudes, as most participants indicated that women should be allowed to breastfeed in public. Despite high levels of support, our results also indicated that key sociodemographic variables predicted support for, and opposition to, breastfeeding in public. Specifically, being a woman, identifying as Māori, being a parent, being in a relationship, being employed and having higher education were associated with greater support for public breastfeeding, whereas being older, identifying with an Asian ethnicity and identifying with a religion were associated with more opposition to public breastfeeding. Collectively, these results provide a snapshot of populations in New Zealand who express more or less support for breastfeeding in public. Future public health initiatives should consider these results when developing and implementing targeted campaigns aimed at increasing support for breastfeeding in public.

Competing interests:
Nil.

Acknowledgements:
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URL:

REFERENCES:
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New Zealand’s experience of the 1918–19 influenza pandemic: a systematic review after 100 years

Jennifer A Summers, Michael G Baker, Nick Wilson

ABSTRACT

BACKGROUND: The 1918–19 influenza pandemic has been New Zealand’s most severe disaster event (around 9,000 deaths). We aimed to review the literature related to this pandemic in New Zealand and among New Zealanders overseas, to identify any remaining research gaps (given ongoing risks of future influenza pandemics and from new pathogens, eg, synthetic bioweapons).

METHODS: Systematic literature searches and comparisons with international findings for this pandemic to facilitate identification of research gaps.

RESULTS: A total of 61 relevant publications were identified. The epidemiological patterns reported were largely consistent with the international literature for this pandemic. These features included the W-shaped age-distribution for mortality, and the much higher mortality rates for indigenous people (ie, seven-fold for Māori vs New Zealand European). But some novel risk factors were identified (eg, large chest size as a risk factor for death in military personnel), and there was an extremely high mortality troop ship outbreak (probably related to crowding). In contrast to some international work, there was an apparent lack of a socio-economic gradient in mortality rates in two studies using modern analytical methods. New Zealand work has clearly shown how the pandemic spread via the rail network and internal shipping routes and the rarity of successful measures to prevent spread in contrast to some other jurisdictions. It has also found a marked lack of memorials to the pandemic (in contrast to war memorials). Nevertheless, some research gaps remain, including on the apparent marked reduction in birth rates in 1918–1919 and the reasons for no socio-economic gradient despite other New Zealand evidence for occupational class variation in lifespan at this time.

CONCLUSIONS: This is a relatively well-studied disaster event but there remain important research questions relating to this pandemic in New Zealand. Filling these gaps may contribute to improved planning for managing future pandemics.
Methods

We aimed to systematically identify all published literature related to the 1918–19 influenza pandemic either in New Zealand or among New Zealanders outside of New Zealand. The searches were conducted using the Cochrane Library, Google Scholar, Embase, PubMed, various University thesis repositories and grey literature for all studies published from 1914 to 2018 (to take into account evidence of pre-pandemic waves3,4). Search strategies used in databases and other archival/thesis catalogues are detailed in the Appendix (Appendix 1, 2 and 3). We also examined the bibliographies of all the identified literature for additional publications.

Results

The experience of the pandemic in New Zealand and among New Zealanders has been evaluated both during and since the pandemic occurred in 1918, from a variety of primary sources from the period (for example military records or personal accounts) and secondary historical/epidemiological publications. A total of 61 publications were identified which relate to the 1918–19 influenza pandemic in New Zealand or among New Zealanders as a primary focus and provide understating of the pandemic (with further details on each publication in Appendix 4). In total, we identified five books, two case-series, nine discussion/commentary pieces, 15 epidemiological studies, 24 reviews and six theses. These publications use a variety of methods and spanned different academic fields, such as social history, epidemiology, public health, health services and biostatistics.

The earliest identified publication was a case series in 1918 of New Zealand military personnel in the New Zealand Expeditionary Force (NZEF), which described post-mortem details of cases. In contrast, the most recent publication was published in 2018 and it reviewed mortality patterns within the Pacific region during the pandemic.6

There has been steady increase in the number of publications on the pandemic and New Zealand, with the vast majority of studies being published in the last decade. This pattern may reflect the increasing availability of records from 1918 such as the digitisation of military files for online archives and online newspaper records (Figure 1). But there has also been a growth in all medical research, including for “seasonal influenza” in the New Zealand context (eg, 63 Medline-indexed publications as of late 2018).

Figure 1: Cumulative frequency of publications related to New Zealand’s experience of the 1918–19 influenza pandemic.
The main impact of the 1918–19 influenza pandemic occurred in New Zealand during November 1918 for both civilian and military populations situated within New Zealand (Figure 2). While for New Zealand military personnel situated either at sea (on board the troopship *HMNZT Tahiti*) or in the Northern Hemisphere, the experience of the pandemic was rather different. Official reports of the troopship outbreak are held at Archives New Zealand and detail the course of the outbreak and the outcomes for the military personnel. These reports have been used in several epidemiological studies of the outbreak as they provide detailed description of the individuals on board.4,10,11 Those on board the *Tahiti* experienced one of the worst ship outbreaks worldwide during the pandemic, and the personnel in the Northern Hemisphere experienced two mortality waves, in November 1918 and in late February 1919 (much like other populations in Europe) (Figure 3).

**Figure 2:** Pandemic-related mortality per week among the civilian populations in the North and South Islands of New Zealand and NZEF personnel who died in New Zealand.4,12

![Graph showing pandemic-related mortality per week among the civilian populations in the North and South Islands of New Zealand and NZEF personnel who died in New Zealand.](image)

Note: some of the civilian data include discharged NZEF personnel.

**Figure 3:** Pandemic-related mortality among New Zealand military personnel by location during the 1918–19 in the defined pandemic periods.4

![Graph showing pandemic-related mortality among New Zealand military personnel by location during the 1918–19 in the defined pandemic periods.](image)
Table 1: Identified literature on the 1918–19 influenza pandemic in New Zealand categorised by major research domains.

<table>
<thead>
<tr>
<th>Research domain</th>
<th>Comment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Epidemiology (including risk factors for mortality)</td>
<td>Various epidemiological methods have been employed to examine the pandemic. For example, one study gave estimates of reproduction numbers (range 1.3 to 3.1) and a seven-day lag period from diagnosis until pandemic death indicating secondary pneumonia as cause of death while another study estimated a generation time (days) of between 2–4 days. Other studies have used case-control and cohort designs with individual level patient data to explore risk factors for mortality among various populations and environments. There was a ‘w’-shaped distribution pattern for mortality rates, with young adults (in particular men) dying at higher than expected rates, which was consistent with international findings. The New Zealand work has clearly shown how the pandemic spread via the rail network and internal shipping routes and rarity of successful measures to prevent spread (ie, there were only some successful moves in a small town and a few institutions).</td>
</tr>
<tr>
<td>Impact on Māori</td>
<td>An estimate of Māori mortality during the pandemic is at 2,160 (registered deaths), but as Rice has argued, the true figure is likely to have been much higher. Both civilian (7.3x higher) and military death rates (2.3x higher) were disproportionately higher among Māori populations compared with European ones. Several authors have theorised that these differences were possibly due to factors such as: less protective exposure to a milder first wave (associated with rural residence), higher rates of chronic disease (eg, tuberculosis) and poorer access to healthcare/social support during the pandemic.</td>
</tr>
<tr>
<td>Social history (also with some overlap with the epidemiology)</td>
<td>In the social history domain, two recent theses concentrate on the impact and role of children during the pandemic, of which they both describe how older children were called upon to provide relief in both their own homes and in the wider community. The impact of housing on mortality outcomes has also been discussed, with particular evaluation of housing/crowding in Wellington, Christchurch, Auckland, and also the poor housing among the Māori population. Local outbreaks have also been evaluated such as in the town of Nightcaps (which experienced one of the highest European mortality rates during the pandemic). Nelson, Temuka and the Coromandel Peninsula. The probable impact of crowds during Armistice celebrations was also described in terms of their impact in spreading the pandemic both within cities and to more rural areas and comparative work with New Zealand compared to Australia, Japan and Iceland.</td>
</tr>
<tr>
<td>Specific impacts on military personnel</td>
<td>The relationship of the pandemic to WW1 and the military environment have been relatively well explored for the New Zealand military beginning in 1918 with Eyre and Lowe’s case series and epidemiological analysis of the pandemic among military personnel. A majority of the publications have been of epidemiological studies using modern-day statistical techniques conducted in the last 10 years. The medical response to the pandemic within the military has been described, including a vaccination study (using a very broad-spectrum vaccine) and outbreaks within military camps. The detrimental effect of crowding was explored, which has implications for today’s pandemic planning. Higher mortality rates were found among Māori/Pacific Island military personnel, ‘fresh recruits’, those with larger chest sizes, those aged around 25 to 29 years, those with earlier WW1 deployment and those with prior hospital admissions for respiratory conditions. The experience on troopships has also been evaluated, in particular the very severe outbreak on the HMNZT Tahiti.</td>
</tr>
</tbody>
</table>
New Zealand’s role in pandemic spread in the South Pacific

The role of the New Zealand ship the SS Talune in spreading the pandemic throughout the Pacific Islands has been described.57 This included Western Samoa (modern day ‘Samoa’) which resulted in approximately 25% of the adult population dying in the pandemic.6,58,59 The Talune also spread the pandemic to Fiji and Tonga.57

Disaster sociology/psychology

There has been little research on the sociological and psychological aspects of the pandemic. One study commented on the possible effect of WW1 involvement (psychological and physical stress) on immune system response during the pandemic among New Zealand military personnel.23 Another study identified the relative lack of memorials to the pandemic (especially compared with war memorials) and the implications of this absence for public education concerning future pandemic disasters.60

Health Systems

Several authors have examined the impact of the pandemic on the health system in New Zealand, the use of temporary hospitals during the pandemic, the limitations of the New Zealand Health Department’s response and the impact of the Minister of Public Health in 1918, Mr GW Russell, having multiple ministerial portfolios during war time.9,12,22,24,44,61–64 One author describes the pandemic as a worst case, with substantial health staff absent due to the war effort and remaining New Zealand-based staff succumbing to the pandemic themselves.63,65 Authors describe the legislative changes and impact upon the New Zealand health system following the 1919 Royal Commission Report on the pandemic9 such as the 1920 Health Act.9,44,66

Pathology and virology

Two studies describe the pathology and post-mortem results among New Zealanders (either in Dunedin, New Zealand67 or among military personnel located in the UK).28 The thesis by Champtaloup (at the University of Edinburgh) is a relatively new finding from this review and as it includes detailed drawing plates and photomicrographs of the NZEF pandemic cases of which examples are included in this review (Figures 4 and 5). Given that there are no known existing specimens of the pandemic in New Zealand and indeed few samples known worldwide, these plates of post-mortem findings are a particularly notable resource demonstrating the care taken in trying to understand the nature of the 1918–19 pandemic. An earlier study by Eyre and Lowe does not specify the post-mortem details as being from New Zealanders.5 In contrast to some other countries, there are no known existing pathological specimens relating to the pandemic held in New Zealand.

Other areas (including multiple domains)

There are several sources that cover multiple domains such as epidemiology and social history, such as Rice’s three books,12,33,34 and Bryder’s two publications which span a whole city.44,45 Known resources (not listed in Appendix 4) used in some of the above references in this table include WW1 Casualty and Roll-of-Honour,68,69 military reports1–3 and other New Zealand Government reports.39,72–74

<table>
<thead>
<tr>
<th>Research domain</th>
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</tr>
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<tbody>
<tr>
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</tr>
</tbody>
</table>
Figure 4: Plate 1 (Coloured) Lung Case 680: ‘haemorrhagic oedema type’.

Figure 5: Plate 2 (Coloured) Trachea & Bronchi: ‘along the trachea and bronchi appear swollen lymphatic glands dotted with haemorrhages’.
Discussion

Main findings and interpretation

A century has passed since the 1918–19 influenza pandemic reached the shores of New Zealand and among the New Zealand military personnel serving in the Northern Hemisphere as part of WW1. The influenza pandemic occurred during the final stages of WW1 and no doubt spread further during Armistice celebrations resulting in the pandemic having the grim record as New Zealand’s worst human disaster. The works of Rice and one of the current author’s thesis, has identified 8,831 deaths as a result of the 1918–19 pandemic among New Zealanders. Rice’s more recent book suggests a more accurate total may be over 9,000 deaths if undocumented deaths among the Māori population are taken into account. The majority of these deaths occurred in New Zealand during a six-week period in November and December 2018. However, the first substantial numbers of New Zealanders dying during the pandemic occurred eight weeks earlier in September 1918 on board the troopship HMNZT 107 Tahiti on route to the UK carrying New Zealand military reinforcements.

Studies in the last decade have increasingly focused on the pandemic’s impact on military populations; due to access to rich and detailed medical records for large volumes of individuals. As roughly 40% of eligible male New Zealanders served in the NZEF during WW1, estimates of morbidity and mortality can be generalised to the wider population, such as the identification of increased pandemic mortality risks associated with being a young adult, being Māori or Pacific, or having had pre-pandemic respiratory admissions to hospital.

Patterns consistent with the international data

In general, the epidemiology of the pandemic in New Zealand was similar to that of other countries. A notable similarity was the w-shaped age distribution for mortality rates (albeit with some more in-depth analysis that may relate to the role of the 1890s influenza pandemic in this pattern). The higher mortality rate for Māori and Pacific soldiers in the New Zealand military (see Table 1), is also consistent with the higher burden for indigenous peoples from this pandemic. Similarly, risk factors for death identified in a New Zealand case-control study were often the same as those reported elsewhere (eg, co-existing chronic disease or being a recent military recruit). The spread of the pandemic via railway and shipping networks was also part of the international pattern—though rarely has it been shown in such detail as in the work of Rice for New Zealand. Our informal observations are that memorials to this pandemic are rare internationally—which is also the case for New Zealand.

Unusual patterns with the New Zealand data

There were unusual patterns for pandemic impacts and response in New Zealand which contrast with other populations around the world, such as the following:

- Some novel risk factors for pandemic-related mortality were identified in a New Zealand case-control study; with males with larger chest size having an increased mortality risk (possibly related to the increased lung capacity of soldiers which might ‘increase the chance of a cytokine storm’).

- There was an apparent lack of a socio-economic gradient in mortality rates for the New Zealand European population with no apparent variation by different housing districts in Auckland. This finding (albeit with only the two military studies using modern analytic methods), is in contrast to some of the international literature. For example, a socio-economic gradient has been described for Norway, Sweden and Chicago, US. The finding of no gradient in New Zealand is also in contrast with evidence for lifespan differences by male occupational class in New Zealand at this time.

- The similar male vs female mortality rates among Māori were also somewhat unusual—in contrast to the relatively higher mortality in males vs females in the New Zealand European population. One of the possible reasons is Māori being exposed to greater crowding (more mixing of
men and women), but possibly also the greater similarities in chronic respiratory disease burdens by sex in Māori (eg, due to greater similarities in smoking prevalence). However, this area requires further research.

- New Zealand was like most settings where there were only a few (or no) successful acts of border control or ‘protective sequestration’ (ie, there were only some successful moves in a small town and a few institutions. In contrast, some other jurisdictions successfully used maritime quarantine, road closures and measures such as school closures and public gathering bans.

Strengths and limitations of this review

A strength of this review is that it is the first systematic review of this pandemic in the New Zealand context in the journal literature. It has also encompassed a wide variety of academic fields. However, this review also has its limitations. For example it has focused on secondary sources mostly as they provide summary accounts/data. Furthermore, there was little review of first-hand accounts, such as newspaper articles, letters or diaries (other than military sources, eg, Summers et al). It is also conceivable that there are journal articles or theses that were published in the early part of last century which have not yet been included in the online medical databases which we searched.

Possible implications for future research

A first step is probably to consider further research around those unusual aspects of the pandemic in New Zealand that differed from the international literature as detailed above (ie, the large chest size as a risk factor for death, the apparent lack of a socio-economic gradient in mortality rates, and the similarity of male and female Māori mortality rates). For example, the use of modern biostatistical methods for additional analysis of other data relevant to socio-economic gradients, eg, by using the suburb data in Rice’s Christchurch research or the Auckland-based work by Bryder.

But other apparent gaps are as follows:

- There is scope for better quantifying the extent of undocumented Māori deaths with studies that compare registered deaths with names on memorials in urupā (Māori burial sites). This type of research by a Māori researcher would also have the benefit of further building Māori research capacity.

- Modern spatial analysis could be applied to data on the spread of the pandemic (as detailed in maps on the rail and shipping networks compiled by Rice). This analysis could then estimate the speed of pandemic spread (eg, in kilometres per day and week).

- The relationship of the natality shocks of 1918 and 1919 in New Zealand to the pandemic have not been thoroughly analysed, although Pool provides a brief assessment of decreased fertility among Māori women. It is known that influenza infection is associated with fetal loss and stillbirth (as documented in Dunedin, New Zealand, during the pandemic) and it is likely to have been a factor in the sudden decline in New Zealand’s annual birth rate in 1918 by 9% and in 1919 by 17% (relative to 1917) [Data calculated from the 1924 Yearbook and based on changes in rates]. This issue only appears to have been studied in a few international settings, eg, US and Scandinavia, Taiwan, and Sri Lanka. This topic has some contemporary relevance given suboptimal vaccination of pregnant woman against influenza.

Given the importance of learning from pandemics, there is perhaps a case for the Ministry of Health to allocate funds to the Health Research Council to specifically support research to address these knowledge gaps. Once this work was done, an updated review of the potential lessons relevant to modern pandemic planning could be conducted, eg, in terms of external border control, internal border control, health system preparedness and provision
of voluntary sector nursing care to neighbours, etc.

Several studies evaluated the effect of the pandemic on the New Zealand health system both during and post-pandemic. There appears to be consensus that the health system was under immense strain, with limited resources/staffing and a crippled administration that was unable to provide clear leadership in the face of an overwhelming influenza pandemic. If anything can be learned from this experience it is that pre-pandemic planning is essential for New Zealand in order to face inevitable future pandemics. Such planning needs to include scenarios of similar intensity to the 1918 influenza pandemic and potentially more extreme events.

A greatly improved Health Act in 1920 was one of the responses to the 1918 influenza pandemic, which aimed to address the limitations of the previous legislation in terms of administrative responsibilities/duties by restructuring the health department and allowing special measures during periods of infectious disease outbreaks.44,66,82 Perhaps New Zealand could use the centennial of the 1918 pandemic as an opportunity to reflect on our readiness for the kinds of pandemics that we may face over the next 100 years and plan accordingly. One example is the need for rapid border closure to prevent entry of particularly severe pandemic diseases. Such measures could be highly cost-effective.83,84

Conclusions
In the centenary year of the 1918–19 influenza pandemic, now is the time for New Zealand to reflect on its impact on New Zealand in terms of its mortality, its long-term effects on the physical and psychological health of survivors, and indeed its role in shaping New Zealand’s health system and society. Most importantly for today’s New Zealanders, the pandemic provides insight into the nature of influenza pandemics and how societies respond to such events. Despite the large body of work to date, there remain important knowledge gaps relating to this pandemic in New Zealand. Filling these gaps may contribute to improved planning for managing future pandemics.

Appendix 1: Literature search criteria

<table>
<thead>
<tr>
<th>Inclusion criteria</th>
<th>Disease</th>
<th>Influenza (specifically the 1918-19 Influenza Pandemic)</th>
</tr>
</thead>
</table>
| Population        | • Cases located in New Zealand during the pandemic period.  
|                   | • New Zealanders who contracted influenza during the pandemic period.  
|                   | • Cases of pandemic influenza as a result of the viral strain in New Zealand.  
|                   | Population groups of interest (based on inclusion criteria):  
|                   | • Māori/Pacific Island peoples  
|                   | • New Zealand Expeditionary Forces |
| Search terms      | See Appendix 2. |
| Language restrictions | Foreign language papers if translation available. |
| Search dates      | 1914 to present day. |

<table>
<thead>
<tr>
<th>Exclusion criteria</th>
<th>Study design</th>
<th>Book reviews</th>
</tr>
</thead>
<tbody>
<tr>
<td>Search dates</td>
<td>Pre-World War One (ie, before 1914)</td>
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## Appendix 2: Database search strategies

### Cochrane Libraries
Search date: 22nd August 2018

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<tr>
<td>#2</td>
<td>Zealand</td>
<td>12,877</td>
</tr>
<tr>
<td>#3</td>
<td>1918:ti,ab,kw</td>
<td>108</td>
</tr>
<tr>
<td>#4</td>
<td>1918</td>
<td>334</td>
</tr>
<tr>
<td>#5</td>
<td>#1 and #2 and #4</td>
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</tr>
<tr>
<td>#6</td>
<td>#3 and #5</td>
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<tr>
<td>#7</td>
<td>pandemic</td>
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<tr>
<td>#8</td>
<td>#7 and #2</td>
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<td>#9 and #2</td>
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<td>#11</td>
<td>#10 and #4</td>
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<td>#12</td>
<td>#10 and spanish</td>
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<tr>
<td>#13</td>
<td>#11 or #12</td>
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### Google Scholar
Search date: 22nd August 2018

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<td>In article: 1918 zealand</td>
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<td>#8</td>
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</table>

### Embase
Search date: 22nd August 2018

- Embase 1974 to 2018 Week 34
- Embase Classic 1947 to 1973
- Global Health 1973 to 2018 Week 32
- HMIC Health Management Information Consortium 1979 to May 2018
- Ovid MEDLINE® Epub Ahead of Print, In-Process & Other Non_indexed Citations, Ovid MEDLINE® Daily, Ovid MedLINE and Versions®
ID | Search | Hits
---|--------|----
#1 | (1918 influenza pandemic and Zealand).af. | 18
#2 | (pandemic and Zealand).af. | 7,660
#3 | (pandemic and influenza and Zealand).af. | 586
#4 | (“1918" and Zealand and influenza).af. | 89
#5 | (“1918" and Zealand and pandemic).af. | 71
#6 | (“1918" and Zealand).af. | 193
#7 | 2 or 3 | 760
#8 | 1 or 4 or 5 or 6 | 193
#9 | (Spanish and Zealand and influenza).af. | 31

**PubMed**
Search date: 22nd August 2018

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<th>ID</th>
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</tr>
<tr>
<td>#2</td>
<td>(Spanish) AND influenza</td>
<td>1,756</td>
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<tr>
<td>#3</td>
<td>((1918) AND influenza) AND zealand</td>
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</tr>
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<td>#4</td>
<td>((Spanish) AND influenza) AND zealand</td>
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<tr>
<td>#5</td>
<td>#1 OR #2 OR #3 OR #4</td>
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<tr>
<td>#6</td>
<td>(1918) OR spanish</td>
<td>411,227</td>
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<tr>
<td>#7</td>
<td>#6 AND influenza</td>
<td>2,767</td>
</tr>
<tr>
<td>#8</td>
<td>#7 AND zealand</td>
<td>40</td>
</tr>
</tbody>
</table>

**Grey literature**
Search date: 22nd August 2018
Grey literature – searched key words such as “1918”, “influenza”, Spanish”, and “Zealand”.

- www.greylit.org/ | 0
- www.opengrey.eu/ | 0
- http://oaister.worldcat.org/ | 20
- ntrl.ntis.gov/NTRL/ | 465
- www.archives.govt.nz – searched “1918 influenza” or “Spanish influenza” | 85 27
- Wellcome Trust 86 http://wellcomelibrary.org/ | 1
- University Library catalogues:
  - New Zealand:
    - http://catalogue.library.auckland.ac.nz
    - http://ourarchive.otago.ac.nz
    - http://mro.massey.ac.nz
  - United Kingdom/International:
    - http://ethos.bl.uk/
    - http://www.era.lib.ed.ac.uk/
    - http://www.openthesis.org/
- Other sources | 3
Appendix 3: PRISMA 2009 Flow Diagram

Appendix 4: Additional detail on the publications (secondary sources) included in this systematic review

Available through external link:
http://www.nzma.org.nz/__data/assets/pdf_file/0003/86655/Appendix-4-FINAL.pdf
Competing interests:
Nil.

Acknowledgements:
We take this opportunity to thank Professor Geoffrey Rice for his long history of scholarship regarding this pandemic in New Zealand. We also thank the various New Zealand Government agencies which have made archival material available to ourselves and other researchers (particularly the digitalisation of military files).

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URL:

REFERENCES:


41. Lange KJ. “Child’s Play?”: The Role of Children in the 1918 Influenza Epidemic in New Zealand. 2015, Dickinson College.


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Zealand Official Yearbook. 1924, Wellington: Eyre and Spottiswoode.


86. Welcome Library. The library at Wellcome Collection. 2017 [cited 2017 November].

Sudden death in patients with serious mental illness

Erik Monasterio, Andrew McKean, Vimu Sinhalage Christopher Frampton, Roger Mulder

ABSTRACT

AIM: Sudden death is used to define a death under suspicious circumstances, where there is no clear indication of existing medical illness (natural cause) that accounts for the death or clear indication for the cause of death. This includes all deaths from suicide, unintentional poisoning, drowning, falls and violence. Sudden death contributes to the increased mortality in people with serious mental illness (premature mortality) but is far less frequently studied and understood. This study analyses data of all sudden deaths of patients who had been under the care of the Canterbury District Health Board’s Specialist Mental Health Service, New Zealand’s second-largest population region. The study identifies key sociodemographic, diagnostic, legal and causative factors in the study population. This study aims to identify targeted interventions to mitigate premature mortality in this population.

METHOD: Data was obtained from the clinical files and the coroner’s findings for all sudden death patients with established contact with Specialist Mental Health Services in the Canterbury region of New Zealand, between 2005 and 2009.

RESULTS: A total of 313 patients were identified. The median age at the time of death was 42 years (IQ Range 32.5–53 years). Of these, 65% (n=203) were male. Seventy-six percent (n=239) were of European descent and 9% Māori (n=29); 68% (n=280) were under care at the time of their death and 15% (n=32) were under the Mental Health Act. The sudden death rate was 0.36% for those under voluntary care and 0.7% for those under compulsory care. The most common primary diagnoses were alcohol or other drug abuse (29%); depression (25%); psychotic disorders (18%); BPAD (9%) and personality disorder (5%). The most common cause of death was suicide (51.8%) followed by motor vehicle crashes and falls, (23.3%) medical causes (17.6%) and homicide (1.3%). Of those that died by suicide, 75% were male. Hanging was the most common method (48%) followed by carbon monoxide poisoning (9.3%); medication overdose (5.8%) and falls from a height (3.5%).

CONCLUSIONS: The most common cause of sudden death was suicide, which was overwhelmingly the leading cause of sudden death in patients discharged or lost to follow up. The most potent predisposing factor appeared to be drug and alcohol problems. Mental health services should therefore advocate for comprehensive and evidence-based alcohol and drug policies, including access and availability to treatment programmes.

ARTICLE
drowning, falls and violence. The Coroner has a statutory responsibility to investigate all such deaths.

Sudden death contributes to but does not entirely account for the increased mortality in people with SMI. However, sudden death is far less frequently studied and understood than premature mortality in SMI. A matching survey linking deaths registered to the State Coroner of Victoria and a database of all patients who had received care from public sector mental health services in Victoria in 1995 found that sudden deaths were five times higher in people with histories of psychiatric contact. Those who had prior contact with mental health services were on average 11 years younger at the time of death than those without a record of prior psychiatric contact and who did not suffer from organic disorders. The sudden deaths in those with prior contact with mental health services were most commonly due to natural causes, suicides and accidents. A more recent study of patients receiving inpatient and community care from a large psychiatric hospital in New York, between 1984 and 2009, focused solely on sudden death from natural causes and found that the incidence of these deaths had increased greatly in the first decade of the 21st Century. The cause of death was only determined in 48% of cases, and was mostly due to acute coronary syndromes.

The Mental Health Service of the Canterbury District Health Board (MHSCDHB) provides secondary and tertiary psychiatric care, in a variety of community and inpatient facilities, to a population of approximately 540,000. This population ranks second in size out of the 16 regions in New Zealand and accounts for 12.7% of the national population.

As part of its routine data collection on adverse incidents, the MHSCDHB collects information in relation to all sudden or unexpected deaths (sudden death register) that occur for all current and previous patients under the care of these services. All such deaths are subject to specialist review and involve an inquest from the Coroner’s Office to determine the cause of death.

The purpose of this study is to examine clinical information and the Coroner’s findings for deceased patients from the sudden death register. Linking information across these two different data sets provides more detailed information on sudden death in SMI than can be obtained from examining the data sets individually. It adds to the very limited pool of research into the characteristics of sudden deaths in patients with SMI, which can assist to identify targeted interventions to mitigate premature mortality from sudden death in this population.

Consistent with national and international findings on premature and sudden death, the authors hypothesised that natural causes, particularly from cardiovascular disease, would be the most common cause for sudden death in patients with SMI. As there have been no publications in this area in New Zealand, the study will assist in determining to what extent sudden death characteristics are the same as those for premature mortality.

Methods

Sources of data

This study analysed data from the MHSCDHB sudden death register between 1 January 2005 and 31 December 2009. As described above, the Coroner Services of New Zealand defines sudden death to be a death under suspicious circumstances, where there is no clear indication of existing medical illness (natural cause) that accounts for the death or clear indication for the cause of death. As the Coroner has a statutory responsibility to investigate all such deaths, cases identified by name, age and gender are referred to the Canterbury Regional Mental Health Service to determine whether contact with specialist mental health services has occurred. This information is cross-referenced to the electronic database for all patients’ contacts with the MHSCDHB. All those identified to have had past or present contact with MHSCDHB are included in the sudden death register, and without exception were included in the study. As the Coroner has a statutory responsibility to investigate these deaths, all sudden deaths are likely to have been identified by this process.

In addition, the Coronerial and clinical files for each patient in the sudden death register, identified by their National Health Index (NHI) number, were manually reviewed by the researchers. All the data
was anonymised. Ethics approval by the Upper South Regional Ethics Committee was obtained (ref: URA/09/07/EXP).

Variables

**Sociodemographic variables**

Age, sex and ethnicity data. Ethnicity was grouped into European (including New Zealand European), New Zealand Māori, Pacific, Asian and other.

**Cause of death**

Suicide, medical, accidental, homicide and ‘unable to be determined’ (as determined by coronial verdict).

**Length of time elapsed since last contact with MHSCDHB and time of death**

Reported in months for all subjects.

**Mental Health Act Status**

Voluntary and involuntary status and whether under the care of the MHSCDHB at the time of death. Involuntary status included those subject to assessment or a community or an inpatient treatment order of the Mental Health (Assessment and treatment) Act 1992 [MHA].

**Diagnosis**

Extracted from the clinical files and/or Coroner’s reports, which utilise ICD 9 or ICD10 coding.

**Specialist mental healthcare provider**

If receiving care from MHSCDHB at the time of death, whether inpatient or outpatient, and which service provided care.

**Identified stressor before death**

Relationship stress, other family stress, criminal charges, death of a loved one, drug/alcohol withdrawal, financial stress, incarceration or recent prison release, major physical illness diagnosis, occupational problem and other (determined from coronial files and/or MHSCDHB clinical files).

### Results

The data sources for determining the appropriate denominator (to calculate the sudden death rate) are limited, therefore the mean number of 11,054 patients/year under the care of the MHSCDHB between 2005 and 2009 has been adopted for this. This includes a number of people under care over more

<table>
<thead>
<tr>
<th>Table 1: Sociodemographic, diagnosis and mental health service variables.</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Median age (interquartile range) (years)</strong></td>
</tr>
<tr>
<td>42 (32.5–53)</td>
</tr>
<tr>
<td><strong>Gender</strong></td>
</tr>
<tr>
<td>Male 203 (64.9%)</td>
</tr>
<tr>
<td>Female 110 (35.1%)</td>
</tr>
<tr>
<td><strong>Ethnic origin</strong></td>
</tr>
<tr>
<td>NZ and other European 239 (76.4 %)</td>
</tr>
<tr>
<td>Māori 29 (9.3%)</td>
</tr>
<tr>
<td>Pacific 6 (1.9%)</td>
</tr>
<tr>
<td>Asian 6 (1.9%)</td>
</tr>
<tr>
<td>Not recorded 33 (10.5%)</td>
</tr>
<tr>
<td><strong>Primary diagnosis</strong></td>
</tr>
<tr>
<td>Alcohol/substance abuse 82 (26.2%)</td>
</tr>
<tr>
<td>Depressive disorder 72 (23%)</td>
</tr>
<tr>
<td>Psychotic disorder 51 (16.3%)</td>
</tr>
<tr>
<td>Bipolar affective disorder 26 (8.3%)</td>
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<tr>
<td>Personality disorder 14 (4.5%)</td>
</tr>
<tr>
<td>Adjustment disorder 13 (4.2%)</td>
</tr>
<tr>
<td>Anxiety disorder 7 (2.2%)</td>
</tr>
<tr>
<td>Dementia 5 (1.6%)</td>
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<tr>
<td>Other* 13 (4.2%)</td>
</tr>
<tr>
<td>Not recorded on data sets 30 (9.5%)</td>
</tr>
<tr>
<td><strong>Primary Mental Health Service</strong></td>
</tr>
<tr>
<td>Community Drug and Alcohol Service 65 (30%)</td>
</tr>
<tr>
<td>Psychiatric Emergency Service 38 (18%)</td>
</tr>
<tr>
<td>Adult Inpatient Service 38 (18%)</td>
</tr>
<tr>
<td>Adult Community Service 35 (16%)</td>
</tr>
<tr>
<td>Adult Specialist Services 15 (7%)</td>
</tr>
<tr>
<td>Psychiatric Services for the Elderly 11 (5%)</td>
</tr>
<tr>
<td>Forensic Service 7 (3%)</td>
</tr>
<tr>
<td>Child, Youth Family Service 5 (2%)</td>
</tr>
<tr>
<td>Not under care of services 99 (31.6%)</td>
</tr>
</tbody>
</table>

*Intellectual Disability, PTSD, Eating Disorder, Conduct Disorder, Paraphilia, Alcoholic Hepatitis, ADHD, Parkinson’s.
than a single year period. Of those, 52% were male; 81% were New Zealand and other European, 12% were Māori, 1.6% Pacific and 1.7% were not coded; 935 patients/year received treatment under the MHA (8.5%).

A total of 313 patients were identified on the sudden death register during the five-year study period. These patient characteristics are discussed in Table 1.

Demographic variables
The mean age at time of sudden death was 43.6 years and the median was 42 years old (interquartile range 32.5–53 years old); 203 (65%) were male and 110 (35%) were female; 239 (76%) were New Zealand and other European, 29 (9%) Māori, 6 (2%) were Pacific, 6 (2%) were Asian and 33 (11%) had no ethnicity recorded.

Mental Health Act Status
Two hundred and fourteen (68%) subjects were receiving care from MHSCDHB at the time of their sudden death, 32 (15%) of those under the MHA and 99 (46%) were also under the care of two specialist services. Fifty (16%) were inpatients at the time of their deaths. Ninety-nine (32%) were not under specialist care. Therefore the sudden death rate from 2005–2009 was 0.36% for those under voluntary care and 0.7% for those under the MHA.

Length of care
The total length of time that MHSCDHB provided (in- and out-patient) care was available for 284 (90.7%) patients. The mean time in care was 1,346 days (median = 565 days, interquartile range = 107–2,105 days).

The mean number of ‘cases’ was 7.8 (s.d. = 10.5), (median = 5, interquartile range = 2 to 10). Each ‘case’ is a separate admission and discharge hospital or community care episode. There were 24 patients (8%) who had total length of stay (LOS) of 0 or 1, which means that they had no specialist follow-up following an initial assessment.

Contact with MHS
The time between the last contact with mental health services and sudden death was available for 258 (82%) patients. The mean was 13.3 months but the median was one month (interquartile range 0 to 12 months). Sixty-five percent had had contact with MHSCDHB within three months of their death.

Cause of death
The cause of sudden death most commonly recorded was suicide (163 patients, 52%) or 0.3% of patients under specialist care. This was followed by accidents, predominantly from motor vehicle crashes and falls (73 patients, 23.3%), medical causes from predominantly cardiovascular and respiratory diagnoses (55 patients, 17.6%) and homicide (4 patients, 1.3%). The cause of death was not able to be determined in 18 patients (5.8%) and in most of these the Coroner was unable to determine whether the death was accidental or from suicide.

Suicide was by far the most common cause of sudden death (87%) for patients discharged from MHSCDHB. A total of 112 (69%) males and 51 (31%) females died by suicide; 26 (16%) were under inpatient
care and 86 (53%) of those were not under specialist care, at the time of death.

Hanging was the most common method of suicide (77 patients, 48%): 58 males (75%) and 19 females (25%) died by hanging. Other means of suicide included carbon monoxide poisoning (29 patients, 9.3%), medication overdose (including both over the counter and prescribed medications) (18 patients, 5.8%) and falls from a height (11 patients, 3.5%). Less common methods included poisoning (5 patients, 3%); cutting throat and/or wrists (4 patients, 2.4%); suffocation (4 patients, 2.5%); recreational drug overdose (2 patients, 1.2%); electrocution (2 patients, 1.2%); drowning (2 patients, 1.2%); car crashes (2 patients, 1.2%); trains (2 patients, 1.2%); gunshot wounds (1 patient, 0.6%); and not clearly determined from multiple causes (3 patients, 0.2%) (Table 2).

The Coroner’s Office has only provided suicide statistics since 2007/08, and from this point to 2009/10 there were a total of 176 deaths for the Canterbury DHB Region. During the period 2007–2009 there were 100 suicide deaths identified in the sudden death register, indicating that a very high proportion of these (approximately 57%) of all suicides in the Canterbury Region had had contact with specialist mental health services.

Diagnoses

The primary diagnosis was available for 283 (90.4%) of the 313 patients. Alcohol and other drug abuse was the primary diagnosis for 82 (29%), depression for 72 (25%), psychotic disorder for 51 (18%); bipolar affective disorder for 26 (9%), personality disorder for 14 (5%), adjustment disorder for 13 (4.6%), anxiety disorder for 7 (2.5%), dementia for 5 (1.8%), intellectual disability for 4 (1.4%), PTSD for 3 (1%), eating disorder for 2 (0.7%) and conduct disorder, paraphilia, ADHD and Parkinson’s disease for one patient each respectively.

For those who died by suicide the predominant primary diagnoses were: depression for 55 (34%), alcohol and other drug abuse for 32 (20%), psychotic disorder for 19 (12%); bipolar affective disorder for 11 (7%), adjustment disorder for 11 (7%) personality disorder for 8 (5%), anxiety for 6 (3.5%), PTSD for 3 (2%), no diagnosis for 14 (9%) (Table 2).

<table>
<thead>
<tr>
<th>Table 2: Causes of death and diagnoses in suicides.</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Cause of suicide death</strong></td>
</tr>
<tr>
<td>-----------------------------</td>
</tr>
<tr>
<td>Hanging</td>
</tr>
<tr>
<td>Carbon monoxide poisoning</td>
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<tr>
<td>Medication overdose</td>
</tr>
<tr>
<td>Fall</td>
</tr>
<tr>
<td>Other poisoning</td>
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<tr>
<td>Other*</td>
</tr>
<tr>
<td>Not recorded</td>
</tr>
<tr>
<td><strong>Diagnosis for suicides</strong></td>
</tr>
<tr>
<td>-----------------------------</td>
</tr>
<tr>
<td>Depressive disorder</td>
</tr>
<tr>
<td>Alcohol/substance abuse</td>
</tr>
<tr>
<td>Psychotic disorder</td>
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<tr>
<td>No diagnosis</td>
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<tr>
<td>Adjustment disorder</td>
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<tr>
<td>Bipolar affective disorder</td>
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<tr>
<td>Personality disorder</td>
</tr>
<tr>
<td>Anxiety disorder</td>
</tr>
<tr>
<td>Other**</td>
</tr>
</tbody>
</table>

*Cut throat/wrist (2.5%), suffocation (2.5%), electrocution (1%), recreational drug overdose (1%), impact by train (1%), drowning (1%), car crash (1%), gunshot (0.5). **PTSD, Paraphilia, ADHD, Parkinson’s Disease, Dementia.

Identified stress before death

Eighty-four (52%) of patients who had sudden death by suicide had an apparent stressful event recorded at the last contact with the service provider. The most common were intimate relationship problems for 33 (39%), incarceration or recent prison release for 18 (21%), financial stress for 9 (11%), death of a loved one for 8 (10%) and work problems for 6 (7%) and ‘other stressors’ for 20 (15%) of patients.

Specialist mental health care provider

The primary mental health teams for patients who were under care were Alcohol and Drug Services for 65 (30%) of patients, Psychiatric Emergency Service for 38 (18%),
Discussion

Main findings

This study examines the sudden death characteristics of patients who previously received care from New Zealand's second largest specialist mental health provider from 2005–2009. Consistent with our clinical experience of treating patients with SMI, over 90% of cases identified in the study received multiple episodes of community and hospital care over several years. The findings are therefore not unduly influenced by patients who had only a single contact with MHSCDHB. The Coronial Service of New Zealand does not have statistical data on the prevalence and causes of sudden death in the general population, to compare with the study population (Information Adviser, Specialist Courts, Ministry of Justice, 2017, personal communication). However, it is clear that the rate of sudden death in those with prior contact with MHSCDHB is significantly elevated, particularly from suicide and within three months of the last clinical contact.

The study findings do not support the authors' hypothesis that natural causes were the most common cause for sudden deaths in patients with SMI with a history of contact with MHSCDHB. These findings are also not consistent with that of a similar study in Victoria, Australia in 1995, which found that sudden deaths in those with prior contact with mental health services were most commonly due to natural causes, then suicides and accidents. It is difficult to account for this. It is possible that there may be a difference in the Coronial process between Victoria and New Zealand, and that the threshold to investigate sudden deaths in patients with known histories of medical problems (which is likely to account for sudden death) is higher in New Zealand. This contention is supported by the finding of a previous study which found that natural causes accounted for the majority of premature deaths among patients with SMI in New Zealand.2

The findings of this study with regard to suicide are probably the most relevant and generalisable. There is a very high likelihood that all suicides have been captured by the study, as there is a statutory requirement that all suspected suicides are reported to the Coroner's Office and there is a robust process to identify these with the MHSCDHB sudden death register. Suicide was the leading cause of sudden death for patients in the study and these suicides, by patients who had received specialist mental health care, appear to account for close to 60% of all suicides in the Canterbury region between 2007 and 2009. This contrasts with findings from England and Wales, which found that only 24% of all suicides had had contact with specialist mental health services in the preceding 12 months.11 The reasons for this difference is likely to include the fact that coroner's inquests into unexpected deaths in England and Wales usually provide “short form” verdicts for the cause of death, and “open” verdicts are recorded when the cause of death is likely to be suicide but the legal criteria (beyond reasonable doubt) has not been met. This is likely to lead to an under reporting of suicide deaths.12 Also the UK study was limited to mental health contacts in the preceding 12 months, whereas the current study examines any past contact with mental health services. It may also suggest that access to specialist mental health care is more readily available in New Zealand than in the UK.

Consistent with most national and international findings, hanging was and remains by far the most common method of suicide across inpatient and community settings.11,13–15 In accord with these findings and international recommendations for suicide prevention, removal and monitoring for potential ligature points, such as non-collapsible curtain rails, door handles and towel rails has been widely introduced.
in New Zealand psychiatric hospitals and prisons to minimise the risk of suicides in these settings.\textsuperscript{16} Stressful life events at the last contact with MHSCDHB were identified in approximately half of all suicides. This finding is consistent with the extant literature, which identifies recent stressful life events and precipitating factors (significantly higher than for control populations) with suicide, principally interpersonal and legal problems.\textsuperscript{17,18} An important finding was that 20\% of suicides occurred in relation to periods of incarceration, mostly after prison release, which sadly mirrors similar findings from the recent Suicide Mortality Review Committee of New Zealand, which found that 27\% of suicides (between 2007–11) had previous contact with the Department of Corrections.\textsuperscript{15} This is not surprising given the high prevalence of untreated SMI in New Zealand’s prisons.\textsuperscript{19} The introduction of the New Zealand Prison Screening Tool in 2012 has significantly improved identification of SMI and treatment among prisoners.\textsuperscript{20} However, there has been no research conducted to determine whether this has led to improved access to mental health care, drug and alcohol treatment or reduction in suicides after prison release, and is a matter for urgent additional research.

Accidents were the second most common cause of sudden death, predominantly from motor vehicle crashes and falls. This is likely to be influenced by the high prevalence of drug and alcohol misuse, as a primary diagnosis and from co-morbid use, which is well established in patient with SMI and premature mortality.\textsuperscript{2,3} Cardiovascular disease was the most common natural cause for sudden death. This is not surprising and is consistent with studies of premature death for patients with SMI and the general population.\textsuperscript{2,5,21,22} High rates of alcohol and substance misuse, including tobacco, higher prevalence of unhealthy lifestyles, and decreased access to primary and specialist medical services is consistently reported for patients with SMI and contributes to cardiovascular disease.\textsuperscript{1–5} Side effects from psychotropic medications, particularly the metabolic complications associated with antipsychotic treatment have also been reported in this population.\textsuperscript{1–5}

**Clinical implications**

‘Real world’ clinical information on the characteristics of sudden death for patients who have received previous care from a large specialist regional mental health provider can lead to targeted interventions to mitigate premature mortality in this population.

The overall suicide rate in this study is likely to be higher than 52\%, as in 6\% of cases the Coroner could not confidently differentiate accidental deaths from suicides. Suicide was overwhelmingly the leading cause of sudden death in patients discharged or lost to specialist service follow-up, indicating that more emphasis needs to be given to preventing loss of contact with services, maintaining treatment adherence and facilitating re-engagement with specialist services. As previous studies have shown that those with a past history of medically serious suicide attempts have a higher long-term risk of suicide mortality, follow-up in this group should be maintained for at least 12 months after a suicide attempt.\textsuperscript{23}

Our review of the clinical files found that suicide risk assessments were not routinely or systematically documented. More emphasis on an organisational approach to structured risk assessments was part of a range of recommendations from Coroners to specialist mental health services in relation to suicide prevention in New Zealand.\textsuperscript{24} While this seems reasonable at face value there is now consistent evidence that risk categorisation is of limited value and may be harmful.\textsuperscript{25} A systematic meta-analysis of controlled studies of suicide within a year of discharge from psychiatric hospitals found that risk categorisation was of no value in attempts to decrease the numbers of patients who will commit suicide after discharge. Sixty percent (60\%) of patients who commit suicide were likely to be categorised as low risk and only about 3\% of patients categorised as being at high risk could be expected to commit suicide in the year after discharge.\textsuperscript{26} No factor or combination of factors was strongly associated with suicide.

In this context the challenge for clinicians is for risk management to be a part, rather than the focus of patient care. At an individual clinical level we argue for a
shift in focus towards engagement with the individual patient's specific problems and circumstances rather than placing them in arbitrary risk categories. Emphasis on stress management, service accessibility, provider education, use of digital media to engage and maintain contact with patients is important.

At a broader service level a number of service provider intervention strategies have been shown to lead to reductions in suicide rates. These include the provision of 24-hour crisis care, clear policies for management of dual diagnosis patients, and multidisciplinary review and information sharing with families after suicide attempts.27

It is noteworthy that one third of those who suicided were not in contact with mental health services at the time of their death. As a significant number of these patients were in contact with primary medical care, more emphasis on collaborative (shared) care between specialist mental health service and primary care, may provide an additional pathway for assessment, treatment and suicide prevention. Collaborative care is also likely to improve access to primary medical services, and lead to improved assessment and treatment of medical problems, in particular cardiovascular and respiratory diseases and cancers, which are under-treated and contribute not only to sudden death but also premature death and disability in patient with SMI.2–5

Multidisciplinary reviews of all suicide deaths should occur to identify gaps in local service provision and to identify additional opportunities for interventions.

Study strengths and limitation

There are several strengths to the study. It is the first study of sudden death for patients who have received care from specialist mental health services in New Zealand. It involves a relatively large sample and Coroner's reports were available in all cases. This study however, also has several potential biases and limitations. Although Coroner's investigations are thorough and take into consideration multiple sources of information, including from family members to improve accuracy of findings, the authors also relied on standard clinical information, which was at times incomplete and of inconsistent quality across different services. The accuracy of the diagnoses were not able to be validated and co-morbid conditions were so inconsistently documented that we were not able to utilise this data. It is well established in the literature and clinical practice that patients with SMI generally present with multiple conditions and therefore the limitation of sudden death data to only primary diagnosis has to be interpreted with caution. It is possible that sudden deaths from natural causes were under reported and investigated as these may have been mistakenly attributed to an already extant medical condition.

In addition there is no reliable data or process to estimate sudden death from natural causes in the general population and therefore there is no comparator population to give context to the findings. Patients with mental illness who have not been treated by the specialist mental health services, and have been treated solely by primary health services or in the private sector have not been captured by the data. It is therefore possible that the data has focused on a more financially and socially disadvantaged group of patients who could not afford to pay for care. Sudden death findings may therefore be more influenced by social disadvantage (such as unemployment and financial hardship) rather than mental illness. As the proportion of patients treated solely in the private sector in Canterbury is very small it is unlikely that this has significantly biased the findings.

Finally the data reflects sudden death causes from 1 January 2005 to 31 December 2009, and the patterns may have changed since then.

Conclusion

Psychiatric patients have high rates of sudden or unexpected death. The most common cause is suicide. The most potent predisposing factor appears to be alcohol and drug problems. This was the most prevalent primary diagnosis and is likely to be a comorbid diagnosis in many other diagnostic categories. In addition it is well established that alcohol and drug use problems are associated with accidents, imprisonment and cardiovascular disease.28 Therefore mental health services should
in particular be advocating for comprehensive and evidence based alcohol and drug policies (such as increasing price and taxes on alcohol, restrictions on advertising, promotion and reducing availability of alcohol), including increased access and availability of drug and alcohol treatment programmes to help reduce sudden deaths among our patients.

Competing interests:
Andrew McKean has received speaker fees from Novartis.

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Reducing the impact of the impending myopia epidemic in New Zealand

Alex Petty, Graham Wilson

ABSTRACT
Myopia is an eye condition that is increasing around the world, reaching epidemic levels in many countries. It is associated with a higher risk of other ocular diseases including myopic maculopathy and retinal detachment. Historically in New Zealand myopia has existed at a low level, however the environmental changes that have increased myopia internationally will affect New Zealanders too. Higher levels of myopia will have a profound social, economic and health burden on our country. Fortunately, proven interventions to limit the onset and degree of myopia already exist. To limit the level of myopia in New Zealand we propose the creation of a multidisciplinary myopia action group (NZMAG). The NZMAG will serve to support local research, raise awareness of the condition and its associated pathologies, facilitate access to myopia control treatments, improve identification of at-risk children via screening programs, and serve as the guiding body for myopia-related information. With prompt action now, the myopia epidemic seen in other countries can be reduced in New Zealand.

The visual condition myopia, colloquially known as short-sightedness or near-sightedness, is the most common ocular problem in the world. Currently an estimated 1.4 billion people in the world are myopic (23% of the world) with 163 million having high myopia of over five diopters (2.7%). In many East Asian countries, where urbanisation and environmental risks for myopia are high, the condition has reached near ubiquitous levels, affecting up to 90% of young adults (Figure 1). Approximately one-third of adult Americans and Europeans are myopic. Closer to home, 30% of Sydney's 17-year-olds are myopic, double the prevalence of myopia reported in Australia more than a decade earlier. The only available New Zealand data is a prevalence of myopia of 4.2% in Dunedin 11-year-olds in 1984. Alarming, an increasing prevalence of myopia is now established in a number of populations.

The blurred sight of a myope can be corrected with glasses, contact lens or surgical vision correction, albeit with cost and inconvenience to the individual. However, the increase in axial length of the eye which occurs in myopia and which is not treatable, is associated with a host of sight-threatening complications (Table 1). In a European population, uncorrectable visual impairment from these sequelae is seen in 4% of 75-year-olds with myopia and 39% with high myopia. In Japan, degenerative myopia is the third most common cause of vision impairment, ahead of age-related macular degeneration (which is estimated to affect 10.3% of New Zealanders aged 45–85) and cataract. Even mild levels of myopia carry a higher lifelong risk of blinding disease. To put this in context, myopia, even in the so-called 'physiological range', represents a major risk factor for ocular disease that is comparable with the risks associated with hypertension for cardiovascular disease and smoking for stroke.

There is a significant economic burden associated with myopia, with global loss of gross domestic product from uncorrected refractive error being estimated at $202 billion annually. Health economic analyses in the US and Australia have consistently shown that the economic burden of refractive correction far exceeds those from other eye disease.
In New Zealand, myopia's risks are largely underappreciated by the medical, educational and public health community. Even many health professionals are not familiar with myopia, its sequelae or its prevention. Currently the focus is on managing uncorrected refractive error, rather than addressing and limiting the more important axial length elongation. Attempting to limit myopia presents a significant opportunity to reduce an individual's lifetime risk of eye disease and visual impairment, in a similar way to reducing eye pressure in glaucoma. So how can we do this?

**Intervention options to reduce high myopia**

Once a child has become myopic, correction of their refractive error with single vision spectacles or contact lenses will improve their vision but will do nothing to slow myopic progression. Neither will deliberate uncorrection or under-correction of myopia slow a child's progression.\(^{23-26}\) However, there are several interventions currently available to eye care professionals in New Zealand that are proven to significantly slow the progression of myopia and limit axial length growth.

Firstly there are optical treatments, of which orthokeratology and multifocal soft contact lenses are the most effective. Orthokeratology involves the wear of a specially designed rigid contact lens during sleep to remodel the surface curvature of the cornea, leading to unaided correction of refractive error during the day. Meta-analysis of the myopia control effect afforded by orthokeratology shows a 45–50% mean efficacy.\(^ {27,28}\) In contrast, multifocal soft contact lenses are worn to correct vision during the day.

**Table 1:** Odds ratio of the increased risk of ocular pathology associated with higher levels of myopia. Adapted from Flitcroft.\(^ {15}\)

<table>
<thead>
<tr>
<th>Level of myopia (diopters)</th>
<th>Glaucoma</th>
<th>Cataract</th>
<th>Retinal detachment</th>
<th>Myopic maculopathy</th>
</tr>
</thead>
<tbody>
<tr>
<td>-1.00 to -3.00</td>
<td>2.3</td>
<td>2.1</td>
<td>3.1</td>
<td>2.2</td>
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<td>-3.00 to -5.00</td>
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<td>-</td>
<td>-</td>
<td>44.2</td>
<td>126.8</td>
</tr>
</tbody>
</table>

**Figure 1:** Estimated prevalence of myopia in 20-year-olds.\(^ {14}\)
include the Misight myopia control daily contact lens, which was developed at the University of Auckland. Multifocal soft lenses show similar slowing of myopia with Misight lenses reducing progression of refractive myopia by 59% and axial growth by 52% over three years compared to controls. Both optical treatments slow myopia by the creation of relative myopic defocus in the peripheral retina, which decreases the stimulus for future eye growth.

Orthokeratology treatment is generally well accepted by families and carries a high level of patient compliance as children see clearly throughout the day and their contact lens wear is supervised in a controlled environment at home. However, orthokeratology is generally only offered by a subset of optometrists with the skill and equipment to fit these specialty lenses accurately and safely and is generally more expensive than other myopia control strategies. Soft contact lenses fitted for myopia control by optometrists do not require additional equipment or training, are well tolerated by children and are of slightly lower annual cost than orthokeratology lenses. There is currently no government funding for contact lenses for myopia control unless the child or family have a valid community services card or high user card, which will cover only a small portion of the costs via the Enable subsidy.

Secondly there are pharmacological treatments. Atropine, an anti-muscarinic agent, has been used as an eye-drop to safely control myopia progression for some time. Recently, lower concentrations of the eye-drop (eg, 0.01%) instilled daily have been shown in randomised control trials to slow myopia progression, without the significant side-effects. The main issue with low-dose atropine in New Zealand is that it is currently not commercially available nor funded. Low-dose atropine needs to be compounded at select pharmacies, increasing the cost and difficulty of access (eg, a month supply is approximately NZD$50 per bottle). If low-dose atropine can become more readily available, it represents the most realistic method for myopia control treatment due to the fact any healthcare professional can offer it.

Lastly, three major environmental factors contribute to childhood myopia: higher levels of education, greater urbanisation and lower levels of outdoor activity. Based on current evidence, the most easily manipulated of these factors is outdoor time. Several studies have shown that school-based interventions aimed at increasing outdoor time reduced the onset and progression of myopia. Encouraging children to increase their outdoor time to approximately two hours per day is likely to have a positive impact in limiting myopia development in a population, as well as being beneficial for reducing other health problems like childhood obesity. This can be done with appropriate sun protection or undertaken earlier or later in the day.

A recent meta-analysis evaluated the methods of slowing myopia by comparing data from all the randomised controlled trials with study duration of over one year and grouped these in a strong, moderate, weak and ineffective strength relative to single vision spectacles or placebo. In terms of axial length control only low-dose atropine, orthokeratology and multifocal soft contact lenses exhibited ‘moderate’ myopia control, with only higher doses of atropine in the ‘strong’ category. This is consistent with the clinical guidelines from international myopia control experts that contact lens options and low-dose atropine on average provide a similar ~50% myopia control effect. Mathematical modelling shows that if myopia progression can be reduced by 50% across a population then the incidence of high-risk myopia above 5 D will be reduced by 97%.

What needs to be done to control myopia in New Zealand?

We have highlighted that myopia is:

• Common and increasing in prevalence worldwide.
• Strongly associated with visual impairment.
• An underappreciated individual burden and public health problem in New Zealand.
• Able to be slowed with myopia control treatments that decrease the eventual degree of myopia and the risk of visual impairment.
• Presently under-managed in that many young myopes receive only single vision refractive correction and not myopia control treatments.
What then are the translational steps that can be taken in the New Zealand setting to minimise the impact of the impending myopic epidemic? We propose the rapid establishment of a New Zealand Myopia Action Group (NZMAG), consisting of ophthalmic, optometric, paediatric, general practice, public health and Ministry of Health and Education representatives. The NZMAG would be a broad-based collaboration because myopia impacts on individuals, schools, communities, DHBs and policy makers.

The Myopia Action Group's immediate priorities would be to:

- Support research to investigate the current prevalence of myopia, and myopia sequelae, in New Zealanders. This will enable us to evaluate our risk of the social and economic burden in context with the rest of the world.
- Increase public and health professional awareness and education of myopia and its risks (eg, promote the first world Myopia Awareness Week in 2019).
- Ensure easy and affordable (publicly funded) access to low-dose atropine drops for the ophthalmic/optometry profession.
- Investigate the validity of establishing DHB myopia clinics (especially in large urban centres) that can provide the range of interventions discussed above.
- Set a minimum standard of care for childhood myopia management.
- Promote outdoor activities at school and home (while still ensuring sensible sun protection).
- Evaluate the pros and cons of an early identification of myopia school programme. Early intervention is more likely to be effective at limiting high myopia. This could be incorporated into the age 11 (year 7) vision check already undertaken by New Zealand Vision Hearing Technicians.
- To keep abreast of worldwide developments in myopia so they can be rapidly translated to the New Zealand scene.

We have written this article as a public-facing document designed to raise awareness of myopia and encourage participation and action within the relevant sectors. Our next step is to reach out to key personnel in these sectors to initiate formation of the NZMAG, and approach public and private groups for financial support to facilitate the necessary plans. China's Ministry of Education has recently announced a significant new scheme to reduce myopia in children, consisting of profound environmental and education changes. This highlights how seriously other countries are taking the threat of myopia; an example that we too should follow to prevent future vision loss in New Zealanders.

Competing interests:
Mr Petty is the director of the private optometry practice Bay Eye Care. He is a board member of the Orthokeratology Society of Oceania, a not-for-profit group supporting optometrists providing orthokeratology and myopia control services. He receives no financial compensation for this role, but does have travel expenses covered for meetings and conferences. He personally is an advocate for myopia management, including orthokeratology and specialty contact lenses. He has been asked recently to be the New Zealand spokesperson for the ‘Child Myopia Report—A Focus on Future Management’, a public health awareness campaign about myopia launched by Coopervision in Australia and New Zealand. He receives no financial compensation for this role.

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REFERENCES:


31. Clark TY, Clark RA. Atropine 0.01% Eyedrops Significantly Reduce the Progression of Childhood Myopia. J Ocul Pharmacol Ther. 2015 Nov; 31(9):541–5.


43. Conrad F, Lecture presented at; Orthokeratology of Oceania Conference 2016, Gold Coast, Australia.

Internationally and within Aotearoa, New Zealand, there has been a substantial increase in the demand for gender affirming healthcare over the past decade. The Youth ‘12 survey estimated that approximately 1.2% of adolescents in Aotearoa, New Zealand identify as transgender. As societal acceptance for trans people grows, it is likely that this level of referrals to health services will continue in the foreseeable future.1,2

Transgender healthcare is rapidly evolving. Table 1 includes some of the terminology healthcare professionals may encounter. The World Professional Association of Transgender Health (WPATH) is the international body responsible for producing standards of care (SOC) for transgender health based on international clinical consensus.3 These are currently being revised and version 8 will inform practice internationally and in Aotearoa, New Zealand.

The Guidelines for Gender Affirming Healthcare for Gender Diverse and Transgender Children, Young People and Adults in Aotearoa, New Zealand4 were developed following the recognition that the previous good practice guide required updating to be in step with current practice and international standards. This article presents a summary of the guideline focusing on puberty blockers, hormonal therapies, access to surgery and other gender affirming healthcare. We hope these guidelines will support the development and provision of services providing gender affirming healthcare around the country and provide helpful guidance to all health professionals involved in the care of trans people.

**Methods**

This guideline was produced in collaboration with trans community members and after consultation with many services and health professionals throughout Aotearoa, New Zealand, who work professionally...
Table 1: Terminology.

<table>
<thead>
<tr>
<th>Term</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Gender identity</strong></td>
<td>A person's concept of their self as male, female, a blend of both or neither. Gender identity can be the same as, or different to, the sex assigned at birth.</td>
</tr>
<tr>
<td><strong>Gender expression</strong></td>
<td>The external presentation of one's gender. This can be expressed through one's name, clothing, behaviour, hairstyle, voice or any other way. A person's gender expression may or may not conform to socially defined behaviours and characteristics typically associated with being either solely masculine or feminine.</td>
</tr>
<tr>
<td><strong>Gender diverse</strong></td>
<td>A term to describe people who do not conform to their society or culture's expectations for males and females. Being transgender can be one way of being gender diverse, but not all gender diverse people identify as being transgender and vice versa. Gender creative or gender expansive are other similar terms that are used when referring to children.</td>
</tr>
<tr>
<td>Assigned male at birth</td>
<td>A person who was thought to be male when born and initially raised as a boy.</td>
</tr>
<tr>
<td>Assigned female at birth</td>
<td>A person who was thought to be female when born and initially raised as a girl.</td>
</tr>
<tr>
<td>Trans or transgender</td>
<td>A term for someone whose gender identity does not align with their sex assigned at birth. This term is often used as an umbrella term, recognising that people may describe themselves in many ways including the use of indigenous terms such as; whakawāhine, tangata ira tāne, tāhine (Māori), mahu (Hawai’i and Tahiti), vakasalewalewa (Fiji), palo-pa (Papua New Guinea), fa’afafine (Samoa), akava’ine (Rarotonga), fakaleiti or leiti (Tonga), fakafifine (Niue).</td>
</tr>
<tr>
<td>Cis or cisgender</td>
<td>A term for someone whose gender identity aligns with their sex assigned at birth.</td>
</tr>
<tr>
<td>Trans boy/male/man</td>
<td>A term to describe someone, assigned female at birth, who identifies as a boy/male/man.</td>
</tr>
<tr>
<td>Trans girl/female/woman</td>
<td>A term to describe someone, assigned male at birth, who identifies as a girl/female/woman.</td>
</tr>
<tr>
<td>Non-binary</td>
<td>A term to describe someone who doesn’t identify exclusively as a man or a woman. There are many different ways that people may be non-binary male or female.</td>
</tr>
<tr>
<td>Gender dysphoria</td>
<td>A term that describes the distress experienced by a person due to the incongruence between their gender identity and their sex assigned at birth.</td>
</tr>
<tr>
<td>Social transition</td>
<td>The process by which a person changes their gender expression in social situations to better align with their gender identity.</td>
</tr>
<tr>
<td>Gender affirming healthcare</td>
<td>Healthcare that is respectful and affirming of a person's unique sense of gender and provides support to identify and facilitate gender healthcare goals. These goals may include supporting exploration of gender expression, support around social transition, hormone and/or surgical interventions. This may also involve providing support to whānau, caregivers or other significant supporting people.</td>
</tr>
<tr>
<td>Pronoun</td>
<td>A word used in place of a noun (or name). Pronouns include: he/him, she/her or they/them. Other gender neutral pronouns in use include ze and hir.</td>
</tr>
</tbody>
</table>
to advance healthcare for trans people. While regional differences in practice exist, the document describes principles and approaches that encompass this diversity. The gender affirming hormonal therapy guidelines in this document draw significantly on those published by the Endocrine Society.5

Principles of gender affirming healthcare

These guidelines are based on the principle of Te Mana Whakahaere; trans people’s autonomy of their own bodies, represented by healthcare provision based on informed consent.6 The informed consent process involves several conversations between the trans person and clinician(s) before starting treatments that have an irreversible component to increase certainty that they are adequately prepared and are making a fully informed decision.7

The use of Sir Mason Durie's Te Whare Tapa Whā as a framework highlights the equal importance of spiritual, family, mental and physical health.8 Health providers have a duty to approach care holistically and in partnership.4 Involving practitioners with expertise in mental health is important for two reasons. Firstly, mental health professionals with the appropriate skills can assist with the informed consent process. Secondly, it is increasingly recognised that discrimination and marginalisation experienced by trans people contributes to high rates of anxiety and depression.9–11 The Youth’12 survey highlighted the mental health disparities experienced by trans young people compared to their cisgender peers with 41% vs 12% experiencing significant depressive symptoms and 20% vs 4% reporting an attempted suicide, respectively, in the past 12 months.1 While there is no New Zealand data for older trans people it is likely that they also experience elevated rates of anxiety and depression as overseas studies have found.2 Because of this, health services that have good links with peer support groups and mental health professionals will be more responsive to the needs of trans people accessing gender affirming healthcare.

Each person presenting to a health service has their own unique clinical presentation and needs. While many trans people will benefit from hormone therapies and surgical interventions, some may require only one or neither of these options.13 Clinicians should not assume that everyone wants to conform to binary (male or female) gender norms and be open to gender affirming healthcare that aligns with non-binary identities.3 When outer gender expression is congruent with an inner sense of self, most trans people will find increased comfort, confidence and improved function in everyday life.13 Avoiding harm is a fundamental ethical consideration for health professionals when considering healthcare. Withholding or delaying gender affirming treatment is not considered a neutral option, as this may cause harm by exacerbating any gender dysphoria or mental health problems. This is no different from harm that can be caused by withholding or delaying other medically necessary care.

Gender affirming healthcare

Gender affirming healthcare may include provision of puberty blockers in children and adolescents, and hormone therapy in older adolescents and adults. The criteria for access to gender affirming hormones are persistent well-documented gender dysphoria, the capacity to make a fully informed decision and to consent for treatment, 16 years of age or older, and significant medical or mental health concerns must be reasonably well controlled. However, it is increasingly recognised that there may be compelling reasons, such as final predicted height, to initiate hormones prior to the age of 16 years for some individuals, although there is as yet little published evidence to support this.5 There is no upper age limit to starting gender affirming hormone therapy. These criteria reflect the WPATH SOC which emphasise that having medical or mental health concerns does not mean gender affirming care cannot be commenced, rather that these need to be managed as part of an informed consent process.3 This readiness can be assessed by a prescribing provider or mental health professional who is experienced and competent at working with trans people.

The informed consent process for readiness for puberty blockers, gender affirming hormones or surgery are detailed in the WPATH SOC.3 The main components include assessing gender dysphoria, discussing social transition, gender expression and physical transition options, and providing a space to consider the implications of these options, with regard to safety, expectations...
and impact on social, emotional, academic/ occupational functioning. For all trans, particularly children and young people, consideration of psychosocial supports, especially family/whānau support is essential. Provide support to families and additional guidance if this support is absent. If this aspect of the assessment is not completed by a medical professional, then communication between the mental health professional and the prescriber/surgeon should occur to ensure a holistic approach to assessment.

Fertility preservation should be discussed prior to starting puberty blockers, gender affirming hormone therapy or gonadectomy. Refer to local fertility services for access to funded cryopreservation of gametes. For those starting feminising hormones, who have reached at least Tanner stage 3, it is recommended that cryopreservation of sperm be considered. For those in early adolescence (Tanner stage 2–3), collection of mature sperm will not usually be possible as mature sperm are produced from mid puberty (Tanner stage 3–4). For those starting masculinising hormones, the option of egg or ovarian tissue storage should be discussed, recognising however, that this involves invasive procedures that are not currently funded where reproductive organs remain. There is no current evidence to suggest that testosterone exposure affects the likelihood of future healthy egg harvesting, and there are many reports of trans men who have ceased testosterone, for the purposes of achieving conception, having successful pregnancy outcomes. However, it is unknown what effect the duration of testosterone therapy has on ovarian function.

Testosterone therapy does not provide a guarantee of adequate contraception and is contraindicated in pregnancy because of potential harm to the fetus from the androgenising effects of treatment. Provide contraceptive advice prior to starting testosterone. Progesterone based Long Acting Reversible Contraception (LARCs) such as (Depo provera®, Jadelle®) or Intrauterine Devices (IUDs) such as Mirena®/ IUCDs are suitable options. Note that IUD insertion may be technically more challenging in those with a degree of cervical atrophy from testosterone therapy.

Puberty suppression using gonadotropin releasing hormone (GnRH) agonists

Puberty blockers can be prescribed from Tanner stage 2 to suppress the development of secondary sex characteristics and may be still beneficial when prescribed later in puberty to prevent ongoing masculinisation/feminisation. Puberty blockers are considered to be fully reversible and allow the adolescent time prior to making a decision on starting hormonal therapies. Monitoring of height is recommended as adult height may potentially be increased if prolonged puberty suppression delays epiphyseal fusing. A bone age may be helpful to assess whether epiphyseal closure has occurred when considering what rate of hormonal induction to use. Concern has been raised regarding the long-term impact of puberty suppression on bone mineral density. It is therefore advisable to encourage young people on puberty blockers to have an adequate calcium intake, provide vitamin D supplementation where needed and encourage weight bearing exercise. Bone density measurements (DEXA) can be considered in those requiring a prolonged period on puberty blockers or have significant additional risks for reduced bone density.

Puberty blockers halt the continuing development of secondary sexual characteristics, such as breast growth or voice deepening, and relieve distress associated with these bodily changes for trans young people. For trans men and others assigned female at birth, the puberty blockers will induce amenorrhoea, reducing distress associated with menstruation. Currently goserelin (Zoladex®) implants have sole subsidy status, although leuprolrelin (Lucrin®) injections are fully funded for children and adolescents who are unable to tolerate administration of goserelin. Table 2 presents clinical recommendations for puberty blockers, and standard dosing schedules. Puberty blockers should be continued until further treatments such as initiating other anti-androgens, accessing orchiectomy or other surgical interventions are decided on.
Gender affirming hormonal therapy

Adults should undergo a medical examination and investigations prior to starting hormones (Table 3). It is important to evaluate and address any medical conditions that could be exacerbated by treatment. As with the use of oestrogen or testosterone in any context, clinicians should consider whether patients are; smokers, have a history of heart failure, cerebrovascular disease, coronary artery disease, atrial fibrillation, or personal risk factors for cardiovascular disease, history or family history of venous thromboembolism (VTE), migraine, history of sleep apnoea or hormone-sensitive cancers (eg, breast, prostate, uterine or testicular). Prescribers are advised to not consider any of the above conditions as absolute contraindications, but to consider and discuss any risks presented as part of the informed consent process.

Feminising hormonal therapy (Table 4)

Oestradiol valerate can be started in conjunction with an anti-androgen agent or added to a GnRH agonist (leuprorelin/goserelin). Goserelin (Zoladex®) is an option where oral anti-androgen agents are not tolerated. Anti-androgens are no longer required following orchiectomy or genital gender reassignment surgery. Start a low dose of oestradiol valerate (Progynova®/Estradot®) and increase the dose every 6–12 months depending on the clinical effect.

Table 2: Clinical recommendations and dosing schedules for puberty blockade.

<table>
<thead>
<tr>
<th>Medical examination and investigations during suppression of puberty</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Examination</strong></td>
</tr>
<tr>
<td><strong>Blood tests</strong></td>
</tr>
<tr>
<td><strong>X-rays</strong></td>
</tr>
<tr>
<td><strong>If major risk factors for osteoporotic # or prolonged time on puberty blockers</strong></td>
</tr>
<tr>
<td><strong>Leuprorelin (Lucrin®)</strong></td>
</tr>
<tr>
<td><strong>Goserelin (Zoladex®)</strong></td>
</tr>
</tbody>
</table>

*Frequency can be reduced to 10 weeks if incomplete LH suppression, puberty progression, or ongoing menses.

Table 3: Medical examination and investigations prior to commencing gender affirming hormonal therapy.

<table>
<thead>
<tr>
<th>Physical examination</th>
<th>Investigations</th>
</tr>
</thead>
<tbody>
<tr>
<td>Blood pressure</td>
<td>Electrolytes if starting spironolactone</td>
</tr>
<tr>
<td>Height</td>
<td>HbA1c if risk factors suggest indicated</td>
</tr>
<tr>
<td>Weight</td>
<td>Lipids if risk factors suggest indicated</td>
</tr>
<tr>
<td>BMI</td>
<td>Prolactin if starting oestrogen</td>
</tr>
<tr>
<td>Tanner stage (in adolescents)</td>
<td>LH</td>
</tr>
<tr>
<td></td>
<td>Testosterone level</td>
</tr>
<tr>
<td></td>
<td>Oestradiol level</td>
</tr>
<tr>
<td></td>
<td>Urine/serum HCG if commencing testosterone</td>
</tr>
</tbody>
</table>
Potential complications for feminising oestrogen therapy include VTE particularly if aged >40 years and within the first two years of treatment. Transdermal oestrogen has lower risks for thromboembolism than oral oestrogen and should be considered particularly if increased risks are present. It is unclear whether oestrogen therapy may adversely affect the lipid profile and blood pressure, but any effect is likely to be modest. Liver dysfunction and gallstones are occasionally seen, although a clinically significant rise in the prolactin level is an uncommon occurrence. There may be alterations in mood and libido.

**Table 4: Feminising gender affirming hormonal therapy dosing regimen and expected effects.**

<table>
<thead>
<tr>
<th>Medication</th>
<th>Dose (adults and older adolescents)</th>
<th>Effect of oestrogen</th>
<th>Reversibility</th>
</tr>
</thead>
<tbody>
<tr>
<td>Anti-androgen agent options (not required post gonadectomy)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cyproterone</td>
<td>Starting dose: 25–50mg po daily Usual maintenance dose: 25–50mg po daily, although smaller doses (12.5mg) may be effective</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Spironolactone</td>
<td>Starting dose: 50–100mg po daily Usual maintenance dose: 100–200mg po daily</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Oestrogen options</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Oestradiol valerate (Progynova®)</td>
<td>Starting dose: 1mg po daily* Usual maintenance dose: 2–4mg, maximum 6mg po daily</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Oestradiol patch (Estradot®)</td>
<td>Starting dose: 25mcg patch twice weekly Usual maintenance dose: 100–200mcg patch twice weekly</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Effect of oestrogen</strong></td>
<td><strong>Expected onset</strong></td>
<td><strong>Expected maximum effect</strong></td>
<td><strong>Reversibility</strong></td>
</tr>
<tr>
<td>Redistribution of body fat</td>
<td>3–6 months</td>
<td>2–3 years</td>
<td>Likely</td>
</tr>
<tr>
<td>Decrease in muscle mass and strength</td>
<td>3–6 months</td>
<td>1–2 years</td>
<td>Likely</td>
</tr>
<tr>
<td>Softening of skin/decreased oiliness</td>
<td>3–6 months</td>
<td>unknown</td>
<td>Likely</td>
</tr>
<tr>
<td>Decreased sexual desire</td>
<td>1–3 months</td>
<td>3–6 months</td>
<td>Likely</td>
</tr>
<tr>
<td>Decreased spontaneous erections</td>
<td>1–3 months</td>
<td>3–6 months</td>
<td>Likely</td>
</tr>
<tr>
<td>Breast growth</td>
<td>3–6 months</td>
<td>2–3 years</td>
<td>Not possible</td>
</tr>
<tr>
<td>Decreased testicular volume</td>
<td>3–6 months</td>
<td>2–3 years</td>
<td>Unknown</td>
</tr>
<tr>
<td>Decreased sperm production</td>
<td>unknown</td>
<td>&gt;3 years</td>
<td>Unknown</td>
</tr>
<tr>
<td>Thinning and slowed growth of body and facial haira</td>
<td>6–12 months</td>
<td>&gt;3 years</td>
<td>Possible</td>
</tr>
<tr>
<td>Male pattern baldness</td>
<td>Variable</td>
<td>b</td>
<td></td>
</tr>
<tr>
<td>Voice changes</td>
<td>None</td>
<td>c</td>
<td></td>
</tr>
</tbody>
</table>

---

a - Complete removal of hair requires laser treatment; b - Familial scalp hair loss may occur if estrogens are stopped; c - Treatment by speech-language therapists for voice training is most effective.
Masculinising hormonal therapy (Table 5)

Testosterone can be added to a GnRH agonist or started on its own. Start a low dose of testosterone and increase gradually. Potential complications include polycythemia, which if severe, increases the risk of a thrombotic event. Periods will usually cease within the first 3–6 months of therapy. For those moving from GnRH agonists to testosterone, continue the blocker until the person is on the full testosterone dose and well virilised to avoid any undesired bleeding. For those not started on a GnRH agonist and not ready to start testosterone other interventions to achieve bleeding cessation include:

- Primolut® (norethisterone) po 5mg bd to 10mg tds. Note: Norethisterone is partially metabolised to ethinyl-
estradiol, which at these high doses is equivalent to levels in the combined oral contraceptive.
- Provera® (medroxyprogesterone) po 10mg tds or 20mg nocte
- Combined Oral Contraception—continuous active pill taking to avoid menstruation
- Depo-provera® (medroxyprogesterone acetate) 150mg IM every 12 weeks
- Mirena® (levonorgestrel)—intrauterine device

The additional consideration of need for adequate contraception may affect the choice made.

Trans people receiving maintenance hormonal therapy should have ongoing medical assessments and investigations as illustrated in Table 6.
Gender affirming surgery
While many trans people are comfortable without, for others surgery is essential to alleviate their body dysphoria and live fully and authentically in their gender. Availability and funding are significant issues within Aotearoa, New Zealand. District health boards (DHBs) have expertise around provision of chest surgery (chest reconstruction to masculinise/breast augmentation to feminise where there has been no response to oestrogen), hysterectomy, oophorectomy and orchiectomy. Some DHBs have expertise in plastic surgical techniques such as laryngeal shaves and facial feminisation. Clinicians should be aware of local services and referral pathways. Currently access to genital reconstruction surgery (metoidioplasty or phalloplasty (masculinising) and vaginoplasty (feminising)) is via the Ministry of Health high-cost treatment pool (see website).

Table 6: Maintenance surveillance for gender affirming hormone therapy.

<table>
<thead>
<tr>
<th>Investigation</th>
<th>Frequency</th>
</tr>
</thead>
<tbody>
<tr>
<td>All persons</td>
<td></td>
</tr>
<tr>
<td>HbA1c—if risk factors suggest indicated</td>
<td>Annual</td>
</tr>
<tr>
<td>Lipids—if risk factors suggest indicated</td>
<td>Annual</td>
</tr>
<tr>
<td>Consider DEXA imaging if major risk factors for osteoporosis</td>
<td></td>
</tr>
<tr>
<td>Feminising gender affirming hormone therapy</td>
<td></td>
</tr>
<tr>
<td>Electrolytes if on spironolactone and after a change in dose</td>
<td>Annual</td>
</tr>
<tr>
<td>Liver function tests</td>
<td>Annual</td>
</tr>
<tr>
<td>Testosterone—aim for &lt;2nmol/L</td>
<td>3 monthly during first year, then annually</td>
</tr>
<tr>
<td>Oestriadiol—avoid supraphysiological levels (target &lt;500pmol/L)</td>
<td>3 monthly during first year, then annually</td>
</tr>
<tr>
<td>Prolactin</td>
<td>2 yearly</td>
</tr>
<tr>
<td>Masculinising gender affirming hormonal therapy</td>
<td></td>
</tr>
<tr>
<td>Testosterone—aim for male reference range&lt;sup&gt;a&lt;/sup&gt;</td>
<td>3 monthly during first year, then annually</td>
</tr>
<tr>
<td>Full blood count&lt;sup&gt;b&lt;/sup&gt;</td>
<td>Every 3 months for first year, then 1-2 yearly</td>
</tr>
<tr>
<td>Liver function tests</td>
<td>3 monthly during first year, then annually</td>
</tr>
</tbody>
</table>

<sup>a</sup> – testosterone should be measured midway between Depo T and Sustanon injections, immediately prior to a Reandron injection, and at least two hours after application of a testosterone patch.
<sup>b</sup>– consider testosterone dose reduction if Hct >0.54.

Table 7 presents the surgical criteria recommended in the Aotearoa, New Zealand guidelines. These are the same as the current WPATH SOC.

Other gender affirming care
Laser hair removal is important, particularly as feminising therapies will not completely halt facial hair growth that is already established. Be aware of local providers and support access where possible. Wearing a chest binder to achieve a more masculine chest appearance may be important; discuss safe use to prevent health risks associated with prolonged use.

Speech and communication are fundamental to people’s genders. The goal of speech-language therapy is to help trans people develop voice and communication that reflects their gender.

General healthcare
All New Zealanders have the right to healthcare that is respectful and non-discriminatory. Ensuring healthcare services...
are inclusive of gender diversity is fundamental to good health care for trans people. Apart from gender affirming healthcare, trans people experience the same health needs as others. Those who have not undergone surgical removal of their breasts, cervix, uterus, ovaries, prostate or testicles remain at risk of cancer in these organs and should undergo screening as recommended. Manage sensitively, as many trans people find cancer screening extremely challenging, both physically and emotionally. Refer trans women for mammograms as per the National Breast Screening programme. Use of internal oestrogen cream prior to cervical smears in trans men may reduce discomfort and reduce the risk of inadequate smear tests.

General recommendations

Based on the guidelines outlined above, to best support the needs of transgender people in Aotearoa, New Zealand, we recommend that:

1. All health services provide equitable and accessible gender affirming healthcare services that align with international standards, evidence-based literature and community feedback.

### Table 7: Aotearoa, New Zealand Guidelines and WPATH SOC v7 criteria for access to gender affirming surgery

<table>
<thead>
<tr>
<th>Criteria for access to chest reconstruction surgery:</th>
</tr>
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<tbody>
<tr>
<td>• Persistent, well-documented gender dysphoria.</td>
</tr>
<tr>
<td>• Capacity to make a fully informed decision and to consent for treatment.</td>
</tr>
<tr>
<td>• Age of majority.</td>
</tr>
<tr>
<td>• If significant medical or mental health concerns are present, they must be reasonably well controlled.</td>
</tr>
</tbody>
</table>

Hormonal therapy is not a prerequisite for masculinising chest surgery but is recommended for a minimum of 12 months prior to consideration of feminising chest surgery.

<table>
<thead>
<tr>
<th>Criteria for access to hysterectomy, salpingo-oophorectomy and orchidectomy:</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Persistent, well documented gender dysphoria.</td>
</tr>
<tr>
<td>• Capacity to make a fully informed decision and to consent for treatment;</td>
</tr>
<tr>
<td>• Age of majority.</td>
</tr>
<tr>
<td>• If significant medical or mental health concerns are present, they must be well controlled.</td>
</tr>
<tr>
<td>• 12 continuous months of hormone therapy as appropriate to the patient’s transition goals (unless the patient has a medical contraindication or is otherwise unable or unwilling to take hormones).</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Criteria for access to metoidioplasty or phalloplasty (masculinising) and for vaginoplasty (feminising):</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Persistent, well documented gender dysphoria.</td>
</tr>
<tr>
<td>• Capacity to make a fully informed decision and to consent for treatment.</td>
</tr>
<tr>
<td>• Age of majority.</td>
</tr>
<tr>
<td>• If significant medical or mental health concerns are present, they must be well controlled.</td>
</tr>
<tr>
<td>• 12 continuous months of hormone therapy as appropriate to the patient’s gender goals (unless the patient has a medical contraindication or is otherwise unable or unwilling to take hormones).</td>
</tr>
<tr>
<td>• 12 continuous months of living in a gender role that is congruent with their gender identity (note that this can include gender identities other than male and female).</td>
</tr>
</tbody>
</table>

In New Zealand, current practice is that the person must be 18 years or older to access publicly funded surgeries as above and in addition to the referral letter from the prescribing clinician, a letter of support from a mental health professional should be provided. The role of the mental health professional is to ensure that the person is psychologically prepared for the surgery (for example, has made a fully informed decision with clear and realistic expectations and is practically prepared for the event).
2. DHBs enable flexible and responsive pathways on the basis of informed consent and self-determination.

3. Health services enable the involvement of trans people, including Māori trans people, in decisions that affect them regarding the development and provision of services.

4. Health services must support the development of culturally appropriate practice within clinical settings that acknowledges kaupapa Māori health frameworks.

5. DHBs provide clear information about pathways to access gender affirming healthcare services. This is inclusive of health services delivered by DHBs and primary healthcare.

Conclusion

The Guidelines for Gender Affirming Healthcare for Gender Diverse and Transgender Children, Young People and Adults in Aotearoa, New Zealand have been developed in acknowledgement of the substantial increase in demand and significant evolution that has occurred in the period since the publication of currently used documents. The above summary provides an overview of gender affirming healthcare, while the full guideline details the role of the healthcare workforce in the provision of holistic healthcare for transgender people. We hope these guidelines will support the development of health services around the country, and provide helpful guidance to all health professionals involved in the care of transgender people.

Competing interests:
Nil.

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Public health and the radio frequency radiation emitted by cellphone technology, smart meters and WiFi

Susan Pickett

ABSTRACT
This paper argues that the prevailing official narrative in New Zealand concerning the relationship between public health and the radio frequency emissions (RF) from cellphone technology, WiFi and electricity smart meters is scientifically and ethically flawed. The main regulatory document in the area, NZS2772.1:1999, is 20 years out of date and ignores existing laboratory evidence disproving its core assumption that the only biological effect of non-ionising radiation is tissue heating. This and further laboratory evidence for harmful effects of RF continues to be ignored, nominally on the contradictory grounds that (a) cellphone manufacturers say their products now emit less RF than early models, so early lab studies exposed tissue to RF levels higher than those now relevant (b) given the lack of actual data on population exposures either then or now, all laboratory evidence is unconvincing anyway. The official narrative further opines that since there exist both laboratory and epidemiological studies concluding that RF is harmful, the appropriate response is to count up the number on each side, declare the “weight of evidence” to be such that “causation is not proven” and, pending unspecified further studies, continue exposing to unmonitored levels of RF the entire population of the country, none of whom has given informed consent to participate in the experiment. This approach is obviously unethical. It is also unacceptable scientifically. First, the algebraic model is flawed: studies that do find a harmful effect of RF are not invalidated by differently constructed studies that fail to find an effect. Secondly, while causation is relatively easy to study in the laboratory, it is difficult if not impossible to prove epidemiologically, given that (1) the very narrative under discussion has ensured that there is now no unexposed control group and (2) interpretation of timeline correlation studies is hampered by changes in the way new cancer registrations have been recorded over the years and the perennial problem of multiple possible causal factors. The present paper concludes that a precautionary approach is justified, and ends with a number of specific suggestions on how to start implementing such an approach.

Properties of the various standard divisions of the electromagnetic spectrum are summarised in Table 1.

Electromagnetic radiation is generally divided into two classes: ionising and non-ionising. Ionising radiation (gamma rays, x-rays and ultraviolet light) has enough energy to knock electrons off molecules, and is a known carcinogen. Non-ionising radiation (visible and infrared light, microwaves and radio waves) carries less energy than needed to knock electrons off molecules, and in the past has been thought to affect biological tissue only by means of heating it. Hence many of the regulatory standards used around the world permit exposure of the public to non-ionising radiation up to limits based solely on intensities that cause tissue heating. Much of North America and Western Europe, Japan, Australia and New Zealand rely on guidelines put out in 1998 by the International Commission on Non-ionising Radiation Protection (ICNIRP). ICNIRP guidelines allow exposure of the public to radiation at the frequencies emitted by cellphone towers and WiFi transmitters up to a power density of 10 watts per square meter.
The relevant regulatory document in New Zealand is NZS 2772.1:1999, a pdf of which can be purchased from the Standards New Zealand website for $128.70 + GST. Since New Zealand law can be downloaded for free, this charge underlines the fact that NZS 2772.1:1999 is not a statutory document, merely a set of recommendations. To emphasise the commercial nature of the document, NZS 2772.1:1999 starts with the statement “Standards New Zealand will vigorously defend the copyright in this Standard. Every person who breaches Standards New Zealand’s copyright may be liable to a fine not exceeding $50,000 or to imprisonment for a term not to exceed three months. If there has been a flagrant breach of copyright, Standards New Zealand may also seek additional damages from the infringing party, in addition to obtaining injunctive relief and an account of profits.” This point being made, NZS 2772.1:1999 goes on with a disclaimer “There is scientific research, including epidemiology, which has suggested associations between some adverse health effects and exposure to RF [radio frequency] fields at levels lower than the basic restrictions specified in this Standard, however causation has not been shown.”

The aim of the present article is to discuss some of the scientific research referred to by this disclaimer, and as a result argue that current public policy in New Zealand is inadequate to protect public health.

Evidence from laboratory studies

Early laboratory studies in this area were largely concerned to investigate the underlying assumption of documents like NZS 2772.1:1999 that heating is the main, if not only, biological effect of non-ionising radiation.

In fact evidence disproving this hypothesis was already plentiful by 1999.

As far back as 1967, a paper in Nature reported that microwaves cause lymphoblastoid transformation of lymphocytes in vitro at intensities specifically shown not to result in any changes in temperature. In 1974, well-controlled interventional experiments showed that microwaves caused chromosome damage in both hamster and human cell cultures, again at measurably non-thermal intensities. By 1993 at least two major reviews had been published summarising a plethora of further evidence for non-thermal effects of microwave radiation. None of these papers is cited in NZS 2772.1:1999’s summary of existing evidence, which discusses only studies reporting negative or inconclusive findings.

Since 1999, considerable further work has appeared. In 2005, Belyaev reviewed 115 papers showing harmful non-thermal effects of RF on a variety of biological factors. Five years later, the same author reviewed the complex dependence of many of the reported effects on various physical and biological parameters, none of which is controlled in a number of studies that purportedly fail to replicate the original findings.

Reading this literature is not easy. One difficulty is that different studies use different metrics to quantify the amount of RF delivered: power density in watts (W) per square metre or microwatts (µW) or milliwatts (mW) per square centimetre; electric field strength in volts per meter; specific absorption rate in watts per kilogram. Another problem is that, because US government funding in the area was reportedly shut down in the late 1970s, a good deal of the work was done in

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### Table 1: Divisions of the electromagnetic spectrum.

<table>
<thead>
<tr>
<th>Region of spectrum</th>
<th>Frequency (Hz)</th>
<th>Frequency (GHz)</th>
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<tbody>
<tr>
<td>Gamma ray</td>
<td>$10^{21}$–$10^{24}$</td>
<td>$10^{12}$–$10^{15}$</td>
</tr>
<tr>
<td>X-ray</td>
<td>$10^{18}$–$10^{20}$</td>
<td>$10^{9}$–$10^{11}$</td>
</tr>
<tr>
<td>Ultraviolet light</td>
<td>$10^{15}$–$10^{16}$</td>
<td>$10^{6}$–$10^{7}$</td>
</tr>
<tr>
<td>Visible light</td>
<td>$4$–$7 \times 10^{14}$</td>
<td>$4$–$7 \times 10^{5}$</td>
</tr>
<tr>
<td>Infrared light</td>
<td>$10^{10}$–$10^{11}$</td>
<td>$10^{3}$–$10^{5}$</td>
</tr>
<tr>
<td>Microwave</td>
<td>$10^{9}$–$10^{11}$</td>
<td>$10$–$10^{2}$</td>
</tr>
<tr>
<td>Radio wave</td>
<td>$10^{8}$–$10^{11}$</td>
<td>$10^{5}$–$10^{7}$</td>
</tr>
</tbody>
</table>
the former Soviet Union and published in Russian: only a summary of this is available in English. However, these are relatively trivial problems compared with the more fundamental complexities the work reveals. Essentially, average RF power density is not the best predictor of biological effect. For some parameters, short pulses of RF such as those emitted by electricity smart meters have worse effects than continuous irradiation. Within any given temporal emission pattern dose-response curves are counterintuitive, showing dose windows where biological effects are greater than those caused by either larger or smaller doses. Nittby et al summarise repeated attempts to replicate Frey’s 1975 report that 30 min of exposure to either pulsed or continuous 1.2 GHz waves with average power densities a fifth of that permitted by ICNIRP guidelines increased the permeability of the rat blood brain barrier (BBB) to fluorescein. These attempts were apparently unsuccessful, until it was realised that an inverted-U shaped dose response curve held—at which point it became clear that the parameters involved in mobile phone use are particularly effective at damaging the BBB. Given that the BBB is vitally important in protecting brain neurons from environmental influences, this effect may underpin the later findings from Kaplan’s lab that exposure of rats to RF levels perfectly legal under NZS2772.1 causes death of pyramidal neurons in the CA region of hippocampus. Since a properly functioning hippocampus is essential for memory formation, this suggests that levels of RF exposure currently legal in New Zealand might well contribute to the development of dementia.

Even more worryingly, there seems to be no lower limit on the amount of RF that can cause harm. Exposure of quail eggs to 900 MHz (0.9 GHz) RF at doses as low as 0.0025 watts per square meter (cf NZS2772.1:1999’s 10 watts per square meter) causes significant oxidative stress—overproduction of free radicals/reactive oxygen species—and oxidative damage to DNA. Given that oxidative stress is “common for many types of cancer cell that are linked with altered redox regulation of cellular signalling pathways” and has also been linked to artherosclerosis, Alzheimer’s disease, arthritis and diabetes, there would seem to be significant reason for concern about allowing the public to be routinely exposed to 4,000 times the level of RF known to cause oxidative stress (10 W/m² = 4,000 times 0.0025 Watts/m²).

In summary, there is laboratory evidence that RF at power densities a tiny fraction of those permitted by NZS2772.1:1999 causes (a) overproduction of free radicals (b) opening of the blood brain barrier (c) damage to DNA (d) death of hippocampal neurons and (e) transformation of lymphocytes to immortal cell lines that spontaneously replicate. Obviously all of these provide plausible mechanisms by which RF exposure might cause any number of disease states, including cancer.

Does all this translate to proven carcinogenesis in lab animals? Surprisingly little has been published on that question, perhaps partly because rats live for only about two years at best, which may not be enough time for cancer to develop. One 1997 report showed that genetically lymphoma-prone mice were more likely to develop lymphomas if exposed to pulsed 900 MHz RF. But later, Adey and colleagues reported that intermittent exposure of rats to 836 MHz RF for two years had either no effect or (counterintuitively) a protective effect on the formation of CNS cancers, with exposed rats developing fewer tumours than controls. As with the in vitro experiments, precise details of exposure parameters may be important in determining biological effects.

**Epidemiological evidence**

Epidemiology is a discipline beset by multiple problems. To ask whether some agent causes a particular harm, the most scientifically watertight methodology is to expose a test group of subjects to the putative agent and compare them with a control group who have never been exposed. Ideally both groups should be uniform with regard to all other possible causes of the harm, or at least randomised from a heterogeneous population. However, this approach becomes significantly problematic when the subjects under study are human. Deliberately exposing humans to potential harm is generally considered ethical if the participants give their informed consent to participate in the experiment. But when no informed consent is ever solicited, there
are multiple, non-randomised factors that might contribute to any increased incidence of harm, and (thanks to the increasingly inescapable exposure of everyone to RF from mobile phones and their base stations, smart meters and WiFi) there now exists no unexposed control group, epidemiology is reduced to studying timelines and trying to draw correlative conclusions.

In this regard, one question that on the face of it should be relatively easy to answer is whether or not the incidence of brain cancers has increased since the introduction of mobile phones. Here, despite the fact that a 2008 editorial in the journal *Surgical Neurology* cites no fewer than seven published reports detailing an increase in the incidence of nerve sheath and brain tumors, particularly very malignant forms such as glioblastoma multiforme, we have repeatedly been assured that the incidence of brain cancer has not increased since the introduction of mobile phones. But quite apart from a concerning refusal even to acknowledge the existence of the many papers that do show increases, a number of confounds render insecure a conclusion from the rest of the literature that the incidence of brain cancers has not increased since introduction of mobile phones.

First, papers in this area need to be read quite closely, because the conclusions in their abstracts sometimes fail to reflect the data reported. For example, Vocht et al report data that clearly indicate an increased risk of brain cancers related to mobile phone use. They then raise and demolish in their discussion section all reasonable arguments against the validity of this conclusion (implying that they believe their own data do show an increased risk). Yet in the abstract of the paper they say “These data do not indicate a pressing need to implement a precautionary principle by means of population-wide interventions to reduce RF exposure from mobile phones.” Aydin et al also adopt this approach. Further examples are described by Kundi and Cherry.

A second type of confound is pointed out by Hardell and Carlberg. The Swedish Cancer Register shows no statistically significant increase in the incidence of brain cancers between 1998 and 2013, which fact has repeatedly been used to dismiss epidemiological evidence of a risk. However, the Causes of Death Register for the same population shows a highly statistically significant annual percentage change of +22.6% between 2008–2013. This appears to be a localised fault with the Swedish Cancer Register, since Hardell and Carlberg report that the Danish Statens Serum Institut Cancerregisteret reveals an increase in age-standardised incidence of brain tumours of +42.2% among men and +46.1% among women during 2003–2012.

The problem with the Swedish Cancer Register is never clarified, but some general possibilities are suggested by the New Zealand Ministry of Health’s database of new cancer registrations. Here cancers diagnosed at death only started to be registered in 1972, cancers diagnosed in private hospitals were not reliably registered until 1974 and in 1994 the Cancer Registry Act mandated reporting of cancers by diagnostic laboratories, leading to a sharp increase in registration rates. Overlapping with this latter increase, introduction of PSA testing in the early 1990s coincided with a sudden increase in the diagnosis of prostate cancers. In the early 2000s some conditions began to be considered malignant (eg, polycythaemia vera in 2003) while others ceased being considered malignant (eg, superficial transitional cell carcinoma of the bladder in 2005). Since many cellphone users seem to have gradually switched over the last decade from holding their phones against their ears to texting or using speaker mode, exposure of trunk organs is now probably greater than exposure of the brain. But the above administrative changes preclude any clean time-line correlation of total cancer rates with changes in cellphone use.

Returning to published work, what about case-control studies of brain tumours? Khurana et al meta-analyse 11 peer-reviewed epidemiologic studies and conclude that using a cellphone for 10 years or more approximately doubles the risk of being diagnosed with a brain tumour on the same side of the head as that preferred for cell- phone use. This study specifically includes no participants who are also included in the pooled case-controlled studies of Hardell et al, which found odds ratios for glioma of 5.9 for analogue cellular phones, 3.7 for digital cellular phones and 2.3 for cordless phones.

In contrast, the largely industry-funded 13 country INTERPHONE study reports...
overall odds ratios (ORs) that are actually less than 1.0 for gliomas in all centres except Australia, France and New Zealand, where <5% industry funding is declared and odds ratios are not specified in the final report. An OR <1.0 implies either a deficit in methodology or a genuine protective effect of cellphone use. Most commentators have assumed the methodological deficit explanation, although some of the animal data cited in the previous section do suggest the possibility of a genuine protective effect at some exposure parameters. One obvious methodological problem with the INTERPHONE study is that amount of cellphone use was determined simply by asking participants to recall the number of hours a week they had used a cellphone over the last n years. Memory is notoriously unreliable, so this methodology could introduce bias in either direction. There is no way of knowing whether such bias contributes to the results, but the highest decile of cumulative time that mobile phones were recalled as being used (>1,640 hours) was associated with significantly increased probability of glioma (OR 1.4; 95% CI 1.03–1.89).

Finally, Kundi and Hutter review a number of studies on the health effects of mobile phone base stations (cell towers) and as a result recommend exposure limits 10,000 times lower than NZS2772.1:1999.

Discussion

So why do regulators still use the 1998 ICNIRP/IEEE exposure limits? One answer is that, while the above emphasises papers that do show harmful effects of weak RF fields, there are also published reports in the literature concluding that RF has no harmful effects. The critical question for public policy is how this dichotomy should be interpreted.

A priori, there are four possible conclusions:

1. Most studies showing no harmful effects of RF are flawed.
2. Most studies showing harmful effects of RF are flawed.
3. Most studies on both sides are OK as far as they go. The important thing is the weight of evidence. This is presently such that causation is not proven. More research is needed.
4. Most studies on both sides are OK as far as they go. Abundant evidence already exists that RF at some intensities and configurations has harmful effects on some aspects of biological function. Therefore a precautionary approach is needed.

How does each of these conclusions stack up?

Conclusion 1 (that many or most studies showing no harmful effects of RF are flawed) is actually supported by a certain amount of published evidence. For example, statistically speaking, papers funded by the wireless industry are twice as likely as papers not funded by the wireless industry to report no harmful effects of RF. Sometimes scientists funded by the wireless industry deliberately design their studies to produce the answer they know their funders want. Sometimes honestly done industry funded work is suppressed if it produces the ‘wrong’ answer. Pearce summarises a number of documented situations in which epidemiologists have failed to declare conflicts of interest in relation to studies of other putative harms, and there is no reason to suppose that the wireless industry is any less active in this regard than the tobacco, pharmaceutical and chemical industries.

Conclusion 2, that most of the peer-reviewed papers which do show harmful effects of RF are less than credible, is on the present author’s understanding not supported by any published evidence. Yet it appears to be a core tenet of the official narrative that the entire corpus of work cited in the Evidence from Laboratory Studies section of the present paper can legitimately be ignored, on the grounds that no data exist on actual population exposures to RF.

Importantly, this approach avoids attacking the scientific validity of the lab studies on their own terms. Rather it argues that, since the emissions of cellphones have reportedly decreased over the last decade or so, all the lab experiments showing harmful effects of emission levels current a decade ago would have to be redone using current emission values before the results could reasonably be taken into account in setting policy. Further, since the wireless industry keeps shifting the goal posts in this regard, there is reason to believe that it will always...
be possible to dismiss future lab studies as not demonstrably reflective of the current exposure environment.

This position is problematic. For one thing, the non-specific demand for population exposure figures sets an impossibly high bar. The RF output of cellphones varies with brand, year of manufacture and, most importantly, distance from a cell tower: the further any given phone is from a tower, the more RF it emits in an attempt to handshake with the tower. Actual measurement of emissions in, for example, a crowded city street populated by hundreds of people all walking purposefully about with their noses in their devices, is not feasible. The “PhoneGate” scandal, which recently revealed that measurements made by the French Government in 2015 showed 90% of the hundreds of phones tested emitting significantly more than the RF figures claimed by the manufacturer, suggests that it is not possible to estimate emissions with any degree of accuracy. There appear to be no official measurements at all available for cell tower emissions, perhaps partly because these (a) depend on both the configuration of individual antennae and local topography and are thus unique to each tower, (b) vary depending on traffic—the more cellphones are attempting to contact a particular tower at any given moment, the more RF the tower emits—and (c) again, the industry keeps changing the goal posts (3G, 4G, now 5G).

WiFi emissions come in either 2.4 GHz or 5 GHz frequencies, at intensities that depend entirely on (i) how many and what kinds of WiFi routers are active in the vicinity at any given moment, (ii) the distances between these routers and the measuring instrument and (iii) what concrete or earth barriers there are in the intervening space.

An arguably even greater problem concerns the fineness of the spatial grain that would be necessary in any meaningful measurement of population exposure. Figure 1 shows power density at various distances from an electricity smart meter. A smart meter is essentially a radio transmitter mounted on the wall of a dwelling: mesh smart meters transmit measurements of electricity usage in their dwelling to neighboring meters in the mesh, then collector smart meters collate the electricity use figures from all surrounding mesh meters and send the results directly to the electricity company. The figures used to construct Figure 1 are taken from a 2008 application to then Auckland City by Metrix (on behalf of Mighty River Power) for a resource consent allowing installation of smart aka ‘advanced’ meters throughout the Hauraki Gulf islands. The resulting consent allows each meter to emit 250ms bursts of RF, 96 times a day, 24/7, at the power densities shown in Figure 1.

Figure 1: RF emissions from an electricity smart aka advanced meter operating according to parameters allowed by Auckland Council.
Figure 1 demonstrates that during the brief emission periods, these meters routinely expose people in their vicinity to very much more than the 0.25μW/cm² of RF reported to cause overproduction of free radicals and indeed at short distances from the meter to considerably more than even NZS2772.1:1999's recommended limit of 1,000μW/cm². This latter fact was hidden from the bureaucrat granting the consent by averaging emitted power over six minutes, during most of which time the meter is not emitting. This practice is reasonable on the assumption that tissue heating is the only biological effect of RF, but otherwise akin to contending that a single bullet is harmless, because if you average the energy it imparts over a month, being hit by a bullet is no worse than being brushed by a feather.

All of this renders the demand for current population exposure levels safely unfulfillable.

But in any case, the main official narrative in New Zealand at present is essentially Conclusion 3: weight of evidence, causation not proven, more research needed (but don't ask us for funding to do it, you'll have to get that from the industry). When analysed a little more closely, this conclusion appears to be based on an algebraic model. The implicit assumptions are that each negative study cancels out one positive study, with an algebraic sum of zero indicating no effect. Therefore, the argument seems to go, we should continue exposing the public to RF and doing epidemiological studies to see if it harms them, until either papers delivering one answer significantly outnumber papers delivering the other answer, or causation is proven. Unfortunately, there are a number of problems with this position, too.

First, it is completely unethical. What university or hospital Ethics Committee would approve such deliberate experimentation on human subjects who, so far from having given informed consent to participate in the experiment, will insist on doing things like demonstrating in the streets in a fruitless attempt to prevent the erection of cell towers metres from their homes?

Secondly, the algebraic model is overly open to manipulation. Given the preponderance of industry-funded studies showing no effect, it might reasonably be seen that all Big Wireless has to do to tip the ‘weight of evidence’ in their favour is fund more studies than can be done without their funding. Given the depth of the industry's pockets and the current scarcity of government funding for any sort of research, this might not prove too difficult.

Thirdly, definitive proof of causation is problematic in general. Psychologist Daniel Wegner argues that any cause-effect attribution is based on three factors: (i) the timing of the perceived cause, which must occur before the perceived effect, but not too far before it. (This makes attribution of cause especially difficult for long-latency disorders like cancer). (ii) The consistency of the perceived cause with the perceived effect. (This boils down to the existence of plausible mechanisms. The laboratory studies documented above show that RF produces a plethora of biological effects likely to result in cancer and any number of other diseases). (iii) The exclusivity of the perceived cause, ie, the absence of any other possible cause of the perceived effect. (As mentioned earlier, this is a perennial problem for epidemiology).

Seen in this light, the wireless industry's familiar mantra “causation not proven” carries little weight. If a particular harm (cancer, for example) has increased since the introduction of a suspected agent (RF of the sort emitted by cellphones and their base stations, WiFi and smart meters)—and the suspected agent has been repeatedly shown to produce biological effects likely to result in that harm (overproduction of free radicals, opening of the blood brain barrier, damage to DNA, transformation of cultured cells to immortal cell lines that spontaneously replicate)—the jury should no longer be out on whether the public should be protected from the agent.

Finally, the “weight of evidence” argument fares no better. If even a fraction of the peer-reviewed papers describing harmful effects of low-level RF are reporting good science, it is unethical to ignore them. Positive results do not go away just because it is possible to design slightly different studies that return negative results.

Conclusion 4 is therefore the author's preferred response to the available evidence. The biological effects of RF are clearly complicated, but there is no longer any reasonable doubt that under some
circumstances, RF levels common in the present environment do have harmful biological effects. Like its cousin ionising radiation, RF is undoubtedly useful. However, until more is known about when and how RF does or does not cause harm, the precautionary principle must be applied as energetically with RF as it is with ionising radiation. In fact, even NZS2772.1:1999 counsels this approach (albeit in the weakest terms imaginable), advocating “minimising, as appropriate, RF exposure which is unnecessary or incidental to achievement of service objectives or process requirements, provided this can be readily achieved at modest expense”.

The next section offers some concrete suggestions about how to make a start on a genuine implementation of the precautionary principle with regard to RF.

**Recommendations**

1. **For government regulators and their advisors**
   - Drag NZS2772.1:1999 into the 21st century. Stop ignoring evidence that heating is NOT the only biological effect of RF. Do not allow the committee considering the revision of NZS2772 to be dominated by bureaucrats with no scientific training, representatives of the wireless industry or scientists with a history of acting as paid industry consultants. Dare to break step with the rest of the English speaking world: look to Europe, China and Russia for examples of more biologically sensitive regulations.39
   - Once NZS2772.1:1999 has been revised, incorporate the revision into a coherent statute, which takes the precautionary principle seriously and sets legally enforçable limits on RF emissions. Repeal legislation permitting telcos to erect cell towers on roadside berms without a permit. Do not allow telcos to adopt measures explicitly designed to “migrate their customers” away from copper landlines. Especially in areas where fibre is not available, force Chorus to invest in replacement of aging copper line networks. Extend to all public transport existing legislation banning the use of cellphones on airplanes—the issue is not whether radio emissions affect the vehicle’s navigation instruments, it is whether sitting in a metal box surrounded by radio transmitters impacts passengers’ health.
   - Monitor compliance—pending the above, at least compliance with NZS 2772.1:1999 as it stands. Measure the emissions of a selection of cellphones, at various distances from a cell tower. Do not then emulate the French Government by refusing until threatened with legal action to make public the power densities measured at distances from the phone relevant to its carriage in a bra or pants pocket. If radiation values a few cm away from any phone do exceed the 1,000µW/cm² limit specified by NZS2772.1:1999, take appropriate action.
   - Ahead of regulatory reform, schools and universities could profitably lead the way in adopting safer practices. Make campuses cellphone and WiFi free zones, with internet access provided by cabled LANs.

2. **For physicians**
   - Ask your patients where they carry their cellphones. See if you can predict from the answer the location of their primary cancer.
   - If you find that you can, do something about it. Communicate with colleagues. Collate data. Write a paper for the **NZMJ**.

3. **For everyone**
   - Find out whether you have an electricity smart meter. If no meter readers come round any more, you probably do. To find out for sure, DO NOT peer closely at the meter (see Figure 1). Ask the power company. If you do have a smart meter, persevere until you find a power company willing to replace it with a dumb meter (ie, a smart meter from which the radio transmitter has been removed). In the meantime, avoid sleeping or sitting for long periods just through the wall from a smart meter.
If you must use a cellphone, avoid lengthy conversations. Do not hold the device against your ear; use speaker mode or text. If you need a long chat, use a landline—preferably not one accessed through a cordless phone. All cordless phones emit RF, although cordless landlines emit less than cellphones.

Do not carry in your clothing any cellphone that is not either in airplane mode or switched off. Cellphones not in one of those conditions continually emit RF, even when not in use. Figure 1 illustrates how much more intense these emissions are very close to the phone.

Do not use a WiFi-enabled laptop on your lap, for the same reason.

Preferably obtain your home internet access through a cable, instead of via WiFi. Failing that, turn off household WiFi at night.

Stop even taking an active phone into the bedroom at night, let alone sleeping with it under your pillow.

Restrict cellphone use to emergencies.

Gradually phase out device use altogether.

Competing interests:
Nil.

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There's more to this than meets the eye
Tom Kai Ming Wang, Mansi Turaga, Jen-Li Looi

A 53-year-old Cook Island Māori woman presented with sudden loss of vision in her left eye, preceded by two days of fevers and malaise. Ocular examination revealed a dense left eye hypopyon (arrow) with corneal haze and vitreous debris (Figure 1) in keeping with the diagnosis of endophthalmitis. Vitreous aspirate with antibiotic injection was performed and the aspirate grew Streptococcus Lancefield Group G. Further clinical examination revealed Janeway lesions (Figures 2A and B), splinter haemorrhages (Figure 2C) and a pan-systolic murmur. Transoesophageal echocardiography demonstrated large mitral valve vegetation (19mm) with moderate regurgitation (Figures 3A and B). Cardiac surgery was considered but not deemed necessary as the vision loss could not be salvaged and she was well with no further embolic event. Thus, she was commenced on six-week intravenous penicillin.

Endophthalmitis is defined as a bacterial or fungal infection within the eye involving the vitreous and/or aqueous humour. It is a rare but potentially vision-threatening medical emergency. Most cases are exogenous from trauma, eye surgery or extension of keratitis, whereas endogenous bacterial endophthalmitis is most commonly caused by endocarditis. This diagnosis should be considered in patients with painful eye or reduced vision in the setting of bacteraemia.

Figure 1: Hyperaemic conjunctiva and hypopyon (arrow).
Figure 2: A and B Janeway lesions, C splinter haemorrhages.

Figure 3: A) Vegetation (arrow) on mitral valve, associated with b) regurgitation on transoesophageal echocardiography.
Competing interests:
Nil.

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URL:
Acquired haemophilia A: a rare cause of postpartum haemorrhage
Philippa Davey, Helen Allen

A rare cause of postpartum haemorrhage (PPH) is acquired haemophilia A (AHA), a condition that arises from the production of auto-antibodies to Factor VIII.1–4 AHA is a rare condition with an incidence of 1–2/million people/year, with a biphasic distribution. The first peak is seen in younger people, predominantly women, and is associated with pregnancy and autoimmune disease.1–4 The second peak occurs in older adults (median age 64–78 years) with malignancy and autoimmune disorders, although 50% is idiopathic.1–4 AHA is associated with pregnancy, with a demonstrated incidence of 1/350,000 births in UK women.6

AHA is diagnosed with an isolated prolonged aPTT in a woman with no history of bleeding problems, which does not correct with the addition of normal human plasma in 1:1 ratio. The reason it does not correct is because of the presence of an inhibitor (antibody), which also inactivates the factor VIII in the normal plasma.1–5 A measurement of coagulation factor levels and inhibitor levels is then undertaken and reported in Bethesda units (BU).

The presence of an isolated prolonged aPTT in a woman with no history of bleeding disorder should be considered AHA until proven otherwise.1

Significant delay in diagnosis of AHA has been frequently observed, thought to be due to lack of clinician awareness, which may result in increased morbidity and mortality.1–3

Case report
A 36-year-old multiparous woman (G7 P4) with four previous vaginal deliveries and no previous history of abnormal bleeding presented to North Shore Hospital with secondary postpartum haemorrhage (PPH) on Day 14 postpartum (PP). Her pregnancy was uneventful and the infant in good health. Ultrasound (USS) demonstrated retained products of conception (RPOC), subsequently evacuation of uterus was undertaken and bleeding settled. The patient was discharged.

She represented eight days later with a further massive PPH (EBL 1.8L); a further USS was undertaken and suggestive of arteriovenous malformation (AVM). Subsequent examination under anaesthetic and balloon tamponade was performed prior to transfer to a tertiary hospital where interventional radiology performed empirical arterial embolisation of bilateral distal uterine arteries; of note no AVM was identified. Multiple blood products were administered. Prior to discharge an abnormal aPTT of 60 sec was noted; this corrected with addition of normal plasma. Review was undertaken by general medicine and the elevated aPTT was thought to be secondary to multiple transfusions. The third admission for abnormal bleeding occurred on Day 30 PP resulting in a total abdominal hysterectomy and HDU admission. Haematology was consulted regarding the abnormal aPTT, which did not correct with the addition of normal plasma; factor and inhibitor levels were undertaken and the diagnosis of AHA was made on Day 32 PP, 16 days following the first presentation with abnormal bleeding and 10 days following the first abnormal aPTT. Lupus anticoagulant was negative. At the time of diagnosis aPTT 78s, Factor VIII assay 2%, Factor VIII inhibitor 8 BU (Table 1).

The patient received both haemostatic and immunosuppressive treatment under the care of haematology. Activated Factor VII (FVIIa) was administered for three days.
which was not effective; treatment was then changed to Factor Eight Bypassing Agent (FEIBA). Immunosuppressive treatment was with Prednisone and cyclophosphamide, with a dose of Ritixumab to which she developed an urticarial skin reaction. A trial of intragram was of no benefit. Slow improvement in aPTT and decrease in inhibitor levels occurred. One further episode of bleeding resulted in increased doses of FEIBA, in conjunction with tranexamic acid. Table 2 describes haematologic response to treatment.

The patient was discharged on Day 46 PP, Day 16 following the diagnosis of AHA, and remained on immunosuppressive therapy for eight weeks. Follow up over 14 months revealed no evidence of relapse.

Table 1: Summary of blood tests.

<table>
<thead>
<tr>
<th>Days postpartum</th>
<th>Hb</th>
<th>aPTT</th>
<th>Corrected with 1:1 plasma</th>
<th>Haematology</th>
<th>Blood products</th>
</tr>
</thead>
<tbody>
<tr>
<td>14 (admission 1)</td>
<td>117</td>
<td>NA</td>
<td></td>
<td></td>
<td>Nil</td>
</tr>
<tr>
<td>22 (admission 2)</td>
<td>82</td>
<td>73</td>
<td>Yes</td>
<td>Lab comment: Recommend factor studies</td>
<td>5 units RRC 4 units FFP</td>
</tr>
<tr>
<td>23</td>
<td>80</td>
<td>62</td>
<td>Yes</td>
<td></td>
<td></td>
</tr>
<tr>
<td>30 (admission 3)</td>
<td>98</td>
<td>61</td>
<td>Partial</td>
<td>Lab comment: factor studies and LAC</td>
<td></td>
</tr>
<tr>
<td>32 Diagnosis AHA</td>
<td>90</td>
<td>78</td>
<td>Partial</td>
<td>Factor VIII 2% Factor VIII inhibitor 8BU Factor IX, XII normal vWF normal LAC normal ACL normal</td>
<td>3 units RRC 4 units FFP 1 unit FVIIa</td>
</tr>
</tbody>
</table>

Table 2: Treatment response.

<table>
<thead>
<tr>
<th>Days postpartum</th>
<th>aPTT</th>
<th>Factor VIII level (%)</th>
<th>Inhibitor level (BU)</th>
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<tr>
<td>32</td>
<td>78</td>
<td>2</td>
<td>8</td>
<td>FVIIa Prednisone/cyclophosphamide</td>
</tr>
<tr>
<td>37</td>
<td>64</td>
<td>3</td>
<td>14</td>
<td>FVIIa Total FVIIa given-19 units. Prednisone/cyclophosphamide</td>
</tr>
<tr>
<td>40</td>
<td>69</td>
<td></td>
<td></td>
<td>FEIBA Prednisone/cyclophosphamide</td>
</tr>
<tr>
<td>45</td>
<td>54</td>
<td>4</td>
<td>4</td>
<td>FEIBA Prednisone/cyclophosphamide</td>
</tr>
<tr>
<td>51</td>
<td>49</td>
<td>26</td>
<td>0.8</td>
<td>FEIBA stopped. Total administered 40,000IU. Prednisone/cyclophosphamide</td>
</tr>
</tbody>
</table>

aPTT—activated partial thromboplastin time, LAC—Lupus anticoagulant, ACL—anticardiolipin, FVIIa—recombinant activated Factor 7, RRC—red resuspended cells, FFP—fresh frozen plasma.

The patient was discharged on Day 46 PP, Day 16 following the diagnosis of AHA, and remained on immunosuppressive therapy for eight weeks. Follow up over 14 months revealed no evidence of relapse.

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aPTT—activated partial thromboplastin time, FVIIa—activated Factor 7.
Figure 1: Algorithm for the diagnosis of patients with suspected acquired haemophilia.

- Postpartum Haemorrhage
  - Check - Tone
  - - Tissue
  - - Trauma
  - Ongoing PPH or massive volume

- Coagulation Screen

- Isolated prolonged aPTT
  - Normal PT, platelets, fibrinogen

- Mixing Test 1:1 with normal plasma
  - Partial or no aPTT correction
    - Exclude heparin
    - Suspect inhibitor of coagulation
    - Consult with Haematology to guide testing
      - - Factor levels
      - - Lupus anticoagulant
      - - Inhibitor testing
        - - F VIII activity level low
        - - + F VIII inhibitor
  - Acquired Haemophilia

- aPTT correction to normal
  - Suspect single factor deficiency
  - Consult with Haematology
  - Measure FVIII, IX, XI, XII, vWF
  - Single factor deficiency

aPTT: activated partial thromboplastin time; FVIII: factor VIII; FIX: factor IX; FXI: factor XI; FXII: factor XII; vWF: von Willebrand factor.
Discussion

AHA in peri-partum women can present with primary or secondary PPH, post surgical, traumatic, muscular or subcutaneous bleeding. Unlike congenital haemophilia, AHA rarely presents with haemarthroses.\(^1\)\(^-\)\(^4\) This bleeding may not respond to usual treatment measures and can be life-threatening, until the cause is established and appropriate treatment provided.\(^1\)\(^-\)\(^5\) AHA is diagnosed following an isolated prolonged aPTT, which does not correct with the addition of normal human plasma. If there is a factor deficiency aPTT will correct with the addition of normal plasma, however if no correction occurs then this can be due to the presence of an inhibitor (antibody), which also inactivates the Factor VIII in the normal plasma.\(^1\)\(^-\)\(^5\) A measurement of coagulation factor levels and inhibitor levels is then undertaken and reported in Bethesda units (BU) (Figure 1). Coagulation studies should be performed in the case of massive PPH, especially when there is no evidence of uterine atony, trauma or tissue retention.\(^7\) In this case, at first presentation, RPOC was treated and the bleeding settled. At second presentation there was thought to be an AVM, however at interventional radiology no AVM was identified. Empirical embolisation was performed with effect. An abnormal aPTT was identified on this admission; it corrected with a mixing test but factor studies were recommended on laboratory comment and not performed. Ideally haematology consult should have occurred at this point. Follow-up of the abnormal aPTT post-discharge to ensure correction would also have facilitated earlier recognition of the deteriorating situation.

Treatment involves two components; the first is the avoidance of invasive procedures along with haemostatic treatment which is achieved by bypassing Factor VIII in the coagulation pathway. The first line options are activated Factor VII (FVIIa) or Factor Eight Bypassing Agent (FEIBA). These treatments have demonstrated similar efficacy, approximately 90%,\(^1\)\(^,\)\(^3\) however neither agent works for all women. It is recommended that the alternative agent be used if the primary choice is unsuccessful.\(^1\)\(^-\)\(^4\)

The second component of treatment is immunosuppressive therapy (IST).\(^1\)\(^-\)\(^5\) Due to the risks of AHA it is recommended that all adults with AHA receive IST. First-line IST includes steroids or steroids and cyclophosphamide.\(^1\)\(^-\)\(^5\) Steroids and cyclophosphamide are more likely to result in stable and complete remission (70%) than steroids alone (48%). Rituxumab has been used as a treatment for AHA with success when initial therapies fail.\(^2\)\(^-\)\(^5\)\(^,\)\(^8\)

The bleeding risk remains until remission is achieved, which can take weeks to months. In the EACH2 cohort of pregnancy-related AHA the mean time to inhibitor negative was 26 days, Factor VIII >70IU/dl was 47 days and duration of IST was 96 days. The risks of IST include infection, steroid-induced diabetes and neutropenia.\(^1\) Pregnancy-related AHA is rare so there is limited and conflicting data about the risk of recurrence in a subsequent pregnancy, haematology referral and close monitoring are recommended.\(^4\)

Conclusion

In summary, pregnancy-related AHA is a rare condition that can cause significant bleeding morbidity. A woman with no personal or family history of bleeding disorders and an isolated prolonged aPTT should be considered to have AHA until proven otherwise.\(^1\) Retrospectively, in this case, the ordering of factor studies when recommended on haematology comment with subsequent follow-up of abnormal aPTT on discharge from hospital may have led to earlier diagnosis. The absence of an AVM at interventional radiology was another potential clue, as without AVM there was no clear cause for haemorrhage. Consultation with haematology at the time of abnormal aPTT is likely to have led to an earlier diagnosis and potentially decreased morbidity. Awareness of this condition is important to enable provision of prompt diagnosis and appropriate management.

The take home message:
An abnormal aPTT in the setting of acute postpartum haemorrhage is pathologic and warrants immediate haematological specialist consult.
Competing interests:
Nil.

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REFERENCES:


David Murray Fergusson
19 May 1944–3 October 2018

PhD (Epidemiology/Paediatrics) University of Otago 1989,
BA (Hons) (Psychology) Victoria University of Wellington 1969,
Elected Fellow of Royal Society of New Zealand (FRSNZ) 2006,
Honorary Fellow of New Zealand Psychological Society (Hon.FNZPS) 2006,
Honorary Fellow of Royal Australasian College of Physicians (Hon. FRACP) 2007,
Distinguished Research Medal, University of Otago 2010

For nearly 40 years, Emeritus Professor David Fergusson was the Director of the Christchurch Health and Development Study (CHDS), a longitudinal study of a cohort of 1,265 children born in Christchurch in mid-1977. His longitudinal research enlightened debate and informed government policy decisions on a wide range of controversial, but significant topics.

In the early days of the study, one of the main areas of interest was lower respiratory illness among the cohort. Emeritus Professor Fergusson found a significant increase in risk of bronchitis and pneumonia for children of smokers. This study was one of the first to quantify the risk of lower respiratory infection related to parental smoking, and in later years these findings were replicated in cohorts around the world.

Another area of interest in the early years of the study was an examination of swimming pool safety fences, which were not mandatory at the time. A CHDS analysis showed that a significant number of children had experienced accidents that may have led to drowning if parents had not been alert, and that fencing would have reduced the number of accidents.
considerably. This research proved instrumental in the development of local by-laws requiring fencing for domestic swimming pools throughout New Zealand, leading to a reduction in the rate of accidental drownings.

A further important area was the study of lead exposure in the cohort. Lead exposure was measured using shed deciduous teeth, and the level of lead exposure was shown to be linked to increased rates of childhood behaviour disorder, and lower levels of school achievement and IQ. This work influenced government policy, contributing to the evidence leading to the removal of lead from petrol in New Zealand.

One of the primary areas of impact from the early years of the study was the study of childhood conduct problems, and the extent to which these impaired school performance and overall adjustment. Later findings would demonstrate that conduct disorders if left untreated had wide-ranging implications for adult functional outcomes, including offending, personal relationships, employment and other life-course outcomes. This series of studies led Emeritus Professor Fergusson champion policy development at government level to enhance treatment and prevention services for childhood behaviour problems.

In the 1990s, as the cohort entered adolescence and early adulthood, the focus of the study changed to examine issues concerning mental health, substance use and psychosocial adjustment. As part of this, Emeritus Professor Fergusson decided to ask detailed questions concerning cannabis use among the cohort. What resulted from this was a quarter-century's worth of data on cannabis use and the problems associated with cannabis use, which constitute some of the best and most complete data on cannabis use in a single cohort in the world. This data led to a series of landmark publications outlining the harms associated with cannabis use.

In later years, as cohort members grew into adulthood, Emeritus Professor Fergusson became interested in questions concerning economic adjustment and family life, as well as looking back at ‘big picture’ issues such as overall exposure to adversity in childhood. One of the key observations he made from this work was that adversity is best understood as being cumulative; young people who experience adverse circumstances are often exposed to a range of adversities, and it is the total burden of adversity, more so than specific kinds of adversity, that are predictive of poorer outcomes in adulthood.

Emeritus Professor Fergusson's proudest achievement was the development of Early Start, an early intervention service for high-needs families with young children. Working with a consortium of providers including Plunket, Pegasus Health and Māori representatives, Emeritus Professor Fergusson and his colleagues developed Early Start as a programme of early childhood home visitation for at-risk families. Early Start has now been in existence for over 20 years, and has been shown via randomised controlled trial data to be one of the most efficacious home visitation programmes in the world for reducing the risk of child abuse among high-needs families. The findings of the randomised trial have been used to benchmark the performance of wider Government Family Start early intervention services.

Emeritus Professor Fergusson is survived by his wife Prue Wignall, and his four children, Jonathan, Rebecca, Jeremy and Matthew.
Trial of Ibudilast in progressive multiple sclerosis

There are limited treatments for progressive multiple sclerosis. Ibudilast inhibits several cyclic nucleotide phosphodiesterases, macrophage migration inhibitory factor, and toll-like receptor 4 and can cross the blood-brain barrier, with potential salutary effects in progressive multiple sclerosis.

Two hundred and fifty-five appropriate patients were randomised to either oral ibudilast or placebo for 96 weeks. The primary endpoint was the rate of brain atrophy.

Ibudilast was associated with slower progression of brain atrophy than placebo but was associated with higher rates of gastrointestinal side effects, headache and depression. Further trials are needed to identify whether the effects on brain atrophy is reproducible and is associated with slowed progression of neurologic disability.


Sulfonylureas as second-line drugs in type 2 diabetes and the risk of cardiovascular and hypoglycaemic events

Metformin is the drug of choice in the management of type 2 diabetes. If this treatment fails, the patient is often switched to treatment with a sulfonylurea. This cohort study evaluates the safety of this change of treatment.

Among 77,138 metformin initiators, 25,699 added or switched to sulfonylureas during the study period. During a mean follow-up period of 1.1 years, sulfonylureas were associated with an increased risk of myocardial infarction, HR (hazard ratio) of 1.26 and an increased risk of all-cause mortality, HR 1.28 and an increased risk of severe hypoglycaemia, HR 7.6.

It was concluded that sulfonylureas as second-line drugs are associated with an increased risk of myocardial infarction, all-cause mortality and severe hypoglycaemia, compared with remaining on metformin monotherapy. Continuation of metformin when introducing sulfonylureas is safer than switching.

BMJ 2018; 362:k2693

Hospitalisation and morbidity due to adverse drug reactions in elderly patients

Adverse drug reaction (ADR) is a leading but under-recognised cause of illness, particularly in frail subjects with multiple comorbidities. In this report from Italy the researchers investigate the frequency, patterns and outcomes of ADR as a cause of hospitalisation in elderly patients admitted to an internal medicine ward.

Their retrospective observational study included every patient aged 65 years or over who was admitted to their department over one year. ADR accounted for 6.1% of the 1,750 admissions. The median age of the patients was 83.5 years and 56.6% were on polypharmacy. Diuretics were the most commonly imputed drugs followed by antithrombotics and central nervous system-active drugs.

The researchers observed that ADR are a common cause of hospital admission in elderly patients and are often associated with adverse outcomes. Their data underline the need of appropriate strategies aimed at identifying high-risk patients and avoiding potentially preventable drug toxicities.

Internal Medicine Journal 2018; 48:1192–1197

URL:
The Influenza Epidemic

December 1918

The influenza pandemic unfortunately reached New Zealand and has caused sickness and death the like of which has never been seen in this country. The brunt of the fight against the scourge fell, of course, on the medical profession, and we deplore the deaths of a considerable number of doctors who fell martyrs to their duty. We know the condition of affairs in Wellington, and suppose that they were typical of the country generally. The people were nervous and to some extent panic-stricken, and not without some reason; but their nervousness, we believe, was intensified by unduly alarming and occasionally sensational statements in the public press. There was far too much talking to the newspapers by the accredited leaders of the people, and the constant stressing of the shortage of doctors disturbed the public mind, and the applications for medical aid soon became so great that not four times the number of doctors at present in New Zealand could have satisfied all the demands made upon their services. The conditions were certainly very abnormal, but there seems to be a prevalent opinion that it is in some way the business of the Government to see that everybody can get the services of a doctor by right at any hour of the day or night simply by telephoning or ringing a door-bell. If this is to be the fulfilment of the aims of a State Medical Service we believe it to be beyond the power and financial resources of the Government to satiate the appetite of the people of New Zealand for medical attention, unless, indeed, taxation is enormously increased.

Two views are held in regard to the origin of the virulence of the disease in this epidemic—one that the ordinary mild influenza became virulent in this country, and the other view is that the virulent,
septic, and pneumonic form was introduced from abroad, and incidentally could have been prevented by quarantine. We think that no medical man, at any rate in the light of after-events, will find it difficult to say which of the two theories is correct. There have been many recriminations—we make none, for we believe that the officials and others directly concerned did the best they could according to their judgment, and as a matter of fact the whole country was unprepared for the calamity that came upon it. In Wellington the Public Hospital had to refuse admission to influenza cases almost at the outset, and temporary hospitals were established and served a makeshift purpose. They were of great service, at all events, in checking the spread of the disease. A part-time district scheme of medical service was also established, and it tended to tranquillise the public mind, but people, of course, applied more to the doctors resident in the district in the usual way than to the so-called district health managers. An army of voluntary helpers sprang up almost in a night and, on the whole, did good service, but a complete lack of training and experience on the part of many of the women who were dressed and addressed as nurses produced a state of affairs by no means safe or commendable. The women who carried food to the sick, took care of children, and endured many a weary vigil at the bedsides of the sick in the temporary hospitals or in private houses did magnificent service.

Out of the disaster good will come if the matter is not left in the hands of politicians alone, who too often talk about what they will do, the great things they are going to do, and as a rule they do nothing. Slums should be quickly and steadily abolished and a comprehensive scheme of town-planning inaugurated.
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