Tinnitus prevalence in New Zealand

Health literacy: from the patient to the professional to the system

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Policies that kill
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Predictors of vitamin D status in pregnant women in New Zealand
Alec J Ekeroma, Carlos A Camargo Jr, Robert Scragg, Clare Wall, Alistair Stewart, Ed Mitchell, Julian Crane, Cameron C Grant
New Zealand has a sun avoidance health policy and minimal dietary vitamin D fortification. Vitamin D deficiency was present in 109/259 (42%) of pregnant women in a south Auckland cohort. Of those enrolled in winter (June-August)/spring (September-November), vitamin D deficiency was present in 43% of European, 67% of Māori, 80% of Pacific and 59% of women of other ethnic groups. Supplementation for all pregnant women during winter/spring could be an appropriate intervention for prevention of vitamin D deficiency during pregnancy in New Zealand.

Tinnitus prevalence in New Zealand
Billy Wu, Grant Searchfield, Daniel Exeter, Arier Lee
Tinnitus is the perception of sound in the head or ears in the absence of an external real sound. It is commonly associated with hearing loss and can vary in effects from mild annoyance to catastrophic effects on quality of life. This is the first nationally representative study of tinnitus prevalence in New Zealand and largest study sample internationally for tinnitus prevalence to date. Tinnitus is a public health problem affecting approximately 207,000 people in the New Zealand population aged ≥14 years. This study has highlighted the importance of sex and age in defining a high-risk tinnitus population.

An audit of paediatric referrals to the Southern Cochlear Implant Programme (2009–2014)
Jill Mustard, Megan Chinnery, Alice K Guidera, Neil Heslop, Philip A Bird
An audit of referrals was undertaken to determine the effect of Universal Newborn Hearing Screening on the age of referral and implantation in the Southern Cochlear Implant Programme. The audit found that the introduction of universal newborn hearing screening has significantly reduced the age at referral and implantation, however some referrals were unnecessarily delayed. Causes for delay were identified. Recommendations are made to further reduce delayed referral.

Endovascular clot retrieval for acute ischaemic stroke: the Auckland City Hospital experience
Peter Alan Barber, Qiliang Liu, Stefan Brew, Ben McGuinness, Ayton Hope, Maurice Moriarty, Doug Campbell, Dominic Tse
Stroke affects 8,000 New Zealanders every year with half dying from the stroke or left being disabled. Current treatments are not very effective. A new therapy is ‘clot retrieval’ where the clot that blocks an artery that causes a stroke is ‘retrieved’ (i.e., pulled out). This restores blood flow to the brain and reduces the permanent brain damage. This study reports the results from the 1st 33 stroke patients treated with clot retrieval at Auckland City Hospital. The outcomes of the stroke patients in Auckland are similar to those seen in a series of five landmark trials published earlier in 2015 in the New England Journal of Medicine (Auckland City Hospital participated in one of these trials.). The authors recommend that District Health Boards group together into regions where clot retrieval is given at a single large centre.
Sperm quality in New Zealand: is the downward trend continuing?
Mary Birdsall, John Peek, Sumithra Valiapan

Studies in many countries have reported that the average sperm concentration in men has fallen over the past 50 years or more. If sperm concentrations continue to fall, doctors are concerned that more people will experience infertility and need help conceiving. Our previous study showed sperm concentration in men presenting to be sperm donors in New Zealand had halved over the period 1987 to 2008. In this follow up study, we found the downward trend has stopped, which is reassuring.

Laparoscopic adrenalectomy for phaeochromocytoma: a case series
Cheri Hotu, Richard Harman, Rick Cutfield, Nicola Hodges, Eletha Taylor, Simon Young

This paper describes the surgical management of 29 patients with phaeochromocytoma at a single centre. In 27/29 cases the tumour was removed laparascopically with low morbidity and no mortality. With careful anaesthetic management and using magnesium infusions and selected IV antihypertensives, excellent BP control was achieved.
Since January 2015, nearly 530,000 people have crossed the Mediterranean Sea, among whom nearly 3,000 have died. Since launching search and rescue operations in May and June, three Médecins Sans Frontières (MSF) boats have rescued 16,350 people making this dangerous journey across the Mediterranean. Their plight has grabbed the headlines around the world and here in New Zealand, but this is but the tip of the iceberg and just one illustration of the extreme difficulties facing people on the move, crossing borders in search of sanctuary and a better life.

Meanwhile, just a short distance from where my colleagues are working in Bangladesh and Myanmar, thousands of stateless and persecuted Rohingyas and people from Bangladesh fled across the Andaman Sea. Here, search and rescue missions like those on the Mediterranean are very difficult while no country will host and offer protection to those desperate to get away. As Asian nations replicated the hard line approach to border protection promoted by Australia, boats with hundreds and thousands of people on board remained stranded at sea for months. In the end, only through the intervention of local fishing communities in Aceh were they rescued at sea.

These people on boats in two very different parts of the world, as well as those trapped in detention centres in Libya, Indonesia and elsewhere, are proof that this ‘migration problem’ is a global one and that the 1951 Refugee Convention and other national and international migration policies established to provide safe haven and protection are spectacular failures. MSF teams are witnessing and hearing similar stories of fear, misery and violence the world over: on the route to Spain through Morocco, across the Red Sea through Yemen, through Turkey, Bulgaria, Greece and southern Europe, across the Andaman Sea and from Mexico into the United States.

A United Nations Refugee Agency report issued in June indicates that there are now more than 59.5 million forcibly displaced people around the world. That is 59.5 million uprooted people trying to escape war, insecurity and poverty.

That numbers are increasing with the Middle East and Sahel region of the African continent in flames comes as no surprise, but that the world’s forcibly displaced population is over 13 times the entire population of New Zealand is surely an astounding reality to accept. When we add to this the millions of undocumented migrants out of official sight, the amount of people on the move around the world soars even higher.

Let’s be clear, as the situation stands today, the international asylum and refugee framework is limited by the political will of the very people tasked with handling it, and even then the standard of protection enshrined in that framework remains unrecognised by many of the countries most concerned. Signatory states fail to meet obligations and basic policy fluctuates with domestic sentiments. While there are many non-signatory states that carry the majority of the refugee burden, they too manage to evade the responsibility of protection. Prosperous governments promote their humanitarian credentials by financing humanitarian aid to refugee camps in Jordan, Lebanon, Kenya, Ethiopia and elsewhere, warehousing people for years on end. At the same time, however, these countries make it difficult, if not impossible, for those living in these extreme conditions to set foot within their own borders. These same countries then reach
agreements to externalise migration, often to third-party countries economically much worse off than themselves. This not only raises barriers to entry, but displaces accountability for what are often violations of the most basic rights. Australia goes one step further, forcibly returning people at sea, detaining would-be asylum seekers offshore while cutting overseas aid commitments. New Zealand remains insulated from this by our isolation, yet the Government has formulated policies to prevent and disrupt arrival of potential asylum seekers.

Politicians seek a ‘successful’ migration policy, but for most, the definition of success is reducing the number of so-called irregular arrivals on their shores and at their borders; these people’s misery must be someone else’s problem. But when one door closes, another one must open; people do not stay put, they look for an alternative, usually via a more dangerous route. Australia was once one of the main destinations for Afghan asylum seekers, particularly persecuted Hazaras. Current policy is now driving these same people onto boats headed for Greece and Italy. Many of those that now remain stranded in Indonesia have handed themselves over to local authorities, preferring overcrowded and often squalid detention conditions to fending for themselves on their own. Politicians claim success for their strict policies, but in reality the ‘problem’ is not solved at all, it’s simply transferred to another place. People on the move continue suffering—elsewhere.

New Zealand once set a great example in taking many of the refugees rescued from their sinking boat by the MV Tampa, who were unable to reach Australia. It should set such an example again, beyond the welcome but modest increase in Syrian refugees who will be accepted into New Zealand over the next few years.

The hardship people endure on these journeys is shocking for our teams around the world to witness. We witness first-hand the devastation war inflicts in places like Afghanistan, Somalia and Syria, the forced labour and violent repression in Eritrea, the systematic discrimination in Myanmar and the subsistence living in many parts of sub-Saharan Africa and South East Asia, which force millions to flee. But we also hear horrific stories of the flight itself—people left to die of dehydration in the Sahara, packed like cattle into warehouses and trucks, or raped, tortured and starved in Libya and Thailand. Indeed, the journey itself, whether for the forcibly displaced or so-called migrants, is quite literally a killer, subjecting them to all manner of physical injury, abuse and psychological trauma, and in some cases death. New Zealand, in its current position on the United Nations Security Council, has an opportunity to find ways to seek resolution of the conflicts that force people to flee, support stronger temporary protection measures and provide attention to the routes people travel while on the move.

In a world afflicted by conflict, poverty and inequality, population movements are inevitable, as the extraordinary numbers illustrate. Our governments must make a choice between implementing policies that will ultimately result in the maximising or the minimising of harm. As a medical humanitarian organisation with more than 40 years of experience providing assistance to people on the move, we advocate for a policy that seeks to minimise harm.

Our request is simple: manage migration so as to minimise suffering, rather than create it. Stop applying policies that kill and prolong the anguish. Instead, provide protection and assistance based on humanitarian imperatives according to needs.

Competing interests: Nil
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Health literacy: from the patient to the professional to the system

Christine Walsh, Carl Shuker, Alan F Merry

The Health Quality & Safety Commission (the Commission) defines health literacy as the degree to which individuals can obtain, process and understand health information and services they need to make appropriate health decisions. In 2006, a survey showed that more than half of adult New Zealanders had health literacy skills “insufficient to cope with the health literacy demands they typically face” (see Box 1). Four out of five Māori males, and three out of four Māori females, had low health literacy levels of one or two (out of five). Groups including the poor, elderly, rural, Māori in older and younger age groups, and almost 90% of Pacific adults scored poorly. However, these groups are no sure guide in a clinical encounter or other health setting—in absolute numbers, Pākehā with poor health literacy outnumber those of all other ethnic groups combined.

Low health literacy is associated both with higher mortality in older adults and with a slew of missed opportunities, mismanagement and misadventure. People who find it hard to understand or interpret health information are less likely to be involved with preventive services such as screening; have less knowledge of their illnesses, treatments and medicines and are thus less likely to manage their long-term or chronic conditions; are more likely to be hospitalised because of a chronic health condition; are more vulnerable to workplace injury; and are more likely to use emergency services.

What is health literacy?—systemic and dynamic in nature

A chasm often separates what health professionals intend to convey in written or spoken communications with patients, and what patients actually understand. The term health literacy was first used in 1974, but there has been no unanimously accepted definition. Health literacy can be defined in terms of a set of capacities patients possess that allows them to successfully navigate the health care environment; or it can be understood as the interaction between the individual capacities, attitudes and behaviors of patients, families and health professionals, and the health care environment in which they operate together. The distinction affects how improvement is sought—do we target the patient, the professional, or the system? The Commission takes the latter, broader view, in line with recent thinking, with the World Health Organization, and with inte-

Box 1: How is health literacy measured?

The 2006 Adult Literacy and Life Skills Survey (ALL), a large-scale, comparative survey used in 13 countries, was used to test a representative national sample of 7,131 New Zealanders aged 16–65 years. A score from 0–500 was assigned, divided into five levels.

The 2006 ALL contained 191 health-related questions across four domains: prose literacy, document literacy, numeracy and problem solving. Questions addressed health promotion (60 items); health protection (64 items); disease prevention (18 items); health care maintenance (16 items); system navigation (32 items).

Respondents scoring at levels one and two (0–275) are defined in the Ministry of Health’s 2010 Kōrero Mārama report as having poor health literacy skills (see Figure 1).
EDITORIAL

grated conceptual models developed from systematic reviews. This is reflected in the Commission’s definition of health literacy (above).

This chasm between communication and comprehension has been and is often still attributed to a deficiency in the person on the receiving end of health or disability services. The view, whether actively articulated or passively assumed, that failures in the transfer of information reflect a deficit in the capacity of the recipient to understand that information necessarily promotes interventions that target the recipient.

In the US, the Institute of Medicine has been emphatic: health professionals have a key responsibility in lifting health literacy levels. It is their skills that drive health literacy levels. The central role of health staff in empowering or disempowering patients has been reinforced by Edwards and colleagues and by the New Zealand Ministry of Health:

“Health literacy should not depend on the skills of the individual patient and whānau alone. It is an organisational value that should be considered core business, incorporated into all levels of service planning delivery and even the way health centers and hospitals are laid out.”

The Ministry, in May 2015, published their Health Literacy Review: A guide, elaborating on this provider-focused approach to improving health literacy, to assist health care organisations in undertaking a health literacy review. The purpose of such a review is “to gain a better understanding of the health literacy demands created by a health service and how they affect consumers and families.” The Ministry’s ‘Six Dimensions of a health literate organisation,’ which underpin the guide, draw on the Institute of Medicine’s ten attributes of a health literate organisation, tailored for the New Zealand setting.

Rather than viewing health literacy as a challenge for individual patients or even individual clinicians, the solution lies in a concerted effort across sectors, including schools, social welfare, ACC and other government agencies, and the entire health care system.

Health literacy should be seen as a construct with multiple dimensions, encompassing all aspects of the health services system (and other systems) each individual patient engages with, including the patient and the providers within that system and the way in which the system is designed and functions. This approach should be operationalised at all levels, including, explicitly, within each organisation delivering health or disability services.

Knowledge and demand

Health literacy includes knowledge and skills—which of these skills and the specific knowledge required by patients and providers in any given situation is determined by the demands created by that situation.

Even a person who knows a great deal about health care in general (a health care professional for example) will have gaps

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Figure 1: The distribution of health literacy, for Māori and non-Māori, by sex, from the 2006 Adult Literacy and Life Skills Survey

Source: Adapted from Ministry of Health, Kōrero Mārama: Health Literacy and Māori 2010; Adult Literacy and Life Skills Survey 2006. Note: Prioritised ethnicity has been used.
in his or her knowledge of the nuances of particular conditions. When he or she becomes ill, the patient’s context-relevant capacity to grasp the highly individualised implications of a specific disease for him or her personally may not be adequate, particularly given the vulnerability created by illness.

Patients vary in relevant generic abilities, such as reading and comprehension, and they vary in their ability to interact with professionals of any type and to comprehend verbal information about technical matters. Even people with good communication and comprehension skills in a general sense can find it difficult to understand health care information.\(^7,23-25\) Furthermore, learning that one is personally unwell and must make decisions about the management of a specific health-related condition creates challenges far beyond those of most everyday interactions.

When acutely or seriously unwell, health knowledge demands increase dramatically—the basic requirement is for an understanding of disease theory and how the body works, knowing when and where to seek health advice, being able to evaluate the appropriateness of that advice (including medication), being able to interpret and describe health symptoms, and to act and speak confidently within a clinical setting. In addition, at least some information specific to the particular diagnosis in the particular individual must also be acquired and understood.\(^7,14,23\) None of the skills and abilities required for any of this can be assumed (not even of doctors, nurses or other allied health professionals). “Even highly skilled individuals may find the systems too complicated to understand, especially when these individuals are made more vulnerable by poor health.”\(^7\)

Health is only one of many competing fields that impact on the lives of people, even for those most motivated to improve their knowledge. It is likely to be more effective to teach providers to communicate well than to try to lift the capacity of patients to cope with a poor system, peopled with poor communicators.

The universal precautions approach—improving the skills of providers

Expert advice now recommends that rather than assessing individuals to evaluate their ‘health literacy’ and identifying those ‘in need of help’, health professionals should assume that all patients may have some degree of difficulty when in health environments. Health care workers should therefore apply the principle of universal precautions to health literacy.\(^24-27\) Universal precautions, familiar from the prevention of blood-borne disease, means using a common approach to all: it involves ascertaining in all patients what they already know, sharing clear information with them and then being active in helping them build their understanding of their health issues (and the relevant aspects of how their body works), and their proposed treatment. This approach has been endorsed by the US Agency for Healthcare Research and Quality,\(^28\) and underpinned the Commission’s recent Health Literacy Medication Demonstration Project training programme (see Box 3).
EDITORIAL

HELPING PROVIDERS AND PATIENTS TO MANAGE THE CHALLENGE

The chasm in health literacy that confronts many patients today must be addressed from both sides.

Providers

There are few published data on effective interventions for improving health literacy within the New Zealand context (see Box 3). Understanding of health literacy and the relevant principles of adult learning theory varies across the health sector and, as such, "opportunities to create effective learning opportunities for patients in the course of meeting health needs appears underdeveloped." The New Zealand Guidelines Group 2011 report on health literacy and medication safety in New Zealand recommended prioritising the up-skilling of the health workforce in understanding and applying principles of adult learning theory to the delivery of health services.

Patients

Effective health care implies providing outcomes that accurately address the true needs and wants of patients. For each individual patient, health providers need to understand not so much "What's the matter with you?" but, "What matters to you?" This is about 'doing the right thing'—which sometimes means agreeing not to intervene. Some of the problem of overtreatment or the wrong treatment lies in a failure by providers to establish what actually matters to people, and also of people being enabled to convey what really matters to them. This communication nuance is critical when discussing treatment options. Patients can be supported and encouraged to ask questions and take information away to better understand their own health and the treatments available. Let's P.L.A.N. for better care is a new tool developed by the Commission to help patients prepare for, understand and engage with their health care encounter so they leave it with clarity, confidence and a satisfactory level of comprehension (see Box 4).

Conclusion

‘Good' health literacy means patients or consumers of health and disability services obtain, process, and understand information relevant to their care sufficiently well to make good health decisions. This depends...
on a combined approach, in which patients and professionals both take responsibility. But the onus lies primarily with health professionals and the organisations they work within, because at times of substantial vulnerability people are simply not up to the considerable challenges of complex interactions within unfamiliar systems.

Improving health literacy is a dynamic systems issue reflecting the complexity of health information being presented, and the health care system being navigated. \[^{35,36}\] Health literacy is a “multi-dimensional construct that develops over time, across different health contexts and through social interactions.” \[^{19}\] It should develop along a continuum towards greater patient knowledge, greater self-management and greater participation in decision making. Health literacy is about both a process and an outcome—the latter being the optimal management of health conditions at all times. \[^{19}\] As individuals take greater control over their own health and the decisions they need to make, care is likely to become more effective, but also more efficient, more equitable, and, by avoiding overtreatment, more cost-effective. \[^{37-39}\]

Koh and colleagues have suggested that recent US federal policy initiatives at the public health level mean that health literacy is, “poised to make the transition from the margins to the mainstream.” \[^{39}\] Now is the opportunity for New Zealand to be at the forefront of this change.
Competing interests: Nil

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30. For more information, see Tool 5, page 28 and pages 138 to 160 of the Universal Precautions Toolkit: www.ahrq.gov/qual/literacy/healthliteracytoolkit.pdf. For a video of USA health literacy expert Dr Rima Rudd giving an example of a teach-back script see: www.youtube.com/watch?v=_tG2ewud-lhs&list=UU8_p3mo72sDxkyzL1HQUA&index=11. For videos of teach-back use see: http://www. nchealthliteracy.org/teachingaids.html.


EDITORIAL

Does it really matter if sperm counts are decreasing?

Simon McDowell, Andrew Murray

The article published in this journal by Valiapan et al raises an interesting issue. Are men becoming less fertile? Are the various hazards in our current environment (pesticides, endocrine disruptors, cellphones, tight-fitting underpants) making men produce less sperm of poorer quality? This has certainly been topical in recent times, and we commend the authors for searching for answers within their own database.

But does it really matter? If sperm counts and quality are truly decreasing, does this mean that men are becoming less fertile? Fertility is defined as the ability to conceive children. In a way, a man who has not conceived a child is ‘infertile until proven otherwise’.

A semen analysis is only a surrogate measure of a man’s fertility. The World Health Organization (WHO) publishes manuals that guide clinics in how to perform standardised semen analyses. They provide references ranges for use in interpretation. The current manual (WHO 2010) is actually the fifth edition, the first having been published in 1980.1

It is commonly thought that men with semen parameters (concentration, motility, morphology) below the lower limit of the reference range are infertile. This is in fact incorrect. The cut-offs are completely arbitrary. The lower limit of the reference range represents the 5th centile of a healthy fertile population of men. These limits were collated by approximately 1,900 men who had conceived a child within 12 months. All men had a solitary semen analysis, the results pooled and the distribution plotted. Succinctly put, 5% of the 1,900 men had sperm parameters less than currently accepted lower limits, and still achieved pregnancy within 12 months.

There are several controversies with regards to the WHO 2010 routine semen analyses criteria. The current cut-offs are markedly lower than those previously reported. They were obtained from a healthy fertile population, and not an infertile population. Of the 1,900 men involved, almost all were from large cities in North America. A small amount came from Australia and none from Asia, Africa, Latin America and the Middle East. It may be that racial and geographical factors affect semen analysis parameters and the ‘fertility’ of men in those areas.

Perhaps we should look at other factors to assess a man’s fertility? Or use a multitude of things in combination. Tests of sperm quality and functioning may better reflect ‘fertility’ as opposed to a simple semen analysis.

Several tests have been developed, such as hypo-osmotic swelling, induced acrosome reaction, zona pellucia binding and sperm DNA fragmentation. Unfortunately these tests have inherent limitations, namely how do we determine ‘cut-offs’ to measure fertility or infertility. Most of these tests, such as DNA fragmentation, are expensive and may not be readily available. Men with high DNA fragmentation have been shown to have a higher rate of miscarriage, and ‘therapies’ to correct those issues have been described.2,3 There is emerging technology, such as Hyaluronic Acid Binding Assays and Intracytoplasmic Morphologically Selected Insemination (IMSI), which may improve sperm selection when high DNA fragmentation is a factor. Whether these techniques actually improve live-birth rates is still debated.4 It may be that functional sperm issues are contributory, not causative.
For woman, age remains the best prognostic indicator of a woman's ability to conceive. A woman at age 25 years has a 25% chance of conceiving per month, at age 35 years this falls to 16%, and at age 40 years it is down to 6%. Emerging data shows that paternal age affects standard semen parameters. Seminal volume, sperm motility and morphology all decline with advancing paternal age. Time to pregnancy increases, miscarriage risk increases and chance of success with IVF decreases.

Advancing paternal age also represents risks for biological offspring. The occurrence of autosomal dominant conditions increase, as do birth defects, such as cardiac malformations, neural tube and limb defects, schizophrenia and autism spectrum disorders.

We propose male fertility should be assessed via a ‘fertility algorithm’. This could examine a triad of factors, including standard semen parameter analysis, sperm functioning and age. This leads us back to our original question. Even if sperm counts and other semen parameters are truly decreasing, does it really matter? Semen analysis is at best a surrogate marker of a man’s fertility, and this may not decrease fertility at all. A man’s ability to conceive is really measured by the time taken to achieve pregnancy. What would be interesting is to find out if the time to conceive is increasing now compared to decades ago, when controlled for female factors, such as advanced maternal age.

What is important is that both women and men attempt to start producing children at a younger age. For those that then have difficulty conceiving, rapid assessment and treatment can take place when ART success rates are reassuringly high. While we should strive to learn more about the impact of the environment on male and female fertility, we should continue to encourage couples to start trying for families earlier than they currently are.

Competing interests:
Drs Murray and McDowell are both colleagues of Drs Birdsall and Peek, co-authors of the Valipan et al paper.

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Tinnitus healthcare in New Zealand

Kim J Wise, Philip A Bird, Greg A O’Beirne

Tinnitus is the sensation of sound in the absence of an evoking sound stimulus and corresponding mechanical activation of the cochlea. It is usually experienced as an endogenous signal localised to one or both ears (or described as emanating within, or just outside the head), and may be described as a ringing, humming, hissing, buzzing, or a combination of these sounds. Tinnitus may be categorised as pulsatile or non-pulsatile, and may be subjective or objective (ie, the rare cases in which the tinnitus is audible to an external observer). Subjective non-pulsatile tinnitus is the larger clinical problem and is the subject of this paper.

In their article in this issue of The New Zealand Medical Journal, Wu et al.3 present a significant study surveying the prevalence of tinnitus in New Zealand. The work is important in that it is a recent, national estimate of prevalence in the New Zealand population, involving a very large survey cohort of nearly 70,000 respondents. The authors have estimated a prevalence of 6% in persons over the age of 14 years. This study and others have shown the prevalence of tinnitus is higher in older populations, and is higher in men, but may potentially arise at any age.4

As highlighted by the authors, the question asked of respondents in this New Zealand study related to ‘any’ tinnitus—what this work does not show us is the proportion of people in whom tinnitus is clinically relevant, and even more importantly, where it is a significant health and quality of life issue. Their results are weighted to give representative sub-group statistics, but their study could be complemented by the gathering of further demographic data informing our understanding of how tinnitus differentially impacts the groups highlighted; especially in terms of ethnicity.

Statistics New Zealand’s most recent figures (June 2015 quarter) estimate that New Zealand’s population includes 3,742,230 people aged ≥14 years.5 Previous international reports indicate 1% to 4% of the overall population may encounter tinnitus as a primary health concern—experiencing its presence as unremitting and debilitating—with functional, life quality, sleep and mental health substantially, negatively affected.3 Comparing New Zealand population data against international estimates for chronic, incapacitating tinnitus suggests that between 37,000 and 150,000 New Zealanders in the ≥14 year age group may be severely affected by tinnitus. By 2050, it is projected the number of people aged 60 or older will grow globally by 30% or greater, which is likely to significantly increase the number of individuals with intractable tinnitus in need of treatment.5

Much is still unknown about the pathophysiology of tinnitus, although valuable information has been obtained from animal models and functional MRI (fMRI) studies in humans with tinnitus, and this data is now becoming clinically relevant. To grossly simplify the theories of pathophysiology, tinnitus is usually associated with a hearing loss and therefore reduced input from the periphery, ie, the cochlea.3 This triggers a cascade of changes in the central auditory pathways: impaired cochlear function leads to reduced cochlear nerve activity, which may down-regulate inhibitory cortical processes and lead to hyper-excitability within central auditory structures. Abnormally high neural synchrony is observed in animal models, as well as reorganisation of tonotopic maps in the auditory cortex.3 The chances of tinnitus sensation reaching consciousness also heavily depend on activity in the prefrontal, parietal and...
limbic brain regions, which contribute to awareness of the symptom and modulate or sustain the emotional distress caused by it. Network theories for tinnitus perception have recently emerged to account for contributions from non-auditory centres controlling attention, emotion and memory.

Tinnitus has myriad causes, and is usually (but not always) associated with hearing loss and occasionally associated with hyperacusis or noise intolerance. It is often approached as if it were a disease rather than a symptom, and is often managed poorly or not at all. While there is often no ‘cure’ resulting in complete elimination of symptoms, it is usually possible to significantly reduce the distress caused by tinnitus with appropriate management.

Most tinnitus sufferers perceive the sound as a minor annoyance only, and while they would rather not have this symptom, they do cope with it. Generally, in terms of both loudness and degree of annoyance, initial symptoms may be readily noticeable for a few weeks to months after they first appear and fade over time. A thorough case history and full examination are crucial in determining appropriate tinnitus management. The initial consultation may include: a neck and jaw examination to account for musculoskeletal, somatosensory, arteriovenous and/or temporomandibular contributions; a review of medications and supplements to identify any potential interactions or primary causal agents; an appraisal of cardiac and metabolic function to rule out hypertension, diabetes and/or thyroid disorders; and determination of affective state, sleep pattern, functional life impact and coping ability. In some cases, a multi-disciplinary approach may be required.

Reassurance and an explanation of the nature of the condition (‘informational counselling’) are important, initial steps. The Tinnitus Research Initiative (TRI)—a foundation comprised of tinnitus researchers worldwide—has emphasised counselling as a principal treatment consideration, either delivered alone or as an adjunct to other therapeutic options, depending on the case. Of the various counselling approaches used in tinnitus management, cognitive behavioural therapy (CBT) received support in a 2010 Cochrane Review for having a beneficial effect on tinnitus. However, the approach can be lengthy and there is currently little data to support CBT’s superiority to other counselling options, including clinical information provision. Some form of counselling is often included as part of current tinnitus treatment modes, potentially managing pre-existing or later-developing psychological distress, or persisting negative attitudes sustaining tinnitus perception.

In addition to a full examination, audiometry is an essential part of management, as up to 90% of individuals presenting with tinnitus as their main concern demonstrate measureable hearing loss. Unfortunately, a small group of individuals go on to have tinnitus, which in terms of loudness and annoyance is a major issue affecting their quality of life. In some cases, this may be at least partially mitigated by assuring them of the quality and variety of current support and treatment options.

Often, correction of underlying hearing loss via a trial of amplification (hearing aids, for example) is an initial management consideration for the majority of cases involving comorbid hearing loss and tinnitus. Although professional tinnitus working groups emphasise the importance of counselling, one study found that those with co-occurring hearing loss and tinnitus who experienced counselling but subsequently proceeded to a hearing aid trial, had significantly reduced tinnitus handicap. A recent (2014) Cochrane Review comparing hearing aids and sound generators showed both treatment approaches were beneficial—ie, no significant difference was observed between the methods investigated. This highlights the importance of case-based individualised approaches and an appropriate diagnostic review of hearing profile, as those with measured hearing loss and associated tinnitus pitch match(es) that are not well-supported by the bandwidth of modern hearing aids, may find other forms of sound therapy preferable. The application of therapeutic sound may also be employed via a desensitisation approach in cases of hyperacusis or marked sensitivity to certain everyday ambient sound(s), to promote normal sound tolerance over time. The above treatment methods, as well as other case-dependent tinnitus control options, can
be broadly organised into seven categories, shown in Table 1.

Awareness of the theories of tinnitus causation is now leading to individualised management of troublesome tinnitus in specialised facilities. New Zealand is home to world-class tinnitus treatment centres and a network of support through local Hearing Associations, dedicated audiology clinics, otolaryngology, and University laboratories. Basic science, translational and clinical approaches continue to be pursued by internationally-recognised researchers across New Zealand. With this important paper by Wu et al, we now have the benefit of current prevalence data to help drive tinnitus healthcare initiatives and focus our efforts for the future—accommodating the growing proportion of our population projected to be significantly affected by tinnitus.

Table 1: Categories of tinnitus treatment, adapted from K Wise, Tinnitus and Attention Training [Doctoral thesis].

<table>
<thead>
<tr>
<th>Category</th>
<th>Details</th>
</tr>
</thead>
<tbody>
<tr>
<td>I. Counselling</td>
<td>This is a recommended treatment consideration, either alone or as an adjunct to other treatment options, and may include cognitive behavioural therapy (CBT), guided therapy, masking therapy, neurofeedback, and/or acceptance and commitment therapy (ACT).</td>
</tr>
<tr>
<td>II. Amplification or sound provision</td>
<td>Amplification not only treats the hearing loss, but also increases the level of speech, background and environmental sounds which may interact with tinnitus perception, rendering it less intrusive. Some devices also include therapeutic sound generators to supplement or promote this aim. Ear-level and/or stand-alone sound generators, music, nature sounds, and emerging smartphone apps fall in this category.</td>
</tr>
<tr>
<td>III. Customised or methodological sound provision</td>
<td>Treatments such as Neuromonics, Tinnitus Retraining Therapy (TRT), or other approaches using tailored sounds, involve specially-trained clinicians and generally require more time for benefits to be realised (6 to 12 months or longer), but have received extensive peer review.</td>
</tr>
<tr>
<td>IV. Pharmacological</td>
<td>The provision of antidepressants, anxiolytics, or tranquilisers may improve or exacerbate tinnitus depending on the case, but current investigations include drug trials and animal prototypes targeting ion channels, or counteracting acute glutamate excitotoxicity.</td>
</tr>
<tr>
<td>V. Non-invasive neurological treatments</td>
<td>Treatments such as transcranial magnetic or direct current stimulation tend to be provided in research settings or dedicated facilities and currently appear to offer short-term relief. Research continues into effective montages and high-definition modes.</td>
</tr>
<tr>
<td>VI. Medical management or surgery</td>
<td>These treatments apply to pathologies such as superior semicircular canal dehiscence (SSCD), glomus tumour, and vestibular Schwannoma, and require specialist otolaryngology referral/intervention.</td>
</tr>
<tr>
<td>VII. Perceptual training</td>
<td>Treatments involve auditory attention-based or auditory scene analysis perceptual training, sound discrimination and/or categorisation, to theoretically promote training related neuroplastic change and thereby diminish the tinnitus signal. Treatment has tended to occur via research settings or dedicated facilities, but take-home versions have been developed.</td>
</tr>
</tbody>
</table>
EDITORIAL

Competing interests:
Kim Wise reports a patent, Interactive Gaming System US 20140171195 A1, issued to Pending.

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Tinnitus prevalence in New Zealand
Billy Wu, Grant Searchfield, Daniel Exeter, Arier Lee

ABSTRACT

AIM: There is a lack of consensus in the international literature pertaining to the prevalence of tinnitus for the overall population, as well as sex and age sub-groups, suggesting the need for country-specific prevalence estimates. We aim to find prevalence estimates of tinnitus that are representative of the New Zealand population.

METHOD: We obtained data from random-digit dialled telephone surveys of households, conducted by Roy Morgan Research Limited between August, 2007, and July, 2013, for people aged ≥14 years in New Zealand (n=69,976). As part of the survey, participants were asked whether they have had tinnitus in the last 12 months. The response options were “yes” or “no”. Estimates were standardised to the New Zealand population structure based on the 2013 national census. Sex, age and ethnic differences were explored.

RESULTS: The overall weighted prevalence for any tinnitus was 6.0% in the total New Zealand population age ≥14 years. Tinnitus was higher among males (6.5%) compared to females (5.5%). Males were 55% more likely to report tinnitus compared to females among young adults aged 14 to 24 years, while males were 32% more likely to report tinnitus compared to females among adults aged 50 to 64 years. Tinnitus prevalence increased with age, peaking at 13.5% for older adults aged ≥65 years. Adults aged ≥65 years are three times more likely to report tinnitus than people aged below 65 years. Tinnitus prevalence was highest among people identifying as European (7.05%) and lowest among people identifying as Asian (1.00%).

CONCLUSION: This is the first nationally representative study of tinnitus prevalence in New Zealand and largest study sample internationally for tinnitus prevalence to date. Tinnitus is a public health problem affecting approximately 207,000 people in the New Zealand population aged ≥14 years. This study has highlighted the importance of sex and age in defining a high-risk tinnitus population, but our knowledge falls short of profiling their ethnic and social-economic characteristics.

Tinnitus is the perception of sound in the head or ears in the absence of an external real sound. It is commonly associated with hearing loss, but appears to be the result of a cascade of neuroplastic events in auditory pathways and central networks. Its effects can vary from slight annoyance to disruption of the individual's life. Prevalence studies of tinnitus face methodological drawbacks due to the ambiguity surrounding the way tinnitus is defined and whether questions used in collecting epidemiological data are appropriately worded. Despite this difficulty, there have been numerous large-scale cross-sectional studies that have examined the prevalence of tinnitus in the overall population. All studies included for review used questions about tinnitus that were adapted from Davis and Palmer, et al. While questions used by the studies differ in wording to varying degrees, they all sought to find out whether tinnitus was experienced by the participant, and allowed only for “yes” or “no” response options. As such, all studies included for review were able to provide a prevalence estimate for any tinnitus experienced by the overall study population.

In the UK, the National Study of Hearing deployed a postal questionnaire and found the overall weighted-prevalence (n=48,313) of self-reported prolonged spontaneous tinnitus (PST) was 10.1% among adults aged 18 to 80 years. Tinnitus was defined by the questions, “Nowadays do you get noises in your head or ears?” and “Do these noises
last longer than five minutes?” Though not recent, the National Study of Hearing offered the largest study sample for tinnitus prevalence. In Sweden, findings from the Swedish Work Environment Survey showed an unadjusted prevalence of tinnitus was 26.2% among the general working population (n=9,569) aged 16 to 64 years, for any degree of frequency and severity.

In the US, findings from the National Health and Nutrition Examination Survey showed an overall adjusted prevalence for any tinnitus (n=14,178) of 25.3% among adults 20 years and over. Participants were asked, “In the past 12 months, have you ever had ringing, roaring, or buzzing in your ears?” In São Paulo (n=1,960), field survey questionnaires showed an unadjusted tinnitus prevalence (n=430) of 22%.

In South Korea, findings from the Korea National Health and Nutrition Examinations Survey showed an overall adjusted tinnitus prevalence (n=21,893) of 19.7% among people 12 years and over. Participants were asked, “Within the past year, did you ever hear a sound (buzzing, hissing, ringing, humming, roaring, machinery noise) originating in your ear?”

There is little consistency among tinnitus prevalence studies regarding the relationship between tinnitus and sex. Studies from the US, South Korea, and Brazil showed tinnitus was more prevalent among women than men. Conversely, studies from the UK and Sweden showed that tinnitus was more prevalent among men. Prevalence studies from Japan and Nigeria did not show statistically significant differences between sexes.

The increasing prevalence of tinnitus with increasing age has been well established. However, there does not appear to be clear consensus pertaining to age-specific tinnitus prevalence rates. For example, while the US National Health and Nutrition Examination Survey and the UK National Study of Hearing both found the highest prevalence of tinnitus among people aged 60–70 years, yet prevalence estimates were 31.4% in the US and 15.8% in the UK.

A number of studies examined the prevalence of tinnitus specifically among localised elderly populations. In Australia, findings from the Blue Mountains Hearing Study found an adjusted prolonged tinnitus prevalence of 30.3% for people aged 55–99 (n=2,015). Following an audiological assessment, participants were asked, “Have you experienced any prolonged ringing, buzzing or other sounds in your ears or head within the past year, lasting for 5 minutes or longer?” Elsewhere in Australia, prevalence data from the Australian Longitudinal Study of Ageing found that 17.8% of people aged 70 years and over (n=1,453) reported experiencing tinnitus. Participants were asked “Do you

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**Table 1:** Previous studies reporting the prevalence of any tinnitus in the general population (aged ≥14 years)

<table>
<thead>
<tr>
<th>Authors</th>
<th>Year</th>
<th>Study</th>
<th>Sample</th>
<th>Tinnitus Definition</th>
<th>General Adults*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Davis &amp; El Rafaie</td>
<td>2000</td>
<td>National Study of Hearing (UK)</td>
<td>n=48,313</td>
<td>PST</td>
<td>10.1%</td>
</tr>
<tr>
<td>Hasson et al.</td>
<td>2010</td>
<td>Swedish Work Environment, Survey (Sweden)</td>
<td>n=9,569</td>
<td>Tinnitus</td>
<td>26.2% unweighted</td>
</tr>
<tr>
<td>Shargorodsky et al.</td>
<td>2010</td>
<td>National Health and Nutrition Examination Survey (USA),</td>
<td>n=14,178</td>
<td>Tinnitus</td>
<td>25.3%</td>
</tr>
<tr>
<td>Oiticica &amp; Bittar</td>
<td>2014</td>
<td>Field survey questionnaires in São Paulo (Brazil)</td>
<td>n=1,960</td>
<td>Tinnitus</td>
<td>21.9% unweighted</td>
</tr>
<tr>
<td>Park et al.</td>
<td>2014</td>
<td>National Health and Nutrition Examination Survey (S. Korea)</td>
<td>n=21,893</td>
<td>Tinnitus</td>
<td>19.7%</td>
</tr>
</tbody>
</table>

*Prevalence estimates have been adjusted to reflect the national population structure of the study. Unweighted estimates, where specified, represent crude estimates.
have ringing or other noises in your ears or head?” By contrast, the South Korean National Health and Nutrition Examination Surveys found a 32.1% prevalence for the same age group; nearly doubling the rate found in the Australian Longitudinal Study of Ageing.

Studies from Japan and Nigeria tested the same age group, had very similar sample sizes, and deployed a tinnitus question using similar wording. In the township of Kurabuchi, Japan, home-based interviews (n=1,320) with residents 65 years and over found a prevalence of 18.6% for both mild and severe tinnitus combined. Participants were all asked, “In the past year have you experienced any ringing, buzzing, or other sounds in your ears?” In Nigeria, face-to-face interviews with participants 65 years and older found 14.1% experienced some degree of tinnitus. Participants were asked whether they had a perception of ringing, swishing, humming, or other type of noise in the ear or head without an external source of sound.

There has been a lack of population data for tinnitus in New Zealand. It is often presumed that tinnitus prevalence in New Zealand is the same as North America or the UK. However, New Zealand has a different population structure compared to other countries and a diverse ethnic mix, comprising of large Māori, Pacific, Asian and non-European groups. Providing a snapshot of tinnitus in New Zealand, the Dunedin Multidisciplinary Study found that 38.2% of people aged 32 years experienced tinnitus “rarely”, while 6.8% experiencing tinnitus “half the time or more”, and found no difference between sexes. Consistent with other international studies, the tinnitus question used in the Dunedin Multidisciplinary Study was adapted from Davis, which asked participants “In the last 12 months, when you are awake and it is quiet, have you experienced tinnitus (ringing, whistling, or buzzing) in the head or ears?” Participants were offered five response options: never, rarely, about half the time, most of the time, and all the time.

The literature provides little consensus pertaining to the prevalence of tinnitus for the general population. There is also no clear consensus over the prevalence of tinnitus by age or sex. The variations seen in the results from prevalence studies discussed above highlight the need for country-specific prevalence estimates of tinnitus, and the closer examination of prevalence by age and sex. In this paper, we use data that have been adjusted for sampling-weights from the Roy Morgan database (a nationally representative survey) to estimate the prevalence of “any” tinnitus in the New Zealand population, which is inclusive of all forms of tinnitus severity, frequency, and disablement.

### Method

**Data Source:** Roy Morgan Research Limited is an independent, Australian-based marketing firm who also conducts tele-

### Table 2: Previous studies reporting the prevalence of any tinnitus in the older adult population

<table>
<thead>
<tr>
<th>Authors</th>
<th>Year</th>
<th>Study</th>
<th>Sample</th>
<th>Tinnitus Definition</th>
<th>Older Adults</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sanchez et al.</td>
<td>1999</td>
<td>Australian Longitudinal Study of Ageing</td>
<td>n=1,453</td>
<td>Tinnitus</td>
<td>17.8%</td>
</tr>
<tr>
<td></td>
<td></td>
<td>(Australia)</td>
<td>70 years and over</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Davis &amp; El Rafaie</td>
<td>2000</td>
<td>National Study of Hearing</td>
<td>61–70 years</td>
<td>Tinnitus</td>
<td>15.8%</td>
</tr>
<tr>
<td>Sindhusake et al.</td>
<td>2003</td>
<td>Blue Mountains Hearing Study</td>
<td>n=2,015</td>
<td>Prolonged tinnitus</td>
<td>30.3%</td>
</tr>
<tr>
<td></td>
<td></td>
<td>(Australia)</td>
<td>55–99 years</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Michikawa et al.</td>
<td>2010</td>
<td>Community-based interviews</td>
<td>n=1,320</td>
<td>Tinnitus</td>
<td>18.6%</td>
</tr>
<tr>
<td></td>
<td></td>
<td>(Japan)</td>
<td>65 and over</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Lasisi et al.</td>
<td>2010</td>
<td>Nigeria Study of Aging</td>
<td>n=1,302</td>
<td>Tinnitus</td>
<td>14.1%</td>
</tr>
<tr>
<td></td>
<td></td>
<td>(Nigeria)</td>
<td>65 years and over</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Shargorodsky et al.</td>
<td>2010</td>
<td>National Health and Nutrition Examination</td>
<td>60–69 years</td>
<td>Tinnitus</td>
<td>31.4%</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Survey (USA)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Park et al.</td>
<td>2014</td>
<td>National Health and Nutrition Examination</td>
<td>70 years and over</td>
<td>Tinnitus</td>
<td>32.1%</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Survey (Korea)</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
In New Zealand, household telephone access ranged between 86% and 92% (Census 2006 and 2013, respectively), while mobile phone access ranged between 74% and 84% (Census 2006 and 2013, respectively). Given this wide coverage, landlines and RDD of mobile numbers was considered the most nationally representative and robust collection method. The household surveys consisted of data including demographic, social-economic indicators, lifestyle behaviour and attitudes, consumer behaviour, and health conditions.

Quality control (recontacting a proportion of respondents) occurred after each round of interviewing. In New Zealand, surveys conducted by Roy Morgan Research Limited equated to approximately 12,000 eligible samples per year, and allowances for design effect were pre-calculated by Roy Morgan.18

Study Population: Between August, 2007, and July, 2013, 69,976 people aged 14 years and older were interviewed and added to the database. Participants who had already taken part in the survey were excluded from subsequent surveys. Table 3 shows the number of people who were surveyed (n) for each sub-group and their distribution as a proportion of the total sample (%). The sample was adjusted using sampling weights by Roy Morgan Research Limited, accounting for age, sex and region, to represent the New Zealand population. The total weight-adjusted New Zealand population was 3,460,726 people aged ≥14 years.

Sampling weight adjustments were necessary since persons living in small households had a higher-than-average chance of selection. A two-tier weighting system was applied. Firstly, an initial design weight (a priori weight) was assigned to each respondent. The sum of these design weights

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>No. of People Surveyed (n=)</th>
<th>Proportion of Total Sample (Crude)</th>
<th>Proportion of Total Sample (Weighted)</th>
<th>Proportion of Total Sample (Census 2013)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total Population</td>
<td>69,976</td>
<td>100%</td>
<td>100%</td>
<td>100%</td>
</tr>
<tr>
<td>Sex</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>27,100</td>
<td>38.7%</td>
<td>48.5%</td>
<td>48.1%</td>
</tr>
<tr>
<td>Female</td>
<td>42,876</td>
<td>61.3%</td>
<td>51.5%</td>
<td>51.9%</td>
</tr>
<tr>
<td>Age</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>14–24</td>
<td>8,421</td>
<td>12.0%</td>
<td>19.9%</td>
<td>19.3%</td>
</tr>
<tr>
<td>25–34</td>
<td>9,727</td>
<td>13.9%</td>
<td>16.0%</td>
<td>14.9%</td>
</tr>
<tr>
<td>35–49</td>
<td>19,286</td>
<td>27.6%</td>
<td>26.6%</td>
<td>25.3%</td>
</tr>
<tr>
<td>50–64</td>
<td>18,539</td>
<td>26.5%</td>
<td>22.0%</td>
<td>23.0%</td>
</tr>
<tr>
<td>65 and Over</td>
<td>14,003</td>
<td>20.0%</td>
<td>15.5%</td>
<td>17.6%</td>
</tr>
<tr>
<td>Ethnicity*</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>European</td>
<td>53,645</td>
<td>75.6%</td>
<td>72.6%</td>
<td>68.1%</td>
</tr>
<tr>
<td>Māori</td>
<td>6,435</td>
<td>9.1%</td>
<td>10.3%</td>
<td>12.4%</td>
</tr>
<tr>
<td>Pacific Islanders</td>
<td>1,639</td>
<td>2.3%</td>
<td>3.4%</td>
<td>5.3%</td>
</tr>
<tr>
<td>Asian</td>
<td>2,843</td>
<td>4.0%</td>
<td>6.0%</td>
<td>11.5%</td>
</tr>
<tr>
<td>Other</td>
<td>6,385</td>
<td>9.0%</td>
<td>9.5%</td>
<td>2.7%</td>
</tr>
</tbody>
</table>

*Census ethnicity structure based on prioritised output
were compared with the population profile to determine the final weights to be applied.

A combination of cell and rim weighting were applied to achieve the population targets that reflect the population structure of the 2013 New Zealand Census (Table 3). For example, the original sample consisted of 38.7% male and 61.3% female. After adjustment, the sample consisted of 48.5% male and 51.5% female, reflecting the sex distribution of the 2013 New Zealand Census. The largest group by age was the 35 to 49 years group (26.6%), while the largest group by ethnicity was European (72.6%).

**Measure:** As part of the Roy Morgan household surveys, participants were asked, “Which of the following illnesses or conditions have you had in the last 12 months?” Among other health conditions, ear and hearing conditions, including tinnitus, were asked. For “Tinnitus”, the response options were “Yes” and “No”. The tinnitus question was loosely modelled on Davis\(^6\) in terms of the “last 12 months”. An explanation of tinnitus, such as ringing or buzzing in the ears, was not provided to the participants. There was no integration or follow-up questioning regarding the frequency and/or severity of tinnitus. As such, the measure of tinnitus in this study is that of *any* tinnitus.

**Statistical Analysis:** The data used in our analysis have been accessible since November, 2013, from the Roy Morgan database, using Asteroid version 5.14 (Roy Morgan Research Ltd, Melbourne). Sampling weight adjusted data (available from the Roy Morgan database) enabled us to provide population estimates in our results. Fisher’s exact tests were carried out to determine the differences in prevalence estimates (expressed as a prevalence rate ratio [PRR]) between males and females, and older-adult and younger-adult sub-groups. Calculations were conducted in R Statistics version 3.2.0 (http://www.r-project.org).

**Results**

**Overall Prevalence:** The overall weighted prevalence for *any* tinnitus was 5.98% (95% CI = 5.95–6.00) in the total New Zealand population aged ≥14 years (Table 4). Among 69,976 participants, 4,771 reported experiencing tinnitus in the last 12 months, equating to approximately 207,000 people in the New Zealand population.
(Table 5). Overall, the prevalence of tinnitus was higher among males (6.45%, 95% CI = 6.42–6.49) compared to females (5.53%, 95% CI = 5.50–5.57). Tinnitus prevalence increased with increasing age, starting at 1.6% (95% CI = 1.57–1.63) for young people aged 14 to 24 years, and peaking at 13.5% (95% CI = 13.41–13.59) for people aged 65 years and over. Tinnitus prevalence was highest among people identifying as European (7.05%, 95% CI = 7.02–7.08) and lowest among people identifying as Asian (1.00%; 95% CI = 0.95–1.04). Notably, tinnitus prevalence was relatively high among people who identified with Other ethnicity (5.31%; 95% CI = 5.23–5.38).

**Prevalence by Sex:** In the total population, males were slightly more likely to report any tinnitus compared to females (PRR = 1.17; 95% CI = 1.16–1.18, p < .01). This higher prevalence seen among males accounts for nearly 10,000 more cases of tinnitus in the total male population (Table 5). Across sub-groups (with the exception of Pacific Peoples), males were more likely to report any tinnitus compared to females (PRR = 1.55, 95% CI = 1.49–1.61, p < .01). A notable difference by sex was also seen among adults aged 50 to 64 years, with males 32% more likely to report tinnitus compared to females (PRR = 1.32, 95% CI = 1.30–1.34).

In addition to differences by sex, there were also ethnic variations in tinnitus prevalence. The largest difference by sex was seen among both Māori (PRR = 1.32, 95% CI = 1.27–1.38, p < .01) and Asian (PRR = 1.32, 95% CI = 1.20–1.45), where males were 32% more likely to report tinnitus compared to females. Pacific Peoples was the only subgroup where females were more likely to experience any tinnitus compared to males (PRR = 0.85, CI 95%, 0.76–0.96, p < .01).

**Prevalence by Age:** Across all groups, tinnitus prevalence was much higher among elderly adults (Table 7). By sex, estimates were highest among older adults who were male (14.28%), while by ethnicity, estimates were highest among older people who were either European (13.69%) or Other ethnicity (13.47%). By contrast, the prevalence estimate for Asian (5.80%) is relatively low when compared to other ethnic groups in the older adult age group.

Overall, older adults aged 65 years and over were nearly three times more likely to report tinnitus than younger adults

### Table 5: Weighted frequencies of people affected by tinnitus in New Zealand

<table>
<thead>
<tr>
<th>Weighted frequencies</th>
<th>Total</th>
<th>Male</th>
<th>Female</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Total Population</strong></td>
<td>206,915</td>
<td>108,329</td>
<td>98,587</td>
</tr>
<tr>
<td><strong>Age</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>14–24</td>
<td>11,032</td>
<td>6,789</td>
<td>4,243</td>
</tr>
<tr>
<td>25–34</td>
<td>14,579</td>
<td>7,659</td>
<td>6,921</td>
</tr>
<tr>
<td>35–49</td>
<td>42,611</td>
<td>21,804</td>
<td>20,807</td>
</tr>
<tr>
<td>50–64</td>
<td>66,345</td>
<td>37,125</td>
<td>29,220</td>
</tr>
<tr>
<td>65 and Over</td>
<td>72,348</td>
<td>34,952</td>
<td>37,396</td>
</tr>
<tr>
<td><strong>Ethnicity</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>European</td>
<td>177,074</td>
<td>93,347</td>
<td>83,727</td>
</tr>
<tr>
<td>Māori</td>
<td>10,279</td>
<td>5,188</td>
<td>5,091</td>
</tr>
<tr>
<td>Pacific Peoples</td>
<td>1,251</td>
<td>509</td>
<td>742</td>
</tr>
<tr>
<td>Asian</td>
<td>2,074</td>
<td>1,358</td>
<td>716</td>
</tr>
<tr>
<td>Other</td>
<td>17,510</td>
<td>8,709</td>
<td>8,801</td>
</tr>
</tbody>
</table>
Table 6: Tinnitus weighted prevalence by sex in the New Zealand adult population (aged ≥14 years)

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Male Weighted Prevalence (%)</th>
<th>Female Weighted Prevalence (%)</th>
<th>Prevalence Rate Ratio</th>
<th>95% CI (p &lt; .01)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total Population</td>
<td>6.45</td>
<td>5.53</td>
<td>1.17</td>
<td>1.16–1.18</td>
</tr>
<tr>
<td><strong>Age</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>14–24</td>
<td>1.94</td>
<td>1.25</td>
<td>1.55</td>
<td>1.49–1.61</td>
</tr>
<tr>
<td>25–34</td>
<td>2.86</td>
<td>2.42</td>
<td>1.18</td>
<td>1.14–1.22</td>
</tr>
<tr>
<td>35–49</td>
<td>4.92</td>
<td>4.34</td>
<td>1.13</td>
<td>1.11–1.16</td>
</tr>
<tr>
<td>50–64</td>
<td>9.95</td>
<td>7.54</td>
<td>1.32</td>
<td>1.30–1.34</td>
</tr>
<tr>
<td>65 and Over</td>
<td>14.28</td>
<td>12.85</td>
<td>1.11</td>
<td>1.09–1.13</td>
</tr>
<tr>
<td><strong>Ethnicity</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>European</td>
<td>7.65</td>
<td>6.48</td>
<td>1.18</td>
<td>1.17–1.19</td>
</tr>
<tr>
<td>Māori</td>
<td>3.36</td>
<td>2.54</td>
<td>1.32</td>
<td>1.27–1.38</td>
</tr>
<tr>
<td>Pacific Peoples</td>
<td>0.98</td>
<td>1.15</td>
<td>0.85</td>
<td>0.76–0.96</td>
</tr>
<tr>
<td>Asian</td>
<td>1.11</td>
<td>0.84</td>
<td>1.32</td>
<td>1.20–1.45</td>
</tr>
<tr>
<td>Other</td>
<td>5.48</td>
<td>5.15</td>
<td>1.07</td>
<td>1.03–1.10</td>
</tr>
</tbody>
</table>

Table 7: Tinnitus weighted prevalence by age (65 years and over) and younger adults (under 65 years)

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Older Adults (≥ 65 years) Weighted prevalence (%)</th>
<th>Younger Adults (&lt; 65 years) Weighted prevalence (%)</th>
<th>Prevalence Rate Ratio</th>
<th>95% CI (p &lt; .01)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total Population</td>
<td>13.50</td>
<td>4.60</td>
<td>2.93</td>
<td>2.91–2.96</td>
</tr>
<tr>
<td><strong>Sex</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>14.28</td>
<td>5.12</td>
<td>2.79</td>
<td>2.75–2.83</td>
</tr>
<tr>
<td>Female</td>
<td>12.85</td>
<td>4.10</td>
<td>3.13</td>
<td>3.09–3.17</td>
</tr>
<tr>
<td><strong>Ethnicity</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>European</td>
<td>13.69</td>
<td>5.48</td>
<td>2.50</td>
<td>2.47–2.52</td>
</tr>
<tr>
<td>Māori</td>
<td>11.23</td>
<td>2.41</td>
<td>4.67</td>
<td>4.44–4.90</td>
</tr>
<tr>
<td>Pacific Peoples</td>
<td>10.39</td>
<td>0.89</td>
<td>11.64</td>
<td>10.00–13.52</td>
</tr>
<tr>
<td>Asian</td>
<td>5.80</td>
<td>0.92</td>
<td>6.33</td>
<td>5.42–7.37</td>
</tr>
<tr>
<td>Other</td>
<td>13.47</td>
<td>4.39</td>
<td>3.07</td>
<td>2.96–3.18</td>
</tr>
</tbody>
</table>

Aged under 65 years (PRR = 2.93; 95% CI = 2.91–2.96, p < .01). By ethnicity, the likelihood of older adults reporting tinnitus, compared to younger adults, was two and a half times for European (PRR = 2.50; 95% CI = 2.47–2.52, p < .01) and over 11 times for Pacific Peoples (PRR = 11.64; 95% CI = 10.00–13.52, p < .01), suggesting greater age-inequality among Pacific Peoples compared to other ethnic groups.

**Discussion**

This is the first nationally representative study of any tinnitus in New Zealand. To our knowledge, this is also the largest study sample for tinnitus prevalence to date, both nationally and internationally. The overall weighted prevalence of any tinnitus in New Zealand was 6.0%, corresponding to approximately 207,000 New Zealanders.
aged ≥14 years. This prevalence estimate is substantially lower than prevalence estimates reported in existing cross-sectional studies internationally, which ranged between 10.1% and 26.2%. Our results correspond closest to the adjusted-prevalence from the UK National Study of Hearing, where 10.1% of adults aged 18 to 80 years reported prolonged spontaneous tinnitus. It is important to note that some tinnitus prevalence estimates cited in this paper have not been standardised to a single population and as such, care should be taken when comparing total prevalence rates from different studies.

Our results indicate that males had a marginally higher, statistically significant (p<.01), adjusted prevalence of any tinnitus compared to females in New Zealand. Our finding for the general population was consistent with the results from the UK, Sweden, the US, and Australia, which showed a higher male tinnitus prevalence compared to female. Our results showed that the difference between sexes was most pronounced in three sub-groups: people aged 50 to 64 years, people who identified as Māori; and people who identified as Asian. While another study based in New Zealand found no difference between sexes for tinnitus overall, those researchers only interviewed people aged 32 years from the Dunedin Multidisciplinary Study birth cohort. When we stratified our results by age, we also found no difference between sexes for the participants aged 30 to 34 years (PRR = 0.98; 95% CI = 0.94–1.03, p=0.43), suggesting that the difference between sexes for tinnitus cannot be adequately captured when sampling is limited to this age group.

The prevalence for elderly people over the age of 65 years was 13.5%; highest of all age groups. Our findings were consistent with two other studies that examined tinnitus prevalence for the same age group; the community-based study in Japan, which showed an 18.6% prevalence of any tinnitus, and the Nigeria Study of Aging, which showed a 14.1% prevalence of any tinnitus. The studies from Japan and Nigeria were similar in sampling and measurement, and despite their obvious ethnic heterogeneity, there was only a 4.5% difference in their results. As age-specific rates, these prevalence estimates can offer some useful comparison between countries. However, care should still be taken for a country, like Japan, where the population is rapidly aging.

However, geographic, age, and ethnic homogeneity may not always provide consistent results. For instance, despite similarities in sampling age and study context, the two Australian studies differ greatly in prevalence estimates; with the Australian Longitudinal Study of Aging finding 17.8% for people 70 years and over, compared to 30.3% for people 55 to 99 years found in the Blue Mountains Hearing Study. We believe these differences in the estimated tinnitus prevalence in these studies may result from the differences in the questions used to identify tinnitus. Where the Australian Longitudinal Study of Aging very broadly asked participants whether they had “ringing or other noises” in their ears or heads, the Blue Mountains Hearing Study asked participants about “prolonged” tinnitus “lasting for 5 minutes or longer”.

In the New Zealand context, our results for adults in the 30–34 year age group for “any” tinnitus (3.68%, 95% CI = 3.60–3.76) did not correspond with the findings from Welch and Dawes, where 6.8% of people age 32 years from the Dunedin Multidisciplinary Study experienced tinnitus half the time. The key difference between our study and that of Welch and Dawes again lies in the structure of questions concerning tinnitus and the response types offered to the participants. The Dunedin Multidisciplinary Study included the words “when you are awake and it is quiet” in the question, and offered “half the time or more” in the response options. We believe that the inclusion of the proportion of time experienced by the individual, while very useful, may have encouraged participants to select responses other than “never”, thus capturing people with very minor “non-clinical” tinnitus. We also believe that providing a description of tinnitus alongside the Roy Morgan survey question would have increased the response rate for tinnitus in our study, since many people may not know what tinnitus is. As such, our results may represent those with clinically significant tinnitus while the Dunedin
Multidisciplinary Study and others may have captured more people who experienced tinnitus, but were not bothered by it.

In general, ethnic variations in tinnitus prevalence remain largely under-explored in the literature. Our results indicate that the New Zealand European group were more likely to report any tinnitus compared to other ethnic groups. This finding is consistent with US National Health and Nutritional Examination Survey, which found a higher overall tinnitus prevalence among the “White” ethnic group compared to the non-Hispanic group. When examining ethnic sub-groups, two key issues exist that may have played a part in skewing our results.

Firstly, ethnic heterogeneity is more common in English-speaking countries—such as New Zealand, Australia, the UK, and the US—compared to countries such as Japan, South Korea, or Nigeria. Indeed, our results show strong ethnic variations in tinnitus prevalence within each “White” or age specific group. For instance, the Pacific group had the largest inequality in prevalence between older adults and younger adults (PRR = 11.64, 95% CI = 10.00–13.52, \( p < .01 \)), which was marked by a high prevalence of tinnitus among the people over 65 years, and a low prevalence among people under 65 years. Similarly, the Asian group shares the same inequality. However, the prevalence of tinnitus among Asian people are relatively low compared to other ethnic groups, for both older adult and younger adult age groups. These ethnic variations, particularly for Pacific and Asian people, may be due to under-reporting as a result of not fully understanding the survey question.

Secondly, while the effects of ethnicity on socio-economic indicators are well established in New Zealand, the effects of socio-economic indicators and access to health services on tinnitus outcome remains unclear. For instance, findings from the Dunedin Multidisciplinary Study found that people from lower socioeconomic backgrounds were more likely to report tinnitus, and that tinnitus sufferers were more likely to be socially withdrawn, reactive to stress, and alienated. While this finding seems plausible given its generalisability to chronic conditions overall, we found that Pacific Peoples had the lowest prevalence of tinnitus (1.08%, 95% CI = 1.02–1.14). Since the Pacific ethnic group is often marked by both poorer health outcomes and lower socio-economic status, it is unclear whether the low tinnitus estimate is a result of underreporting or service underutilisation. Similarly, it is unclear whether the very low prevalence of tinnitus found among the Asian group (1.00%, 95% CI = 0.95–1.04) was a result of service underutilisation or the healthy migrant effect.

Another limitation in this study relates to the sampling method deployed by Roy Morgan. Since low-income earners tend to have no access to a landline or mobile phone, we may not have adequately sampled low-income earners, resulting in bias. Furthermore, our survey did not include follow-up questions to determine the frequency or severity of tinnitus experienced by survey participants. As such, we were restricted to prevalence estimates for any tinnitus and were unable to estimate tinnitus by level of severity (eg, “mild” vs. severe) or frequency (eg, sometimes vs. always). The restriction of response items to “yes” and “no”, and the lack of follow-up questioning, may have reduced the response rate in our study. However, even with its inclusion, follow-up questions are useful only in understanding the variations of tinnitus frequency and severity in a study population. Nevertheless, the inclusion of follow-up questions would do little to remove the uncertainty in results that arise from subjective tinnitus self-assessments, or the lack of objective measure for the symptoms of tinnitus. These limitations highlight the need for longitudinal studies that integrate audiological methods for determining tinnitus severity. Another limitation was the lack of ethnicity weighting applied to the survey population.

This paper provides a preliminary investigation into the sex, age, and ethnic profile of people who experience some form of tinnitus in New Zealand. This also provides an opportunity to further explore the predictors or comorbidities of tinnitus suffers in the New Zealand context. Furthermore, given New Zealand’s ethnic heterogeneity, community-based sampling for tinnitus research may be explored. Follow-up questions may be included in future research to understand...
the frequency of tinnitus experienced by the study participant, while audiological assessments such as the Tinnitus Functional Index (TFI), Tinnitus Handicap Inventory (THI), or Tinnitus Handicap Questionnaire (THQ) may be carried out to understand the severity of tinnitus.

**Conclusion**

Tinnitus is a chronic public health problem affecting over 207,000 people in the New Zealand population aged ≥14 years. Better understanding the prevalence of tinnitus contributes toward meeting health service needs and identifying high-risk groups in New Zealand. This study has highlighted the importance of sex and age in defining a high-risk tinnitus population, but our knowledge falls short of profiling their ethnic and social-economic characteristics. While our study has revealed some insight into ethnic variations in tinnitus prevalence in New Zealand, the effect of ethnicity on tinnitus remains largely unexplored.

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**REFERENCES:**

ARTICLE


Laparoscopic adrenalectomy for phaeochromocytoma: a case series
Cheri Hotu, Richard Harman, Rick Cutfield, Nicola Hodges, Eletha Taylor, Simon Young

ABSTRACT
AIM: To describe our 13-year experience in laparoscopic adrenalectomy for phaeochromocytoma.

METHOD: We performed a retrospective analysis of case notes of 29 patients who underwent laparoscopic adrenalectomy for phaeochromocytoma between 2000 and 2013.

RESULTS: Twenty-nine patients (16 female), aged 16 to 67 years, underwent laparoscopic adrenalectomy for phaeochromocytoma. All patients were treated preoperatively with alpha-blocking agents. 80% were prescribed additional preoperative antihypertensive agents. 90% received antihypertensive agents intraoperatively. All patients received intraoperative magnesium sulphate for haemodynamic stabilisation. The mean operative time was 160 minutes. Nearly all of the patients experienced haemodynamic stability during surgery. Two patients required conversion to open adrenalectomy, due to severe intraoperative hypertension during tumour handling, and due to extensive intra-abdominal adhesions. Postoperative complications were minimal, and included blood loss, superior epigastric artery damage, and cellulitis at the laparoscopic port site. There was no perioperative mortality. The median length of stay postoperatively was 4 days. 24% were prescribed antihypertensive medication on discharge.

CONCLUSION: In our experience, favourable perioperative outcomes were achieved, demonstrating that laparoscopic adrenalectomy for phaeochromocytoma is a safe and effective procedure in the setting of experienced and skilled surgical, anaesthetic and medical teams delivering the perioperative care.

The laparoscopic approach to adrenalectomy, first described in 1992 by Gagner et al., has become the preferred option over open laparotomy for the removal of most adrenal tumours, functioning or non-functioning, and is considered a safe and effective surgical method. Although often associated with longer operative times when compared to open laparotomy, the advantages of laparoscopic adrenalectomy are in its association with less intraoperative and postoperative morbidity and complications. These include lower rates of intraoperative trauma and blood loss, a decreased need for postoperative analgesia, quicker recovery times and shorter hospitalisation periods. These benefits can lead to increased cost-effectiveness in most but not all cases. Vascular injury and bleeding can still occur with laparoscopic adrenalectomy, and when compared to the removal of aldosterone-secreting tumours, laparoscopic adrenalectomy for phaeochromocytoma removal has been associated with larger tumours, longer operative times and increased complication rates.

Intravenous (IV) magnesium sulphate has been shown to be an effective adjunct in the anaesthetic management of open adrenalectomy for phaeochromocytoma removal through its ability to decrease catecholamine release and control the cardiovascular instability associated with this procedure. One case report has described the effectiveness of magnesium sulphate during laparoscopic adrenalectomy for phaeochromocytoma in a paediatric patient. Publications on the use of magnesium sulphate in this setting are few. We found no published retrospective, clinical case series on laparoscopic adrenalectomy for phaeochromocytoma using adjunctive IV magnesium sulphate intraoperatively.
**Method**

We carried out a 13-year retrospective analysis of experience in laparoscopic adrenalectomy for phaeochromocytoma at a tertiary hospital in New Zealand between 2000 and 2013. The study was approved by the local district health board research review committee. As a clinical audit, it was given exemption from review by the regional ethics committee. Patient demographics, co-morbidities, family history, clinical presentation, biochemical and radiological investigations, preoperative blood pressure (BP), and medications were reviewed. The use of intraoperative antihypertensive agents, vasopressor agents and magnesium sulphate was recorded. Intra- and postoperative outcomes, including mean operative times, intraoperative BP, blood loss, postoperative complications, IV analgesic requirements and postoperative duration of hospital stay were reviewed, as were BP and antihypertensive medication at discharge. The surgery was performed by a laparoscopic surgeon, experienced in performing laparoscopic adrenalectomy for the removal of adrenal tumours, including phaeochromocytoma. Anaesthetic support was provided by an experienced anaesthetic team. Perioperative care was also provided by experienced nursing staff. Pre- and postoperative antihypertensive therapy was overseen by an endocrinologist.

**Results**

Twenty-nine patients (16 female and 13 male) underwent laparoscopic adrenalectomy for phaeochromocytoma. Ages ranged from 16 to 67 years; the mean age was 46 years. There were 22 European, three Māori, two Samoan, one Niuean and one Thai patient. Most cases involved sporadic tumours. One patient had a history of Von Hippel-Lindau (VHL) syndrome with associated renal, ocular and intra-cerebral stigmata. His father and brother also had VHL syndrome. Another patient had a simultaneous renal cell carcinoma and a positive family history for phaeochromocytoma, but tested negative for the VHL gene mutation. One patient had multiple endocrine neoplasia (MEN) 2B with a history of medullary thyroid cancer. Another patient had a history of bilateral phaeochromocytomas and had previously undergone a left adrenalectomy for phaeochromocytoma removal. Three patients had one or more first-degree relatives with a history of phaeochromocytoma.

The majority of patients underwent investigation for phaeochromocytoma based on clinical suspicion from their presenting symptoms and signs. Nineteen patients presented with either sustained or paroxysmal hypertension, and hypertensive crises during surgical procedures were reported in five patients. Episodic headaches and palpitations were reported in 14 patients respectively. Seven patients experienced profuse sweating, and five patients had episodic chest pain. Four patients experienced anxiety attacks and one patient presented with a manic episode. Four patients had incidental findings of an adrenal mass, detected in one patient during a renal tract ultrasound scan for investigation of chronic kidney disease, and during computed tomography (CT) scanning in the other three patients. One patient had undergone a staging CT scan for bowel cancer, the second patient had an abdominal CT scan for investigation of abdominal pain, and the third patient underwent a pulmonary CT scan following an episode of haemoptysis.

All of the patients underwent measurement of 24-hour urinary catecholamines or metanephrines, or plasma metanephrines, and in some cases both tests were done. Elevated catecholamine or metanephrine levels were seen in all of the patients.

The patient with previous resection of a contralateral phaeochromocytoma, and the patient with VHL syndrome, were both found to have elevated urinary catecholamines during routine surveillance screening. Diagnostic imaging modalities used included CT imaging in 16 patients and magnetic resonance imaging (MRI) in 16 patients. Six patients had a metaiodobenzylguanidine (MIBG) scan in addition to MRI or CT.

Eighteen patients had right-sided adrenal phaeochromocytomas, the remainder had left-sided lesions.

All of the patients received alpha-blocking agents preoperatively. Phenoxybenzamine...
was used in 26 patients, doxazosin in two
patients, and labetalol in one patient. Twenty-
three patients (80%) were taking other
antihypertensive medications preopera-
tively in addition to the above medications.
Beta blockers were prescribed in 15
patients, calcium channel blockers in 10
patients, thiazide diuretics in two patients,
and an angiotensin converting enzyme
(ACE) inhibitor and an angiotensin receptor
blocker (ARB) in one patient, respectively.
At hospital admission, the mean (SD) preop-
erative systolic and diastolic BPs were 142
(24) mmHg and 86 (12) mmHg respectively.
Median (IQR) preoperative systolic and
diastolic BPs were 144 (124-155) mmHg and
85 (80–90) mmHg respectively.
The mean operation time was 160
minutes (59–260 minutes). The patient with
renal cell carcinoma underwent a right
laparoscopic adrenalectomy and right
nephrectomy. Another patient underwent a
simultaneous right hemicolectomy for colon
cancer. All of the patients received intraop-
erative magnesium sulphate, administered
as boluses of 2.5 to 4 grams (g) and in infu-
sions of 1 to 2.5 g/hour. Twenty-six patients
(90%) received IV antihypertensive medi-
cation intraoperatively. Twenty patients
received esmolol, five patients received
glyceryl trinitrate, and 10 patients were
administered sodium nitroprusside. Ten
patients received more than one antihy-
pertensive agent intraoperatively. Four
patients experienced systolic BP spikes of
≥200 mmHg intraoperatively but this was
for a brief duration (<2 minutes) in most
cases. Two patients required conversion to
open adrenalectomy, one patient developed
severe intraoperative hypertension (270/160
mmHg) during tumour handling, and
the other patient had significant saccing
present between the tumour and the aorta.
Thirteen patients received intraoperative
vasopressor infusions. Noradrenaline
was the most common vasopressor agent
used. Five patients experienced brief
episodes of intraoperative hypotension
(systolic BP<80mmHg), but this was quickly
corrected with the use of volume expanders
and vasopressor administration. None
of the patients developed intraoperative
arrrhythmias. Blood loss was <500 ml in 14
of the 16 patients who had this quantified.
The maximum recorded blood loss was
1,200 ml. One patient sustained intraopera-
tive damage to the left superior epigastric
artery which required repair. Prolonged
neuromuscular blockade was not reported
in any of the cases.
Three patients required IV analgesia
for >24 hours postoperatively. The patient
who underwent open adrenalectomy after
developing severe intraoperative hyper-
tension received bupivacaine and fentanyl
via an epidural infusion for 4 days post-
operatively. Postoperative complications
included cellulitis at a laparoscopic port
site, urinary retention, and pneumonia
in three respective patients. The median
length of stay was 2 days preoperatively
and 4 days postoperatively. Twenty-six
patients had 6 days or less hospital stay
postoperatively. The other three patients
had 7, 13 and 14 post-operative days stay
respectively. There was no perioperative
mortality. On histological inspection, the
mean tumour size was 45 mm (25–75 mm).
Twenty-seven of the tumours were benign,
one was multifocal and one was malignant.
At hospital discharge, the mean (SD) systolic
and diastolic BPs were 123 (18) mmHg
and 73 (12) mmHg respectively. Median
(IQR) systolic and diastolic BPs were 120
(110–140) mmHg and 72 (60–80) mmHg
respectively. Seven out of 29 patients (24%)
were prescribed antihypertensive medi-
cations on discharge from hospital. Beta
blockers were prescribed in four patients.
Calcium channel blockers, ACE inhibitors,
ARBs and thiazide diuretics were prescribed
in one patient respectively.

Discussion
Phaeochromocytomas are rare, catecho-
lamine-secreting tumours that arise from
the chromaffin cells of the adrenal medulla.
The annual incidence is approximately
0.8 per 100,000 person years.\textsuperscript{21}
Untreated phaeochromocytomas are associated with a
high incidence of morbidity and mortality.
The most common symptom of phaeo-
chromocytoma is sustained or paroxysmal
hypertension. Other common symptoms
include episodic headache, sweating and
palpitations. Panic attack-type symptoms,
gereralised weakness, tremor and pallor
are less common symptoms. Phaeochro-
mocytoma has been associated with
cardiomyopathy due to excess catecho-
lamine release, similar to stress-induced takatsubo cardiomyopathy.

Whilst most phaeochromocytomas are sporadic, approximately 30% are familial. VHL syndrome, MEN2, and neurofibromatosis type 1 (NF1) are the familial disorders associated with phaeochromocytoma. Following biochemical confirmation of the diagnosis, clinical practice guidelines recommend CT scanning of the adrenal glands as the initial imaging test, however MRI should be considered when there is evidence of metastatic disease or when limitation of radiation exposure is crucial, for example during pregnancy. MIBG scintigraphy is useful for locating metastatic paragangliomas, however positron emission tomography (PET)/CT scanning is the preferred imaging modality in patients with metastatic paragangliomas.

The definitive treatment for phaeochromocytoma is surgical removal of the tumour.

Laparoscopic adrenalectomy has been shown to be a safe and effective procedure for the removal of adrenal tumours including phaeochromocytoma. For favourable outcomes to be achieved in the surgical management of patients with phaeochromocytoma, it is important that adequate perioperative care be delivered. While it is unclear whether all patients awaiting surgery for phaeochromocytoma removal need preoperative hypotensive treatment, there is evidence to suggest benefit in patients with BP >180/115 mmHg, and in those with complications of hypertension, including heart failure, coronary artery disease, stroke and dysrrhythmias, and during pregnancy.

Haemodynamic changes, including an increase in heart rate and BP, are part of the normal physiologic response to stress and these predictably occur during laryngoscopy and tracheal intubation for any surgical procedure. Haemodynamic instability, in particular intraoperative hypertension, is common during phaeochromocytoma surgery due to an exaggerated release of catecholamines occurring throughout the different stages of airway management and surgery, with one series reporting intraoperative hypertension (systolic BP >200mmHg) in 58% of cases. Intraoperative hypertension can be severe and sustained, often requiring the use of potent antihypertensive agents to control it. Pneumoperitoneum induced during laparoscopic adrenalectomy, and in particular, handling of the phaeochromocytoma tumour can result in marked catecholamine release resulting in severe hypertension. Effective intraoperative management of BP is therefore crucial during phaeochromocytoma surgery. Careful handling of the tumour tissue, limited intra-abdominal pressure, adequate anaesthesia and the use of vasoactive agents are important components of achieving intraoperative BP stability and reducing the risk of complications secondary to elevated intraoperative BP. Rapid-acting antihypertensive agents that allow for a reduction of BP, without exerting a prolonged effect, can be particularly beneficial at the time of tumour removal. Intraoperative hypotension may also occur during surgery for phaeochromocytoma, particularly following tumour removal, with one series reporting intraoperative hypotension in 53% of cases. Proficient anaesthetic management with the use of volume expanders and vasopressor administration can prevent sustained episodes of hypotension from occurring.

There is limited information in the literature on the efficacy of adjunctive therapeutic agents to achieve haemodynamic stability intraoperatively in phaeochromocytoma removal. Magnesium sulphate, which acts as a calcium channel antagonist, has been shown to enhance cardiac and haemodynamic stability by inducing peripheral vasodilation and increasing anti-arrhythmic effects by inhibiting catecholamine release from the adrenal medulla, and by decreasing alpha-adrenergic receptor sensitivity to catecholamines. The resultant peripheral vasodilation leads to a decrease in systemic vascular resistance and a lowering of arterial systolic BP. The effectiveness of magnesium sulphate has been described in the control of severe hypertension in the setting of phaeochromocytoma crisis. Studies and case reports have shown high dose magnesium sulphate to be effective in reducing catecholamine levels during anaesthetic induction and
intubation, leading to a decrease in BP and heart rate.\textsuperscript{18,19,29} Serum magnesium levels between 2–4 mmol/l are associated with a significant attenuation of catecholamine output during tracheal intubation.\textsuperscript{18,19,27} Although catecholamine release resulting from tumour handling is not inhibited by the use of magnesium sulphate, the effectiveness of this agent during tumour handling is thought to be due to its ability to reduce alpha-adrenergic receptor sensitivity to catecholamines.\textsuperscript{18} Potential complications associated with magnesium sulphate include prolonged neuromuscular blockade,\textsuperscript{30} emphasising the importance of monitoring neuromuscular function in the immediate postoperative period, and the cautious dosing of muscle relaxants.

Our case series demonstrated favourable perioperative outcomes in patients undergoing laparoscopic adrenalectomy for phaeochromocytoma. Apart from one patient who developed severe, sustained intraoperative hypertension requiring conversion to open adrenalectomy, haemodynamic stability was maintained in the majority of patients, and while 10 of the patients required more than one antihypertensive agent during surgery, BP was controlled without difficulty in most cases, and sustained elevations of BP were not seen. Intraoperative hypotension also occurred infrequently and was non-sustained. Postoperative complications were minimal and there was no mortality. More than two-thirds of patients treated with antihypertensive therapy preoperatively (in addition to adrenergic receptor blockade) did not require these medications on discharge from hospital. Experienced surgical, anaesthetic and medical teams delivering a high standard of surgical and perioperative care to the patients likely contributed to favourable outcomes achieved.

Several limitations were identified in the study. The clinical data reviewed came from a single centre only, and the study’s retrospective design precluded our ability to identify any causal relationship between intervention and perioperative outcomes. Another important limitation was around the accuracy and precision of manual recordings in the anaesthetic records of eight patients, resulting in difficulty to calculate parameters such as the mean and median intraoperative BP. The precise duration from incision to wound closure was difficult to ascertain in some of the cases due to limited recording of the specific stages of the operation within the patient notes. The mean operation time is likely to have been overestimated due to this factor. Also, the lack of a control group makes it difficult to conclude how much benefit magnesium sulphate had in addition to adequate preoperative alpha blockade and intraoperative antihypertensive use. A blinded placebo controlled study is therefore needed to further evaluate the utility of magnesium sulphate during laparoscopic adrenalectomy for phaeochromocytoma.
Competing interests: Nil

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REFERENCES:


An audit of paediatric referrals to the Southern Cochlear Implant Programme (2009–2014)

Jill Mustard, Megan Chinnery, Alice K Guidera, Neil Heslop, Philip A Bird

ABSTRACT

AIM: To determine the effect of the Universal Newborn Hearing Screening and Early Intervention Programme on the age of referral and implantation of prelingually deaf children in the Southern Cochlear Implant Programme.

METHOD: A retrospective review of data collected prospectively from March 2003 to August 2014.

RESULTS: 123 children were referred to the programme with prelingual deafness in the time period. There was a significant decrease in the age of referral (median 6.23 months vs. 21.50 months) and age at implantation (12.66 months vs. 24.0 months) in those that underwent newborn hearing screening. Reasons for delay in referral and implantation were identified.

CONCLUSION: The introduction of universal newborn hearing screening has significantly reduced the age at referral and implantation of prelingually deaf children. However, the screening programme must continue to undergo monitoring and regular audit. Efforts must also be made to reduce the time to referral, including reducing non-attendance rates, education for parents and service providers, and earlier referral of those with comorbidities so as to reduce the time to implantation.

The Southern Cochlear Implant Programme (SCIP) was established in 2003 in Christchurch, New Zealand, and expanded to include a clinic in the Wellington region in 2014. SCIP provides cochlear implant assessment, surgery, audiological and rehabilitation services for children and adults throughout the South Island and the lower North Island. A cochlear implant is a device that can replace the auditory function of the inner ear by electrically stimulating the cells of the spiral ganglion within the cochlea. It consists of a surgically implanted electrode array and an externally worn sound processor. Cochlear implants are a suitable treatment for people who get limited benefit from hearing aids. Cochlear implantation in prelingual infants has undergone marked advances in the past decade. Studies have proven that early detection of hearing loss and early intervention significantly improve long term language skills and cognitive ability. Children who receive cochlear implants by 12 months can demonstrate age appropriate speech perception and language skills at 3 years post implant. The US Food and Drug Administration (FDA) has approved cochlear implants for infants at 12 months of age since 2000, but there is now evidence that implantation prior to 12 months of age results in improved auditory outcomes, without an increased risk of complications.

Earlier cochlear implantation is supported by findings that primary and secondary neonatal auditory cortices are disorganised and thought to be overlapped by visual projections. As the primary auditory cortex is stimulated, it makes sophisticated reciprocal connections with the secondary auditory cortex essential for language development and the visual projections become concentrated in the normal visual pathway. If there is no input, there may be atrophy of connections or compensatory abnormal projections, which can mean cochlear implantation is less successful. This auditory development begins at approximately 26 weeks
of gestation, major developments occur within the first 12 months with significant ongoing cortical change until four years of age and refining up until 15 years of age. \(^5\) Children who receive implantation before 12 months of age do significantly better in terms of auditory and spoken language outcomes than those implanted between 12 and 24 months. \(^2\) There is now evidence that even earlier implantation yields even better results with no significant increase in risks to the child. \(^3,4\)

As a result of these findings, Universal Newborn Hearing Screening (UNBHS) has been introduced following World Health Organization (WHO) guidelines. \(^7\) Implementation of these guidelines was anticipated to reduce the age of referral and implantation. \(^8,9\) A recent dual centre retrospective study in the Netherlands and Germany confirmed a reduction in age in both centres following the introduction of newborn screening, though the scale of this reduction was markedly better in the Dutch population. \(^10\) The difference may be explained by a difference in follow-up systems. In the Netherlands, children are referred by the screening programme to an audiology clinic and are subject to a national tracking system. In Germany, parents are advised to contact an otolaryngologist for a diagnostic hearing test, but there is not a national tracking system.

A previous audit was undertaken by the Southern Cochlear Implant Programme (SCIP) prior to the introduction of UNBHS. At that time, infants hearing was only screened if risk factors for sensori-neural hearing loss were present, or if there were parental concerns. The audit found that the median age of referral was 21.5 months and median age at implant was 24 months, for children with prelingual deafness. \(^11\) At that time, analysis of national data found the mean age for confirmation of profound loss was 13 months, and the mean age of confirmation of severe hearing loss was 34 months. \(^12\)

The national implementation of Universal Newborn Hearing Screening and Early Intervention Programme (UNHSEIP) in New Zealand was a phased process spanning 3 years, from 2007–2010. \(^13\) Since August, 2010, all 20 District Health Boards (DHBs) have been offering screening to families of all newborn babies. The SCIP provides services to 15 of these DHBs.

The purpose of this audit is to determine the effect of the UNBHS on age of referral and implantation, with a focus on those who were considered to have delayed referral, so that preventable delays can be avoided in the future.

**Method**

The SCIP database prospectively collected data from all referrals to the service from March, 2003, to August, 2014. At referral, an assessment is made as to whether the child is pre/peri lingual or post lingual. After initial count, postlingual children were excluded from further analysis. Children referred peri/prelingually were identified; fields used in calculations were: date of birth, date of referral, and date of implantation. It was also recorded if these children had undergone UNBHS. Individual case notes of those implanted following UNBHS who were implanted after 14 months of age were reviewed to identify contributing factors for the delay in implantation.

**Statistical Analysis**

Data were analysed using Microsoft Excel for Mac (2011) version 14.2.5 and GraphPad software (2014). The data were mostly normally distributed. However, the Mann-Whitney U test was used to compare the median data, as there were several major outliers from the mean in all datasets. Data pertaining to the reasons for delay are presented descriptively.

**Results**

In total, 219 children were referred to the programme, of which 123 were prelingual or perilingual at time of referral; the remaining 96 were referred post lingually. The first infant to be referred to the SCIP from UNBHS was in April of 2010, 44 were subsequently referred following UNBHS. The remaining 79 were referred prior to UNBHS.

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The infants referred to SCIP who underwent UNBHS were significantly younger (median 6.23 months vs. 21.50 months, Mann-Whitney p=0.001), and underwent implantation at a significantly younger age (median 12.66 months vs 24.00
Table 1: Age at referral and implantation.

<table>
<thead>
<tr>
<th></th>
<th>Prior to UNBHS</th>
<th>Following UNBHS</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age at referral (months)</td>
<td>79</td>
<td>44</td>
</tr>
<tr>
<td>n</td>
<td>21.50 (1.38–80.88)*</td>
<td>6.23 (1.41–50.66)</td>
</tr>
<tr>
<td>Median (Range)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age at implantation (months)</td>
<td>77</td>
<td>36</td>
</tr>
<tr>
<td>n</td>
<td>24.00 (4.08–83.64)*</td>
<td>12.66 (7.20–55.79)</td>
</tr>
<tr>
<td>Median (Range)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Time (months) between referral and implantation</td>
<td>4.08 (0.36–14.96)</td>
<td>5.65 (1.68–18.71)*</td>
</tr>
<tr>
<td>Median (Range)</td>
<td></td>
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</tr>
</tbody>
</table>

* p<0.001

Figure 1: Age of individual infants at referral and implantation (Prior to UNBHS vs UNBHS)
ARTICLE

months, Mann-Whitney p<0.001) than those who did not undergo UBHBS, but there was a longer mean time between referral and implantation in those that underwent UBHBS (median 5.65 months vs. 4.08 months, Mann-Whitney p<0.001) (Table 1). Figure 1 demonstrates the range of ages at referral and implantation, and compares those that underwent UBHBS and those that did not (the median is depicted by a black line).

Thirteen children who underwent UBHBS were implanted after 14 months of age, which we consider clinically unacceptably late. The following causes for delay were identified, with some children presenting with more than one contributing cause for delay:

- Additional disabilities (3)
- Auditory Neuropathy Spectrum Disorder (3)
- Did not attend appointments (3)
- Late referral from audiology (2)
- Progressive hearing loss (2)
- Health issues requiring other interventions (1)
- Screener error (1)
- Passed screening test (1)
- Passed screening in another country (1)

Discussion

This audit has confirmed that the introduction of UBHBS has significantly reduced the time to referral and surgery for cochlear implants in children with prelingual deafness. The median age of implantation of screened infants was 13 months, compared to 24 months for unscreened infants.

It is noted that there was a small, but significant, increase in the time from referral to implantation in the infants that underwent UBHBS. This can be explained, as the screened infants were referred at a significantly younger age than their unscreened counterparts, sometimes as young as 2 to 3 months of age. This necessitated a longer wait time to implantation—until they were of an appropriate age for surgery. Also, their unscreened counterparts, who were referred at an older age, were processed with some urgency so as to achieve the best possible results. The Ministry of Health UNHSEIP has stated a core goal of “initiation of appropriate medical and audiological services ... by 6 months of age”, which was largely achieved (median referral age was 6 months). The SCIP aims to implant these children by 12 months of age and was still able to achieve this in half the population, with only a slight increase in delay from referral to implantation. However, there is emerging evidence that even earlier implantation is beneficial and the SCIP is moving towards implantation as close to 6 months of age, as is possible.

Two infants who experienced significant delays in referral and implantation were reported to have progressive loss—initially, they did not meet the severity criteria for cochlear implantation, but their hearing went on to deteriorate. These are examples of unavoidable delay, as it would be inappropriate to implant mild-moderate hearing loss. These children had been fitted with hearing aids and underwent appropriate ongoing monitoring, which is essential to prevent subsequent delay in referral should there be progression of the hearing loss.

Two infants who had undergone newborn hearing screening were reported to have passed. It is not known whether they were true passes and the children's hearing rapidly deteriorated, or whether these were false passes. At the time of the study, in New Zealand the initial method of screening for well babies included otoacoustic emissions (OAEs), those that fail are referred for diagnostic Auditory Brainstem Response (ABR) testing. Those that are deemed to be high risk (eg, family history, intrauterine infection or NICU admission) undergo Automated ABR automatically (AABR) by screeners. The sensitivity of OAEs is reported to be between 67–100% and AABR 99–100%. These methods of screening are adequate for population-based screening, but they are not 100%. There must be an awareness that the test can be wrong and considered when there are parental concerns or failure to respond. Similarly, a test that requires human administration is susceptible to error, as was evidenced in one case. The equipment used is mostly automated, but adequate provider training must be given to reduce the chance of error. Following a review of newborn hearing screening in March 2014, a revised screening regime is currently being rolled-out nationally,
whereby all babies will be screened using only one test, automated Auditory Brainstem Response (aABR) testing, with one standard screening device. The new regime is expected to reduce risk of protocol error, provide more concise screener scripts and explanations to parents, potentially reduce workload stress, and potentially earlier referral to audiology. A screening incident in 2012, whereby some screeners did not screen babies according to the screening protocol, resulted in “delayed referral from audiology” for one of the two children in this category. It is estimated that non-protocol screening occurred in 1.4% of all babies who have completed screening in New Zealand since the programme began full implementation across all DHBs in 2010.19 All babies identified as incorrectly screened were invited for rescreening. Only one baby was identified with profound congenital hearing loss and was referred for bilateral cochlear implants at 10 months and implanted at 14 months. This incident highlights the importance of vigilance in monitoring any screening programme, regular quality control checks and adequate education of the screeners. The revised screening regime eliminates the possibility for this screener error to recur.18

Delay in referral and implantation due to lack of attendance is preventable. Children ‘lost to follow-up’ have been recognised as problematic and an area for improvement in the UNBHS Programme in New Zealand, and also in UNBHS programmes in other countries.7,20 The significant reduction in age at implantation in the Netherlands, compared to the more modest reduction in Germany, reflects the national programmes of those countries; the first providing targetted follow-up and automatic referral, and the second relying on parent self-referral and follow-up following a failed screening result.10 The first few months of an infant’s life are a challenge for parents however this is, as has been explained, a critical period for auditory and language development. Enhanced education of parents, audiologists and the primary care physicians will emphasise the importance of timely treatment and potential consequences of treatment delay. The introduction of telephone and SMS reminders have been shown to decrease the rate of non-attendance across many disciplines internationally21 and should be considered in areas where this is a problem.

A diagnosis of Auditory Neuropathy Spectrum Disorder (ANSD) contributed to later referral for three children. Two of these children also presented with additional disabilities, one received poor follow-up from Audiology. Management of ANSD can be a challenge. Outer hair cell function is preserved and therefore these children are not always identified by otoacoustic emissions, so detection and diagnosis may be delayed. Sound may be detected, but the signal may be distorted and lack clarity, causing delays in speech and language development. It is only recently that cochlear implants have been confirmed as a successful treatment in cases of ANSD.22,23 Children with a diagnosis of ANSD, without associated cognitive or developmental disorders, can acquire speech and language outcomes comparable to other children who receive a cochlear implant.24 Some children with ANSD benefit from hearing aids. However, ANSD patients who do not benefit from conventional amplification do well when implanted at a young age.25 Careful monitoring of the functional benefit derived from hearing aids should facilitate prompt referral for a cochlear implant in cases of ANSD.

Prelingually deaf children are an extremely heterogeneous group, and include children with congenital malformations or co-morbidities that may delay suitability for general anaesthesia. Additional disabilities are no longer a contraindication for cochlear implantation, although outcomes may be significantly different than for children with no additional disabilities.26,27 Speech and language outcomes may be poorer than for children without additional disabilities, however benefits have been noted in general communication, and it is appropriate to provide children with additional disabilities with the same opportunity to access audition as any other child with a hearing impairment.28 It is critical that referral for cochlear implantation is not delayed until other issues are ‘sorted out’, as this leads to further delays to implantation and language development.
Finally, age of implantation is only one of the variables known to affect outcomes post implant, together with duration of deafness, additional disabilities, number of active electrodes, neural survival and mode of communication.\textsuperscript{29,30} However, the age of implantation is one variable that we can aim to improve.

Conclusions

- The introduction of newborn hearing screening has significantly reduced the age at which children are referred for cochlear implantation.
- The Southern Cochlear Implant Programme can continue to improve its practice, as international trends move towards implantation even earlier than 12 months.
- Children with moderate to severe loss must be regularly monitored so as not to delay referral, should the hearing loss progress.
- Parents of children with hearing loss must be supported and educated so they understand the importance of early intervention. Efforts must be made to reduce non-attendance of appointments.
- Screening programmes and the screeners must be audited and regularly monitored. Adequate training must be given to screeners and they must be educated as to the importance of early intervention.
- Children with other co-morbidities should not have their referral delayed.

\textbf{Competing interests:}

Philip Bird reports he is a trustee of the Southern Charitable Hearing Trust which administers the Southern Cochlear Implant Programme.

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Sperm quality in New Zealand: is the downward trend continuing?

Mary Birdsall, John Peek, Sumithra Valiapan

**ABSTRACT**

**AIM:** To investigate whether the decline in sperm concentration in New Zealand sperm donors observed from 1987 to 2007 continued in the period 2008–2014.

**METHOD:** A retrospective study from 2008 to 2014. The first semen sample of 285 men presenting as sperm donors in Auckland and Wellington was analysed for sperm concentration, seminal fluid volume and the percentage of motile sperm. These results were compared to results from 1987 to 2007 from the same clinics.

**RESULTS:** The decline in semen volume and sperm concentration observed between 1987 and 2007 did not continue in 2008–2014. Sperm concentration decreased from 1987 until some time between 1997 and 2001, and has remained stable at an average of 62x10^6/ml between 2001 and 2014. Sperm motility declined significantly (8%) in the period 2008–2014, but there was no significant change over the total period studied, between 1987 and 2014.

**CONCLUSION:** After a decline between 1987 and sometime during 1997–2001, the sperm concentration in men presenting as donors remained unchanged between 2002 and 2014, suggesting semen quality has not changed in New Zealand men over the last decade.

There have been concerns over a possible global decline in semen quality since the 1930s. In 2008, we reported an annual reduction of 2.5% in sperm concentration in a study of sperm quality among New Zealand men presenting as sperm donors over 20 years. This trend exceeded the 1% average global decline reported by Carlsen et al. Subsequently, Swan et al reported a 2.3% and 0.8% annual decline for European and American men respectively. Rolland et al reviewed one of the largest study populations to date, and reported a 1.9% decline among French men.

A group in Israel found deterioration in sperm quality in their intrauterine insemination (IUI) sperm donation program, leading them to postulate they may need to utilise in-vitro fertilisation instead of IUI in the future.

Recent papers from France, Spain and Finland have also reported deterioration in sperm quality. However, other researchers have reported different results; Jorgensen et al found an increasing trend in sperm concentration and total sperm count among Danish men and, in Sydney, Costello et al found no decline in semen quality among their sperm donors.

There is ongoing debate that this geographical heterogeneity is due to diverse influences from environmental, occupational and lifestyle factors. A systematic review recently concluded that there is a lack of evidence to confirm a worldwide decline in sperm counts.

The present study adds another 7 years of data to our original analysis to test whether the trends of falling semen volume and sperm concentration have continued. The implication is that a continuing fall in semen quality among men presenting as donors may reflect a continuing decline in male fertility, and the prospect of more New Zealand couples requiring Assisted Reproductive Technology in the future.
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Methods

Subjects: This study added 285 men, recruited between January, 2008, and July, 2014, to the 975 men included in the original study. The median ages of men in the two periods were 36 and 35. The men were potential sperm donors recruited by Fertility Associates. The study excluded men recruited by patients as personal donors. Recruitment was by advertising in local newspapers, magazines and billboards. The clinic had an upper age limit of 50, which was reduced to 45 in 2005. Proven fertility or marital status was not required nor mentioned in advertising.

Semen analysis: Samples were collected by masturbation, with two to four days abstinence recommended. Semen volume, sperm concentration and percentage motile sperm were measured, from which were calculated the total number of sperm and the total number of motile sperm.

Samples were analysed within two hours. Semen volume was measured by aspirating the whole liquefied sample into a 5 ml or 10 ml graded pipette. Between 1987 and 2002, sperm concentration was determined using formalin immobilised sperm in a hemocytometer. Motility was assessed on a slide with cover slip, which had a sample depth of about 20 microns. From 2002 onwards, 20 micron deep counting chambers (MicroCell) were introduced for measuring both concentration and motility. At least 200 sperm were measured for both these parameters.

Statistical analysis: For the initial analysis, semen volume, sperm concentration, motility, total number of sperm and total motile sperm were cube root transformed before multivariate linear regression to look at temporal trends. Since analysis of transformed and untransformed data gave similar results, untransformed data was used in this paper for simplicity, as in the previous paper.

Results

Temporal changes in semen volume, sperm concentration and motility between 1987 and 2014 are shown in Figures 1, 2 and 3. There were statistically significant falls in semen volume and sperm concentration over the period 1987–2007, as presented in the initial report, and over the whole period 1987–2014 (Table 1).

Semen volumes for 2008–2014 were 6% higher than predicted by the trend seen in the original study, but this was not significant (p=0.14). The mean semen volume in the periods 2001–2007 and 2008–2014 were similar, at 3.3 and 3.2 ml, suggesting no change between these periods.

Sperm concentrations for 2008–2014 were 39% higher than predicted by the trend seen between 1987 and 2007, which was significant (p<0.001). The mean sperm volume in the periods 2001–2007 and 2008–2014 were similar at 63 x 10^6/ml and 61 x 10^6/ml, indicating that sperm concentrations fell from 1987 and sometime between 1997 and 2001, but have remained unchanged since (Figure 3, three order polynomial regression line).

Sperm motility was 16% lower in the period 2008–2014 than the trend predicted from the initial study (p<0.001). Mean motility in the periods 2001–2007 and 2008–2014 were 61% and 53%. However, the trend over the total period 1987–2014 was slight and not significant (Table 1).

Table 1: Change in semen quality over time in 1,260 potential sperm donors

<table>
<thead>
<tr>
<th></th>
<th>Mean</th>
<th>Trends</th>
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<tr>
<td></td>
<td>1987–2007 Previous study</td>
<td>2008–2014 This study</td>
</tr>
<tr>
<td>Volume (ml)</td>
<td>3.5</td>
<td>3.2</td>
</tr>
<tr>
<td>Sperm concentration (million/ml)</td>
<td>79</td>
<td>62</td>
</tr>
<tr>
<td>Motility (%)</td>
<td>59</td>
<td>53</td>
</tr>
</tbody>
</table>


Figure 1: Sperm volume in 1,260 potential sperm donors recruited between 1987 and 2014

![Semen Volume (mL)](image1)

Figure 2: Sperm motility in 1,260 potential sperm donors recruited over 27 years recruited between 1987 and 2014

![Sperm Motility (%)](image2)
Figure 3: Sperm concentration in 1,260 potential sperm donors recruited between 1987 and 2014. Linear (solid) and three order polynomial (dashed line) regression lines.

Discussion
This study has shown that the decline in sperm concentrations in New Zealand sperm donors reported in 2008 has not continued.

Our previous study showed a significant decline in sperm concentration over the period 1987 to 2007. Post hoc analysis suggested the decline was limited to the first half of the period studied. The findings from the present study confirm this observation, so we can conclude that sperm concentration declined from 1987 to sometime between 1997 and 2001, but has remained stable at a mean of 61–63 x 10⁶/ml from 2001 onwards.

More than one hundred peer reviewed articles have been published on trends in sperm counts, with varying conclusions. One extensive review suggested a decline in sperm counts from 1938 to 1972, with no decline over the next 20 years.

The present study did show lower sperm motility in 2008–2014 compared to 1987–2007, but there was no trend when the whole period was considered.

It is difficult to know whether this observed reduction in sperm motility will be part of a trend or whether it is due to fluctuations in laboratory processes. Quality control for sperm motility measurement over many years is more difficult than for sperm concentration. Among those who have reported falling sperm concentration, some have observed a concomitant fall in motility, while others have not.

There have been a number of theories proposed to explain deteriorating semen quality, and these have included both environmental and lifestyle factors. Reductions in semen quality have also been associated with an increasing rate of testicular cancer, cryptorchidism and hypospadias, as well as a decline in levels of androgen hormones.

One postulated cause for reduced semen quality is exposure to chemicals in the environment that are endocrine disruptors. Industrialisation has resulted in the release of endocrine disruptors originating from pesticides, herbicides, cosmetics, preservatives, cleaning materials, private waste and pharmaceutical products into the environment. Many of these chemicals have long half-lives and have been detected in the environment decades after their release.

Exposure to pesticides at both occupational and environmental levels may be associated with reduced sperm quality.

Another putative cause is exposure to toxins and/or environmental estrogenic compounds during fetal growth, which would reduce the level of spermatogenesis in the testes as an adult. Recent studies on
smoking in pregnancy indicate an association between prenatal tobacco exposure, lower sperm concentration and testicular cancer in the male offspring.

We have no information with respect to the presence or absence of toxicants or pollutants in our population during the time period of our study. Determining exposure is difficult because good quantitative exposure data is challenging to acquire and exposures in utero are even more difficult to measure. It is important to note that some toxins are being reduced, which may affect our findings and sperm concentrations into the future. For instance, DDT (dichlorodiphenyltrichloroethane) was widely used in New Zealand agriculture as an insecticide, but its use was phased out from the 1970s and finally banned in 1989. DDT exposure has been shown to have detrimental effects on male fertility. Similarly, cigarette smoking is declining, with fewer women smoking during pregnancy.

A limitation of our study is that it is a retrospective analysis. Men who choose to be sperm donors may also not be representative of the general population; for instance, sperm donors tend to be well educated. Although there are valid concerns about how representative of the general population sperm donors might be, such men constitute a fairly homogenous population in age and background, and thus trends in this group may reflect trends in the whole population. A further limitation is that we did not collect lifestyle information from potential donors at the time of their first semen sample, such as smoking, alcohol intake, recreational drug use, obesity and self-assessment of stress. These are common confounding factors which have been associated with a reduction in semen quality, although better quality evidence is needed to confirm the impact of most of these effects.

Merzenich, et al found that older age contributed significantly to a decline in sperm concentration and motility. Older paternal age is negatively associated with time to pregnancy as well as a declining likelihood of pregnancy. Age is associated with an approximately 4% reduction in fecundability per increasing year. The average age of our participants was 35 years, and increased only slightly between 1987 and 2014. This is older than in most studies of donors, but similar to the age of men trying for pregnancy in New Zealand, where the average age at birth is 30 for women and 32 for men.

The latest systematic review on sperm quality published recently concluded that there is insufficient strong evidence to confirm a worldwide decline in sperm counts, with no scientific proof of a causative role for endocrine disruptors. However, there is sufficient evidence to entertain that there may be regional changes in semen quality, especially in sperm concentration, over time. It is prudent to consider what effect these might have if maintained on human fertility and fecundity, since sperm concentration has been found to be associated with time to pregnancy in natural conception. Sperm concentration is associated with various aspects of sperm quality, so a decline in sperm concentration may signal an increasing need for fertility services. The present findings are reassuring, in that if there was a decline in sperm concentration in New Zealand men, as indicated between 1987 and 2001, it has stopped.
Competing interests: Nil

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Endovascular clot retrieval for acute ischaemic stroke: the Auckland City Hospital experience

Peter Alan Barber, Qiliang Liu, Stefan Brew, Ben McGuinness, Ayton Hope, Maurice Moriarty, Doug Campbell, Dominic Tse

ABSTRACT

AIMS: In acute ischaemic stroke, endovascular therapy with the Solitaire FR stent retriever has been shown to double recanalisation rates and the numbers of patients who recover to be functionally independent, when compared to standard therapy. We present the Auckland City Hospital experience of clot retrieval.

METHODS: Previously independent ischaemic stroke patients with contraindications to, or no response following, i.v. alteplase, were treated with clot retrieval. All patients had proximal large artery occlusions on CT angiography and many also had CT perfusion scans showing salvageable ischaemic tissue.

RESULTS: Clot retrieval was performed in 33 patients (10 women, mean (SD) age of 54 (17) years) since 2011. Twenty-two (67%) patients were first treated with alteplase. Patients fell into three groups: 17 (52%) had anterior circulation occlusion, similar to those in recent clot retrieval studies; 10 (30%) had posterior circulation occlusion; and six (18%) had ‘Rescue’ clot retrieval, usually with stroke that followed a procedure. Patients with anterior circulation occlusion had a median time from symptom onset to groin puncture of 225 (range 95–450) minutes, full recanalisation occurred in 76%, and by day 90, all 17 were alive and living at home, with 63% functionally independent (modified Rankin Scale (mRS) 0–2). At day 90, eight of 10 posterior circulation occlusion group patients were alive and living at home, four with a mRS of 0–2. In contrast, four of six ‘Rescue’ patients had died, and another was functionally dependent with a mRS of 4.

CONCLUSIONS: Endovascular clot retrieval can be safely and effectively performed in a New Zealand setting with similar results to recent trials in anterior circulation occlusion patients. We suggest that District Health Boards develop clot retrieval services as part of regional hyperacute stroke treatment pathways.

Sroke is the third leading cause of death worldwide and a major cause of long-term adult disability. The lifetime costs of stroke per person in New Zealand are estimated to be $73,600, with a total cost to the country of over $450 million annually.1 Intravenous (i.v.) thrombolysis with alteplase, administered within 4.5 hours of symptom onset, has been shown to improve clinical outcome in acute ischaemic stroke.2,3 However, i.v. alteplase results in recanalisation rates of only <10% for internal carotid artery (ICA), and 30% for the M1 segment of middle cerebral artery (MCA), occlusion.4 As a consequence, 60–80% of such patients are dead or dependent at 90 days despite therapy.

Endovascular clot retrieval has been explored in a number of randomised-controlled trials. Five studies published in early 2015 examining stent retriever devices reported clear superiority of intra-arterial therapy over standard therapy.5–9 Auckland City Hospital (ACH) has been performing clot retrieval since 2011 in highly selected ischaemic stroke patients with severe deficits, including several patients enrolled into the EXTEND IA clot retrieval study. We present our experience with clot retrieval.
Methods

In 2011, the Neurology and Radiology Departments, in conjunction with the Departments of Critical Care Medicine (DCCM) and Anaesthesia, developed a protocol for the use of clot retrieval at ACH, in 2011. Patients had to have evidence of distal ICA, MCA (M1 or M2 segments) or basilar artery occlusion on computed tomographic angiography (CTA). Anterior circulation patients also had CT perfusion (CTP) studies to identify potentially salvageable ischaemic brain tissue where possible.

Treatment was restricted to previously independent patients presenting with ischaemic stroke who had contraindications to i.v. alteplase, no response to i.v. alteplase, or who were enrolled in the EXTEND IA study. An arbitrary age limit of 60 or less was imposed for the first 18 months while experience was gained with what was an experimental treatment at the time. Patients or next of kin provided consent to be enrolled in the EXTEND IA study, which had been approved by the Health and Disabilities Ethics Committee (NTY/12/023/AM04), or for treatment with this ‘off label’ therapy. Ethics Committee approval was not required for the audit presented here.

There were three groups of patients: those with anterior circulation occlusion who were either enrolled in, or would have met the eligibility criteria for the EXTEND IA study and other recent clot retrieval studies; those with basilar artery occlusion; and those with iatrogenic stroke or contraindications to enrolment into EXTEND IA study, which we have termed ‘Rescue’ patients.

Alteplase was given at a dose of 0.9 mg/kg, as per standard care where indicated. Groin puncture had to be commenced within 6 hours of symptom onset in patients with anterior circulation occlusion, and 12 hours for posterior circulation occlusion. The use of conscious sedation or general anaesthesia was at the discretion of the neurointerventionist and anaesthetist. The Solitaire FR retrievable stent (Covidien) was deployed at the site of intracranial vessel occlusion and then removed under negative-pressure aspiration. Recanalisation was determined from post-procedure digital substraction angiography (DSA).

Stroke severity at presentation was determined by the National Institutes of Health Stroke Scale (NIHSS) score, where a score of 0 is normal and 42 is dead. Early neurologic recovery was defined as an NIHSS score drop of 8 or more points, or 0 or 1 at 24 hours. Functional outcome was determined using the modified Rankin Scale (mRS) score (range, 0 (asymptomatic) to 6 (death)) at 90 days. Functional independence was defined as mRS of 0-2 at day 90.

Safety measures included symptomatic intracranial haemorrhage (sICH), procedural adverse events, (namely subarachnoid haemorrhage, vessel dissection and angioedema) and death at 90 days. sICH was defined as large parenchymal haematoma (>30% of infarct volume with mass effect) and ≥4 point increase in NIHSS as per the NINDS criteria.10

Data for all patients treated with clot retrieval, including demographic, clinical, treatment, timing and outcome information, were prospectively recorded and entered into Microsoft Excel (2011) by stroke nurse specialists and reviewed regularly by one of the investigators (P.A.B.).

Results

Thirty-three patients (10 women, mean (SD) age of 54 (17) years) with acute ischaemic stroke have been treated with clot retrieval with the Solitaire FR stent retriever since 2011 (Table 1). Five of 33 (15%) patients had stroke while an inpatient with another condition—12 (36%) had been transferred from Counties Manukau (7 patients) or Waitemata (5 patients) District Health Boards (DHBs).

Twelve (36%) were admitted after office hours. Data on day 90 mortality was available for all 33 patients and functional outcome was known for 32 patients. One patient who was transferred to Waikato Hospital post-procedure was known to be alive and living at home, but had an unknown functional status.

Anterior circulation occlusion group

There were 17 (52%) patients (seven women, mean (range) age of 47 (16–82) years) in the anterior circulation occlusion group (Table 1). These patients were moderately severely disabled at
Table 1: Results

<table>
<thead>
<tr>
<th>Demographic characteristics</th>
<th>Anterior circulation</th>
<th>Posterior circulation</th>
<th>Rescue</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number (%)</td>
<td>17 (52)</td>
<td>10 (30)</td>
<td>6 (18)</td>
<td>33 (100)</td>
</tr>
<tr>
<td>Age, years – mean ± SD (range)</td>
<td>47±20.4 (16–82)</td>
<td>59±8.2 (44–70)</td>
<td>62±6.6 (54–71)</td>
<td>54±17 (16–82)</td>
</tr>
<tr>
<td>Female sex (%)</td>
<td>7 (41)</td>
<td>2 (20)</td>
<td>1 (17)</td>
<td>10 (30)</td>
</tr>
<tr>
<td>Ethnicity (%)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>European</td>
<td>7 (41)</td>
<td>2 (20)</td>
<td>5 (83)</td>
<td>14 (42)</td>
</tr>
<tr>
<td>Pacific</td>
<td>4 (24)</td>
<td>4 (40)</td>
<td>1 (17)</td>
<td>9 (27)</td>
</tr>
<tr>
<td>Māori</td>
<td>3 (17.5)</td>
<td>1 (10)</td>
<td>-</td>
<td>4 (12)</td>
</tr>
<tr>
<td>Asian</td>
<td>3 (17.5)</td>
<td>3 (30)</td>
<td>-</td>
<td>6 (18)</td>
</tr>
<tr>
<td>Location of occlusion (%)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>ICA</td>
<td>4 (24)</td>
<td>-</td>
<td>2 (33)</td>
<td>6 (18)</td>
</tr>
<tr>
<td>M1</td>
<td>10 (59)</td>
<td>-</td>
<td>2 (33)</td>
<td>12 (36)</td>
</tr>
<tr>
<td>M2</td>
<td>3 (17)</td>
<td>-</td>
<td>0</td>
<td>3 (9)</td>
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<td>Basilar</td>
<td>-</td>
<td>10 (100)</td>
<td>2 (33)</td>
<td>12 (36)</td>
</tr>
<tr>
<td>Intravenous thrombolysis (%)</td>
<td>16 (94)</td>
<td>6 (60)</td>
<td>0 (0)</td>
<td>22 (67)</td>
</tr>
<tr>
<td>Time from onset—median (range)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hospital arrival (minutes)*</td>
<td>60 (18–187)</td>
<td>100 (18–293)</td>
<td>-</td>
<td>65 (18–293)</td>
</tr>
<tr>
<td>IV alteplase</td>
<td>150 (60–223)</td>
<td>128 (110–157)</td>
<td>-</td>
<td>149 (60–223)</td>
</tr>
<tr>
<td>Groin puncture</td>
<td>225 (95–450)</td>
<td>283 (120–600)</td>
<td>177 (100–255)</td>
<td>225 (95–600)</td>
</tr>
<tr>
<td>Full recanalisation (%)</td>
<td>13/17 (76)</td>
<td>7/10 (70)</td>
<td>4/6 (67)</td>
<td>23/32 (72)</td>
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<tr>
<td>NIHSS score—median (range)</td>
<td></td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>On admission</td>
<td>16 (8–24)</td>
<td>35 (9–35)</td>
<td>34 (19–38)</td>
<td>22 (8–38)</td>
</tr>
<tr>
<td>24 hours</td>
<td>8 (2–24)</td>
<td>9 (0–42)</td>
<td>35 (0–42)</td>
<td>9 (0–42)</td>
</tr>
<tr>
<td>mRS, 90 days(^1)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Median (range)</td>
<td>2 (0–4)</td>
<td>3 (1–6)</td>
<td>6 (0–6)</td>
<td>3 (0–6)</td>
</tr>
<tr>
<td>mRS 0–2 (%)</td>
<td>10/16 (63)</td>
<td>4/10 (40)</td>
<td>1/6 (17)</td>
<td>15/32 (47)</td>
</tr>
<tr>
<td>mRS 4–6 (%)</td>
<td>2/16 (13)</td>
<td>4/10 (40)</td>
<td>5/6 (83)</td>
<td>11/32 (34)</td>
</tr>
<tr>
<td>Alive 90 days (%)</td>
<td>17/17 (100)</td>
<td>8/10 (80)</td>
<td>2/6 (33)</td>
<td>27/33 (82)</td>
</tr>
<tr>
<td>Home by 90 days/total (%)</td>
<td>17/17 (100)</td>
<td>8/10 (80)</td>
<td>2/6 (33)</td>
<td>27/33 (82)</td>
</tr>
<tr>
<td>Length of stay—median (range)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Acute stroke unit (days)</td>
<td>10 (2–12)</td>
<td>7 (3–13)</td>
<td>29 (0–52)</td>
<td>10 (0–52)</td>
</tr>
<tr>
<td>ADHB</td>
<td>32 (4–99)</td>
<td>11 (1–70)</td>
<td>13 (0–52)</td>
<td>22 (0–99)</td>
</tr>
<tr>
<td>All healthcare facilities</td>
<td>33 (2–99)</td>
<td>30 (1–79)</td>
<td>13 (0–52)</td>
<td>28 (0–99)</td>
</tr>
</tbody>
</table>

* All but one ‘rescue’ patient had an in hospital stroke
\(^1\) One patient alive and living at home at 90 days but with unknown functional outcome
admission with a median (range) NIHSS of 16 (8-24). Sixteen patients were treated i.v. alteplase; one woman with anaemia due to menorrhagia was not thrombolysed. The time from stroke onset to i.v. alteplase was a median (range) of 150 (60-223) minutes and to groin puncture was 225 (95-450) minutes. After the procedure, four patients required a short intensive care unit (ICU) stay but the remainder were transferred to the stroke unit. Thirteen of 17 (76%) patients had fully recanalised on follow up imaging. At day 90, 10 (63%) anterior circulation patients were functionally independent and all 17 were alive and living at home.

Posterior circulation occlusion group

There were 10 (30%) patients (mean (range) age of 59 (44–70) years) in the posterior circulation occlusion group (Table 1). These patients were severely disabled at admission, with eight having an NIHSS of 22 or more. Six patients were treated with i.v. alteplase; three were outside the treatment window and one was being treated with dabigatran. The time from stroke onset to i.v. alteplase was a median (range) of 128 (110–157) minutes and to groin puncture was 283 (range 120–600) minutes. At day 90, four posterior circulation occlusion group patients were functionally independent, eight were alive and living at home and two had died.

‘Rescue’ patients

There were six (18%) patients that we termed ‘Rescue’ patients (mean (range) age of 54 (16–82 years)) (Table 1). Five had strokes while in hospital; three following myocardial infarction (2 after percutaneous coronary intervention), one following lung transplantation and one following cerebral aneurysm coiling. Another patient with multiple medical co-morbidities presented with a fixed dilated pupil at admission. The ‘Rescue’ patients were very severely disabled at baseline, and all but one had an NIHSS of 24 or more. The site of arterial occlusion was the ICA in two patients, M1 MCA in two and the basilar artery in two. All six patients required a post-procedure ICU stay. These patients did poorly, with only two of six still alive at day 90, one of whom was dependent on others for care and one post-MI patient who was neurologically normal.

Safety outcomes

Symptomatic ICH was seen in two patients, one in the posterior circulation occlusion group and one in the Rescue group, both of whom died. One patient developed subarachnoid haemorrhage following injury of the right posterior cerebral artery. This was treated with coils and he did reasonably well with a day 90 mRS of 2. One patient developed angioedema, a recognised complication of alteplase, and this was successfully treated.

Discussion

In 2015 five studies, MR CLEAN,5 ESCAPE,6 EXTEND IA,7 SWIFT PRIME8 and REVASCAT,9 reported clear superiority of intra-arterial over standard therapy in ischaemic stroke. Together, these studies enrolled 1,287 patients (mean ages 65–71 years, with three of the studies having no upper age limit). Patients had moderate to severe stroke (baseline NIHSS scores of 17). Patients were randomised 1:1 to standard therapy (in most cases alteplase) versus standard therapy followed by clot retrieval. All patients had proximal anterior circulation occlusion (distal ICA, MCA M1 ± M2) on screening CTA. The numbers needed to treat to achieve functional independence in one patient ranged from 6–7 in the MR CLEAN and REVASCAT studies5,9 to 3–4 in the other three studies.6-8 Clinical benefit was consistent across all pre-defined subgroups including age (older or younger than 80 years), sex, the presence of cervical ICA occlusion, baseline clinical scores and time from randomisation. Serious adverse events, such as procedural complications, sICH and death were uncommon in all five studies.

Clot retrieval therapy at ACH was started four years before the results of these studies were known. We have reported all patients treated, and not just those matching the patients in the recent trials, as there are a number of lessons to be learnt. Firstly, in the anterior circulation group of patients we achieved similar efficacy and safety results as the randomised controlled trials. Our mean onset-to-groin puncture time of 225 minutes was that same as that seen in SWIFT-PRIME, and shorter than the 260 to 285 minutes for the MR CLEAN, ESCAPE and REVASCAT studies.5,9 By three months,
there had been no deaths and approximately two-thirds of the patients were functionally independent and living at home. This compares favourably with the recent studies, where 33–71% of patients had an outcome mRS of 0–2. The only major difference is that all of our anterior circulation patients had the procedure performed under general anaesthesia (GA), compared to 7% in REVASCAT and 38% in MR CLEAN.5,9 There has been controversy about the use of GA, with some suggesting that it should be avoided if possible, but others in our group questioning this assertion.12

Secondly, the 10 posterior circulation occlusion group patients (all with basilar artery occlusion) had a reasonable outcome. Eight survived and were able to be discharged home, and 40% were functionally independent at three months. These results compare favourably with a mortality rate that approaches 80% in patients, with basilar occlusion receiving standard therapy.13 It is unlikely that clot retrieval studies will be completed in patients with basilar artery occlusion. This is because clinical equipoise has now shifted, and of the anecdotal good outcomes with, and the almost universally dismal prognosis without, clot retrieval in this patient group.

Finally, we included six ‘Rescue’ patients where clot retrieval was seen as a last resort therapy. Five of these patients did poorly. There is no trial evidence to support the use of clot retrieval in these often desperate situations. However, these were the patients where the pressure to ‘do something’ was greatest, particularly in those with iatrogenic stroke. The lesson to be learnt here, is that while understandable, this pressure should be resisted, although as always in clinical medicine final decisions should be made on a case by case basis.

Clot retrieval has been shown to be cost-effective in patients with anterior circulation occlusion. In the EXTEND IA study, which provides important ‘local’ data, clot retrieval patients spent a median of 73 days at home in the first 90 days following stroke, compared to only 15 days in the alteplase-only patients (p=0.006).7 The costs of endovascular consumables and staffing were offset by shorter acute stroke unit stays (mean of 8 days versus 12 days in the alteplase only arm, p=0.04) and shorter inpatient rehabilitation time (mean 14 days versus 33 days, p=0.03). Further cost savings could be expected from more survivors living independently and fewer severely disabled survivors requiring costly care in the community.

How do we proceed from here? The Northern Region Clinical Practice Committee has recommended that ACH provides a clot retrieval service for the northern region DHBs. This service will be a single component of a regional hyperacute stroke care pathway. This is because almost all clot retrieval patients will be first treated with i.v. alteplase. A successful service is therefore dependent on rapid assessment and short ‘door to needle’ times. Furthermore, an overall increase in the numbers of stroke patients treated with alteplase is required to realise the full potential of clot retrieval.

Clot retrieval will be limited to previously independent patients with occlusion of the distal ICA or MCA M1 segment (and select M2 segments). Those with basilar artery occlusion could be considered for treatment on a case by case basis. Clot retrieval is equally effective in older people and there will be no upper age limit.

We envisage treating approximately 50 patients per year, based on current alteplase treatment rates. This relatively small number, and the need for neurointerventionists to provide an on-call service and maintain clinical skills, means that it would be inappropriate for clot retrieval to be provided at an individual DHB level. For this reason, we suggest DHBs around New Zealand develop clot retrieval services as part of regional hyperacute stroke treatment pathways to provide this effective and safe therapy.


New Zealand Society of Gastroenterology Guidelines for the Management of Refractory Ulcerative Colitis

Elena Eliadou, Andrew S Day, Mark W Thompson-Fawcett, Richard B Gearry, David S Rowbotham, Russel Walmsley, Michael Schultz, Stephen J Inns, on behalf of IBDNZ

ABSTRACT

The management of patients with ulcerative colitis who are dependent on corticosteroid for control of symptoms, or refractory to corticosteroids or standard immunosuppressive therapy, is challenging. The development of newer medical therapies has increased the options for managing patients in this situation, but access and funding remain limited. This guideline summarises the literature regarding this situation and provides guidance as to the management of refractory colitis in the New Zealand setting.

Ulcerative colitis is a chronic inflammatory condition of unknown aetiology typically causing continuous, non-granulomatous mucosal inflammation of the colon. It affects the rectum and a variable extent of the colon in continuity. The disease is characterised by a relapsing, remitting course leading to bloody diarrhoea, cramping and abdominal pain.¹

Due to the limited knowledge of the underlying cause, current drug treatments are empiric, aimed at controlling the inflammatory process and are not curative. First-line therapy for mild to moderate disease focuses on the use of 5-aminosalicylic acid (5ASA) preparations, depending on the extent of the disease, either in a topical formulation per rectum or as tablets. For disease refractory to 5ASA and for more severe disease, immunomodulating or suppressing medicines become necessary. Because of their rapidity of action and effectiveness, corticosteroids are often used as first-line immunosuppressants, usually as a bridge to agents of slower onset, such as the immunomodulator 6-Mercaptopurine, or its prodrug, Azathioprine.

The goals of treatment include induction and maintenance of remission of symptoms and of mucosal inflammation, which can be assessed by clinical examination, normalisation of blood tests and endoscopic assessment looking at mucosal healing. Long-term goals would include improvement in quality of life and minimisation of cancer risk. An important tenet of modern disease management is the reduction of the need for long-term corticosteroids.² Even though corticosteroids can be beneficial in inducing remission, they are associated with side effects. Early adverse effects include cosmetic side effects (such as acne, moon facies, weight gain and oedema), sleep and mood disturbance, glucose intolerance and dyspepsia. Dose related effects with prolonged use (usually >12 weeks of use) include cataracts, osteoporosis and osteonecrosis of the femoral head, myopathy and susceptibility to infections. Despite this, 25% of patients one year after diagnosis are dependent on corticosteroids for control of disease, and it is not uncommon for disease to be refractory to first-line immunosuppressant agents.³ Patients in this situation are said to have “refractory” colitis. The focus of this practise guideline is to raise awareness of the importance of identifying the “refractory” patients early, and to provide information and guidance regarding the options available in New Zealand for escalation of therapy.
Definitions
Refractory ulcerative colitis comprises patients in 3 main situations: Steroid refractory; steroid dependent; and standard immunomodulator (Azathioprine/6-Mercaptopurine) refractory disease. For the purpose of this guideline, these groups will be defined using the ECCO consensus statement4

- **Steroid refractory colitis**: Patients who have active disease, despite prednisolone up to 0.75 mg/kg/day over a period of 4 weeks
- **Steroid dependent colitis**: Patients who either are unable to reduce steroids below the equivalent of prednisolone 10 mg/day within 3 months of starting steroids, without recurrence of disease activity, or who relapse within 3 months of stopping steroids
- **Immunomodulator refractory colitis**: Patients who have active disease or relapse in spite of thiopurines at an appropriate dose for at least 3 months (i.e azathioprine 2–2.5 mg/kg/day or mercaptopurine 0.75–1 mg/kg/day in the absence of leukopenia)

Clinical assessment of severity
For the purposes of this guideline, “clinically active disease” is defined as disease where the treating clinician has evidence to suggest there is ongoing inflammatory disease, either because of documented mucosal inflammation or symptoms consistent with ongoing inflammation. The treatment decisions required in the setting of refractory colitis are weighty and it is often reasonable, in the first instance, to ensure after clinical assessment and basic laboratory investigations:

1. That adherence to medications is adequate
2. Adequate delivery of medication to the mucosa
3. Absence of concurrent disease (eg, proximal constipation or superimposed infection)
4. Concomitant diseases that might contribute to symptoms (eg, irritable bowel syndrome and coeliac disease) have been ruled out
5. Confirmation that it is UC and that Crohn’s disease has been excluded
6. Stool cultures to exclude the presence of pathogenic organisms including *Clostridium difficile*, *Giardia lamblia* and other common causes of infectious diarrhoea should generally be undertaken
7. Endoscopic assessment with flexible sigmoidoscopy is often warranted. As well as allowing objective assessment of the degree of inflammation, endoscopy allows microscopic and immunohistochemical assessment of mucosal biopsies for CMV infection. Colonoscopy may be indicated if the extent of the disease is unknown or there are concerns it may have altered.

Often, response to therapy is evident. However, the objective scoring of disease activity aids decision making, particularly if there are delays between decision points or if multiple clinicians are involved in decision making. A commonly used scoring system for the assessment of the clinical activity of colitis in the New Zealand setting is the simple colitis activity index (Table 1).5 This score defines remission as less than 3 points. A score of 4 or more is required for public funding of infliximab for UC in New Zealand.

Additional tools that can be used to monitor activity, include biochemical or laboratory markers such as C-reactive protein (CRP) and faecal calprotectin (FC). CRP has the advantage of being freely available, with result provided rapidly. FC is a heat-stable protein released into the intestinal lumen as a consequence of leukocyte trafficking to the gut. It has the disadvantage of being slow to process. CRP and FC are predictive of endoscopic disease activity; however, no lower threshold has been identified that reliably predicts mucosal healing by strict criteria.6 At this stage, CRP and FC should be considered ancillary to endoscopic assessment.

Treatment options
One of the cornerstones of the management of refractory colitis is the minimisation of chronic steroid exposure. The choice of alternative treatment needs to be a balance between drug potency,
side-effect profile, patient choice, age, sex, current medication and previous response to therapy, and the presence or absence of extra-intestinal symptoms. Prior to instituting novel immunosuppressant strategies it is important that standard first- and second-line treatments are optimised. Beyond this, second-line immunomodulators, biological agents and surgery might need to be considered.

### Optimising treatment

#### Optimising 5 Aminosalicylates (5ASA)

5ASAs are commonly used in the treatment of UC. They are metabolised within the large bowel via various mechanisms and help in mucosal healing.

Two studies comparing low-dose (2.4 gram) and high-dose (4.8 gram) mesalazine therapy showed improved mucosal healing and remission rates with the higher dose strategy.\(^7\)\(^8\) Once daily dosing improves adherence and is as effective as twice-daily dosing at inducing remission in mild to moderate active UC.\(^9\) In the presence of active disease, the dose of oral mesalazine should be maximised to at least 4 grams, preferably given once a day to improve adherence, as well as adding topical therapy in the form of mesalazine enemas 1 to 2 grams per day.\(^10\) Pentasa granules are available for those who find large 5ASA tablets difficult to swallow.\(^11\)

### Table 1: Simple colitis activity index

<table>
<thead>
<tr>
<th>Symptom</th>
<th>Score</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Bowel frequency (day)</strong></td>
<td></td>
</tr>
<tr>
<td>1–3</td>
<td>0</td>
</tr>
<tr>
<td>4–6</td>
<td>1</td>
</tr>
<tr>
<td>7–9</td>
<td>2</td>
</tr>
<tr>
<td>&gt;9</td>
<td>3</td>
</tr>
<tr>
<td><strong>Bowel frequency (night)</strong></td>
<td></td>
</tr>
<tr>
<td>1–3</td>
<td>1</td>
</tr>
<tr>
<td>4–6</td>
<td>2</td>
</tr>
<tr>
<td><strong>Urgency of defecation</strong></td>
<td></td>
</tr>
<tr>
<td>Hurry</td>
<td>1</td>
</tr>
<tr>
<td>Immediately</td>
<td>2</td>
</tr>
<tr>
<td>Incontinent</td>
<td>3</td>
</tr>
<tr>
<td><strong>Blood in stool</strong></td>
<td></td>
</tr>
<tr>
<td>Trace</td>
<td>1</td>
</tr>
<tr>
<td>Occasionally frank</td>
<td>2</td>
</tr>
<tr>
<td>Usually frank</td>
<td>3</td>
</tr>
<tr>
<td><strong>General well being</strong></td>
<td></td>
</tr>
<tr>
<td>Very well</td>
<td>0</td>
</tr>
<tr>
<td>Slightly below par</td>
<td>1</td>
</tr>
<tr>
<td>Poor</td>
<td>2</td>
</tr>
<tr>
<td>Very poor</td>
<td>3</td>
</tr>
<tr>
<td>Terrible</td>
<td>4</td>
</tr>
<tr>
<td><strong>Extracolonic manifestation</strong></td>
<td>1 per manifestation</td>
</tr>
</tbody>
</table>

*Arthritis, pyoderma gangrenosum, erythema nodosum, sclerosing cholangitis and uveitis.\(^\)\(^\)\(^\)\(^\)

(Remission <= 3 points, significant change = 2 points)
active disease. There are limited data on the use of thiopurines in ulcerative colitis, but a meta-analysis of 30 non-controlled studies and 7 controlled studies confirmed that thiopurines are more effective than placebo for the prevention of relapse in UC with a number needed to treat of 5, and absolute risk reduction of 23%.

Thiopurines demonstrate wide inter-individual variability in terms of response, due their complex metabolism. Their metabolism is mainly regulated by Thiopurine S-methyltransferase activity (TPMT). Therefore checking TPMT activity prior to initiating thiopurine is recommended.

The standard dose of azathioprine is up to 2.5 mg/kg/day and 6-mercaptopurine 0.75–1.5 mg/kg/day and dosage should be guided by TPMT activity.

Failure to respond to thiopurines can relate to non-adherence, inadequate dosing, or the preferential metabolism of the drug to the hepatotoxic metabolite 6-methyl mercaptopurine (6-MMP), rather than the immunosuppressive metabolites, the 6-thioguanine nucleotides (6TGN). Monitoring of 6TGN and 6MMP levels may, therefore, be useful in maximising the effect of thiopurines. The target level for 6TGN is 235–450 pmol/8*10E8 RBC. The threshold of 6TGN level of 235 had a significantly greater therapeutic response (p<0.001) in a prospective study of paediatric IBD patients. Since then, there have been several prospective studies reporting a correlation between 6TGN and clinical response with a therapeutic cut-off above 235 pmol/8*10E8 RBC. Monitoring the metabolites can identify “shunting”, which is defined by a ratio of 6TGN:6MMP of >20:1. When shunting occurs, the addition of allopurinol 100 mg reverses the effect. The thiopurine dose must be reduced to 1/4–1/3 of the regular dose and 6TGN and 6MMP levels monitored to guide dosing. Levels are best performed approximately 4 weeks after any change in dose.

Second-line Immunomodulator Therapies

Methotrexate
Methotrexate and its breakdown products inhibit several enzymes in the metabolic pathway of folic acid. While the cytotoxic and antiproliferative effects of high-dose methotrexate are ascribed to inhibition of dihydrofolate reductase, with consequent inhibition of DNA, RNA, and protein synthesis, the anti-inflammatory and immunomodulatory actions of low doses are probably due to inhibition of other folate dependent enzymes. Long-term low-dose methotrexate may lead to accumulation of adenosine, a lymphotoxic, immunosuppressive, and anti-inflammatory autacoid. Other effects include interleukin 1 (IL-1) receptor blockade, increased production of the regulatory cytokine IL-2, decreased production of soluble IL-2 receptors, IL-6, IL-8, leucotriene B4, and antibodies, and impairment of neutrophil chemotaxis.

Limited data exist for the use of methotrexate in UC. Benefit has been suggested in small, uncontrolled studies of patients with steroid dependent disease who failed to respond to, or were intolerant of, thiopurines. A previous randomised double-blind placebo controlled trial used the low dose of 12.5 mg of oral methotrexate weekly in 67 patients with UC. This showed no significant difference in the induction or maintenance of remission between the two groups. A Cochrane database systematic review then concluded there was insufficient evidence to support its use in UC. However, a recent randomised-controlled study, currently only available in abstract form, showed clinical benefit for steroid-dependent patients, using the higher dose of 25 mg weekly, given parenterally. We conclude that Methotrexate 25 mg weekly should be considered and discussed with patients, particularly for those who are steroid dependent.

Tacrolimus
Tacrolimus is a calcineurin inhibitor that acts via a mechanism similar to cyclosporine by inhibiting T lymphocyte activation and also production of interleukin 2. Two randomised, double-blind, controlled trials demonstrated that tacrolimus is effective in induction of remission for steroid refractory, moderately active UC. Moreover, the dose of tacrolimus is an important determinant of induction and maintenance of remission. In a recent double-blind, randomised, controlled study of 60 patients with
resistant UC, there was better response when dosing was aimed at achieving higher tacrolimus trough level (10–15 ng/mL) compared to low trough level (5-10 ng/ml) and placebo.\textsuperscript{25} One long term prospective study of 27 patients with refractory UC from Japan has shown a cumulative colectomy-free survival of 62.3% at 65 months.\textsuperscript{26,27} However, in the absence of larger, randomised, controlled trials with lengthy follow-up periods, tacrolimus cannot yet be considered standard second-line immunosuppression for UC. In addition, tacrolimus is currently only available in New Zealand via the Named Patient Pharmaceutical Assessment (NPPA) scheme.

**Cyclosporin A**

While there is extensive experience with the use of cyclosporin A in the setting of acute severe colitis,\textsuperscript{28} no prospective data exists for its use in refractory colitis,\textsuperscript{25} no prospective data exists for its use in refractory colitis.

**Anti TNF-alpha monoclonal antibodies (Infliximab and Adalimumab)**

**Infliximab**

Tumour necrosis factor (TNF)-\(\alpha\) is a proinflammatory cytokine with a central role in the pathogenesis of inflammatory bowel disease. Infliximab is a chimeric monoclonal antibody directed against TNF-\(\alpha\).

The ACT1 and ACT2 studies are the seminal studies that investigated the use of infliximab in UC.\textsuperscript{29} They were large, randomised, placebo-controlled trials that evaluated the efficacy of infliximab for induction and maintenance of remission in more than 700 patients, with moderately active UC in the outpatient setting. ACT1 was a 364 patient study comparing infliximab 5 mg/kg, 10 mg/kg or placebo at 0, 2 and 6 weeks, then every 8 weeks for a year. The primary endpoint was clinical response or remission at week 8. Response rates were achieved in 37.2% in placebo group, 69.4% in the 5 mg/kg and 61.5% in 10 mg/kg (\(p<0.001\)). Remission rates at week 8 were 38.8% in the infliximab 5 mg/kg (\(p<0.001\)), and 32% in infliximab 10 mg/kg group (\(p=0.002\)) compared to 14.9% in placebo group.

Also, patients who received infliximab 5 mg/kg and 10 mg/kg had a 45% and 44% clinical response at week 54, compared to placebo 20% with \(p<0.001\) for both. Clinical remission rates at week 54 were 34.7% in the infliximab 5 mg/kg group and 34.4% (\(p=0.001\)) in the infliximab 10 mg/kg (\(p=0.001\)) dose group, compared to 16.5% for placebo.

ACT2 was almost identical, but included 364 patients with disease refractory to 5ASA alone—which was 26% of the population—with a 30-week follow-up. The response at week 8 was 29.3% in the placebo group, 64.5% in the 5 mg/kg group and 69.2% in 10 mg/kg group, with a \(p\)-value of \(p<0.001\) for the comparison between both infliximab groups and placebo. Remission rates at week 8 were 33.9% (\(p<0.001\)) in the infliximab 5 mg/kg, and 27.5% (\(p<0.001\)) for the infliximab 10 mg/kg, compared to 5.7% in placebo group.

The long-term data arising from ACT1 and ACT2 were recently published. 229 of 484 infliximab treated patients from these trials entered the long-term extension for 3 years. Overall 70 (30.6%) patients discontinued infliximab infusions for adverse events (24 [10.5%]), lack of efficacy (11 [4.8%]), required colectomy (1 [0.4%]), or for other reasons (34 [14.8%]). The proportion of patients who maintained a physician's global assessment score indicative of no or mild disease (score=0 or 1) during the extension studies was 76.5% at extension week 0, and ranged between 90.0% and 94.3% through to extension week 52. The improvement in the inflammatory bowel disease questionnaire scores observed in the main studies was maintained. During the long-term extension, the safety profile was consistent with that of the main studies and no new or unexpected safety issues were identified.\textsuperscript{30}

**Adalimumab**

Adalimumab is a recombinant human monoclonal antibody directed against TNF-\(\alpha\). Currently in New Zealand, adalimumab is not funded for use in UC. The efficacy of adalimumab has been investigated in two placebo controlled trials, ULTRA1 and ULTRA2, conducted in patients with moderately to severely active UC despite oral corticosteroids and standard immunosuppressants. ULTRA 1 compared
adalimumab 160/80 mg and 80/40 mg to placebo for the induction of clinical remission after 8 weeks of treatment. At week 8, 18.5% in the adalimumab 160/80 group (p=0.031 vs placebo) and 10% in the adalimumab 80/40 group (p=0.833 vs placebo) were in remission, compared with 9.2% in placebo group. Serious adverse events occurred in 7.6%, 3.8% and 4.0% of patients in the placebo group, adalimumab 80/40 and adalimumab 160/80 respectively. There were two malignancies in the placebo group and none in Adalimumab groups.34

ULTRA2 was a study of 494 patients that looked into the induction and maintenance of disease using adalimumab 160/80/40 mg versus placebo in moderate to severe chronic active ulcerative colitis. Primary endpoints were remission at weeks 8 and 52. Overall rates of clinical remission at week 8 were 16.5% in the adalimumab group and 9.3% in the placebo group (p=0.19), corresponding values for week 52 were 17.3% and 8.5% (p=0.04). Serious adverse events occurred in 12% of patients given adalimumab or placebo. Serious infections occurred in 1.6% of patients given adalimumab and 1.9% given placebo.32, 33

Combination therapy (Azathioprine and antiTNF-α)
The question as to whether standard immunosuppression should be used in combination with antiTNF-α therapy has not been well investigated. UC SUCCESS was a 16-week trial in biologic naïve patients with moderately severe UC.34 Patients were failing corticosteroids and either naïve to azathioprine, or had stopped azathioprine more than 3 months before entry. Patients were randomised to infliximab, azathioprine or combination azathioprine and infliximab (induction and maintenance). The primary endpoint was steroid-free remission at week 16. Combination therapy with infliximab and azathioprine was found to be superior to both azathioprine and infliximab monotherapy in inducing remission in patients with moderately severe UC. Steroid-free remission at week 16 was achieved in 23.7% (18/76) of patients on azathioprine monotherapy, 22.1% (17/77) of patients given infliximab monotherapy and 39.7% (31/78) of patients given infliximab and azathioprine combination therapy (p=0.032 for combination vs azathioprine monotherapy and p=0.017 for combination vs infliximab monotherapy).

Access to antiTNF-α therapy for UC in New Zealand
In New Zealand, infliximab is now funded by PHARMAC and the current criteria for its use are all of the below:

- Patient has histologically confirmed ulcerative colitis; and
- The Simple Clinical Colitis Activity Index (SCCAI) ≥4; and
- Patient has tried but had inadequate response to or has experienced intolerable side effects from, prior systemic therapy with immunomodulators at maximum-tolerated doses for an adequate duration (unless contraindicated) and corticosteroids; and
- Surgery (or further surgery) is considered clinically inappropriate; and
- Patient must be reassessed for continuation after 3 months

Surgery
Thirty percent of patients with ulcerative colitis will eventually come to proctocolectomy and this includes some with troublesome distal colitis. The decision as to whether to proceed to surgery is obviously a big one, with life-long consequences. The discussion about the possibility of surgery should be started early if a patient has troublesome disease. There are many aspects to be considered. Introducing the need for surgery late in the process is difficult for all. Care must be managed by a multidisciplinary team comprising the patient and their family, gastroenterologist, colorectal surgeon, stoma-therapist and other expertise as required. A clinical psychologist can be valuable, especially for younger patients.

Removing the colon and rectum in poorly controlled ulcerative colitis restores physical well-being and quality of life. Long-term concerns about neoplasia are put aside. Patients are understandably very concerned about avoiding a “bag”. However the starting point of a discussion with the patient about surgery should focus on whether or not the time has come to remove
the colon and rectum. Although the patient will often have a strong preference for an ileal pouch, the type of reconstruction—ileal pouch or permanent ileostomy—should be a secondary consideration. The goal for most requiring proctocolectomy is an ileal pouch, but patients must accept that if they have complications they may require a permanent ileostomy. Long-term pouch failure rates are in the order of 5%. Reassuringly, patients with either an ileal pouch or a permanent ileostomy typically have the same quality of life, matching that of the general population. However, quality of life is likely to be reduced if the patient is troubled by difficult chronic pouchitis (5%), or is a teenager or young adult with an ileostomy. For a typically functioning pouch, patients empty their pouch 4–8 times a day. Although this sounds frequent, patients don’t have urgency and can usually defer for greater than 20 minutes. So, typical frequency is not a concern. Up to 30% may have a degree of minor leakage at night and 10% during the day.

Surgery provides a cure for the colitis, but carries a risk of a variety of short- and long-term complications. To reduce the risk of post operative complications, surgery is usually staged. Post-operative complications occur more frequently in patients who have been on greater than 20 mg of prednisone per day for 6 weeks or longer. Postoperative complications are not significantly increased with the use of thiopurines, calcineurin inhibitors or biological agents. Great care is needed with the occasional malnourished and immunosuppressed patient, where there may have been too much delay making treatment choices. If a patient is malnourished, septic, or on higher dose steroids, a colectomy, leaving the rectum, is usually the first operation to get the patient well. During later surgery a proctectomy is carried out, usually with the formation of an ileal pouch.

In the post-operative period, the most common serious problems from ileal pouch surgery are an anastomotic leak and subsequent pelvic abscess (5–10%). After creating an ileal pouch, it is usually covered with a temporary ileostomy to mitigate the effects of an anastomotic leak. The ileostomy is closed after about 3 months. Overall, there is a 30% chance of peripoerative morbidity, but the mortality rate in large series is very low. Patients choosing a permanent ileostomy have a lower risk of perioperative complications and, particularly in older patients, this can be a factor in some patients’ decision making.

Long-term complications of surgery need to be discussed with patients prior to surgery. There is about a 10% life-time risk of adhesive small bowel obstruction, which may require reoperation. In women who have not completed their family, if the rectum is removed there is probably a 20 to 30 percent reduction in fertility due to scarring in the pelvis. Laparoscopic surgery is associated with less adhesions and may reduce infertility rates. For these women, consideration can be given to an initial colectomy with end ileostomy and then waiting until child bearing is complete before later proctectomy and pouch formation. An ileorectal anastomosis is an option that may come up in discussion, but this is not favoured outside Scandinavia due to poor functional results and a high-rate of later proctectomy.

Thirty to 50% of patients will experience an episode of pouchitis. Acute pouchitis is usually episodic and settles quickly with antibiotics. The most common long-term problem with an ileal pouch is chronic pouchitis and this occurs in about 5%. Chronic pouchitis is managed with ongoing medical therapy, usually antibiotics, but in 1% may lead to pouch removal. If there is peri operative pelvic sepsis from an anastomotic leak, this can lead to a variety of chronic problems including fistulas, sinuses and strictures that can lead to poor function. Between 5 and 10% may also turn out to have Crohn’s disease in the long-term, with problems of strictures or fistulas. Any of these problems can lead to further surgery, revision of the pouch or in some cases removal of the pouch and a permanent ileostomy. The outcomes of surgery are influenced by the experience of the surgeon and the volumes of colectomies being performed by the centre.

In summary, surgery is a major undertaking that is currently required in 30% of patients with ulcerative colitis. There is significant potential for morbidity, but overall greater than 90% of patients are pleased with their resulting health state and bowel function.
Appendicectomy

The inverse relationship between ulcerative colitis and appendicectomy has been investigated in epidemiological studies. A Swedish cohort study demonstrated that the protective effect of appendicectomy was restricted to appendicectomy performed under the age of 20 years for appendicitis or lymphadenitis, but not for non-specific abdominal pain without objective evidence of inflammation. The theoretical explanation, based on T-cell population studies of resected appendixes, is that the appendix provides an inflammatory site and might play a role in the development of ulcerative colitis.

A recent meta-analysis regarding the effect of appendicectomy on ulcerative colitis activity compared five case-controlled and one cohort study, all with conflicting results. Due to the diversity of outcomes, insufficient adjustment for confounders and heterogeneous methodology, the pooled data were not comparable in this meta-analysis and no recommendation regarding any benefit of appendicectomy could be made. Currently, it is not possible to recommend appendicectomy for refractory ulcerative colitis, except in the setting of a clinical trial.

Biological treatments of proven benefit other than Anti TNF-α monoclonal antibodies

The treatments described in this section are neither freely available, nor funded in New Zealand at this time, but it is likely that some will become available in the future and many of these treatments (and other upcoming therapies) are available via clinical trials.

Other antiTNF-α therapies

Golimumab

Golimumab is a fully humanised anti-TNFα agent, which has been investigated in the treatment of moderately active UC and is administered in a 4 weekly subcutaneous injection. The use of golimumab was investigated in an integrated phase 2 dose-finding and phase 3 dose confirmation clinical trial of 1,064 patients with UC who were naïve to biological treatment and had failed immunomodulator, steroid and/or 5ASA therapy (774 pts in phase 3). Patients were randomised to groups given golimumab doses of 100 mg and then 50mg (phase 2), 200 mg and then 100 mg, or 400 mg and then 200 mg 2 weeks apart. The phase 3 primary endpoint was clinical response at week 6. The secondary endpoint was clinical remission at week 6. The clinical response rates at week 6 were 51% and 54.9% among patients given 200 mg/100 mg and 400 mg/200 mg respectively, vs 30.3% among those given placebo (both p<0.0001). Rates of clinical remission were significantly greater in both golimumab groups vs placebo (p<0.0014). Golimumab was approved for the treatment of UC by the US Food and Drug Administration (FDA) in May, 2013, and also by the European Medicines Agency (EMA), but is currently not available in New Zealand.

Antibodies to adhesion molecules (integrins)

Vedolizumab

Vedolizumab is a monoclonal antibody that selectively blocks α4β7 integrin expressed on lymphocytes. α4β7 integrin is responsible for T-cell homing into gut-associated lymphoid tissues through its binding to mucosal addressin cell adhesion molecule (MAdCAM), which is present on high endothelial venules of mucosal lymphoid organs.

A phase III trial investigated the induction and maintenance efficacy of vedolizumab in 895 patients with moderate to severe treatment refractory UC. Induction treatment consisted of two infusions of 300 mg on day 1 and day 15. The clinical response rate at week 6 was significantly higher in the treatment arm compared to placebo (47.1% vs 25.5 % p<0.0001). A maintenance study revealed clinical remission rates at week 52 of 44.8% for 4 weekly treatments compared to 15.9% for placebo p<0.0001. Vedolizumab has been approved by FDA in 2014, and also in many European countries, for the management of moderate to severe UC.

Inhibitors to Janus Kinases

Tofacitinib

Tofacitinib is an oral inhibitor of Janus Kinases (JAK) 1, 2 and 3, resulting in...
blocking of interleukin 2, 4, 7, 9, 15 and 21 pathways. Its use has been investigated in a double-blind placebo controlled phase II trial in 194 adults with moderate-severely active UC. Patients were randomised to receive twice daily tofacitinib at doses 0.5, 3, 10 and 15 mg and placebo for 8 weeks. Clinical remission rates at 8 weeks of 48% and 41% of patients were seen at doses of 10 mg (p<0.001) and 15 mg (p<0.001) respectively compared to the placebo rate of 10%. No long-term data are available. A dose-dependent increase in both low- and high-density lipoprotein cholesterol was seen, which might restrict this agent’s use in the future.

Other treatments of uncertain benefit

Leucocytapheresis

This technique involves removal of neutrophils, monocytes and lymphocytes via an extracorporeal system of either cellulose acetate beads or a polyester fibre filter. Each session lasts an hour, during which 2–3 litres of blood is drawn from one arm, filtered, and then returned to the other. A course of treatment takes up to 5–10 sessions at 1–2 weekly intervals. Its use has been investigated, mostly in Japan, with observational and randomised studies. In 2010, an attempt at metaanalysis of the existing studies highlighted methodological concerns (lack of controls, small sample size and short duration follow-up).

One well-designed, randomised, double-blind, sham-controlled study comparing active leucocytapheresis to sham treatment did not show any significant benefit for the treatment of moderate to severe UC patients. While leucocytapheresis is a relatively safe procedure, technical issues, such as the need for adequate venous access, the cost, and the lack of data would suggest it is not ready for widespread use.

Faecal microbiota transplantation (FMT)

Part of the pathogenesis of inflammatory bowel disease could be related to dysbiosis of the gut microbiota interacting with individual genetic predispositions via the mucosal immune system. One way of manipulating the gut microbiota is via faecal transplant. The process consists of the transfer of gastrointestinal microbiota from a healthy donor, via intestinal installation of a liquid suspension, to restore the intestinal microbiota of a diseased individual.

A recent meta-analysis of the use of faecal transplantation in the treatment of inflammatory bowel disease included nine studies of FMT for maintenance or treatment of IBD, and eight related to the treatment of infectious diarrhoea in IBD. It was not possible to conduct the meta-analysis due to the lack of randomised controlled trials, small number of reports and heterogeneity of protocols and outcomes. Of the 17 case series/reports of patients treated for IBD, the majority experienced reduction of symptoms (19/25), cessation of IBD medications (13/17) and disease remission (15/24). There was also resolution of Clostridium difficile infection in all those treated for this.

More recently, two randomised controlled studies of FMT for active UC in the absence of infection have given directly opposing results, with one showing no benefit of FMT over placebo, and the other showing clear benefit. An interesting finding in the positive study was that response related directly to the donor used. Seven of the nine patients in remission after FMT received fecal material from a single donor.

Thus, we conclude that currently there is some evidence that FMT might be a potential effective and safe treatment in UC, but that issues, such as the most advantageous microflora in the donor stool, need to be carefully considered before it can be recommended in routine practice.

Paediatric considerations

Many of the above issues and consideration are also relevant to children and adolescents with refractory UC. UC is typically more extensive in children than in adults, with the majority having pan-colonic involvement and only a small number having limited distal disease or proctitis. Further, reports illustrate early extension of disease in those with limited involvement at diagnosis.

Active UC may impact adversely upon weight, linear growth and pubertal development in children. Consequently, important aspects of monitoring children and adolescents with UC include: serial
measurements of weight and height; assessment of pubertal status (in adolescents); along with symptom review and consideration of the impact of the disease upon daily activities (eg, school, sporting and social activities).

Disease activity in children with UC can be assessed by the use of the Pediatric UC disease index (PUCAI), a well-validated composite score, ranging from 0 to 85, with a score of <10 indicating remission. In terms of standard drug therapies, corticosteroids have further particular concerns in paediatric populations with UC. The common short-term side effects of steroids (such as moon facies and increased acne) are poorly accepted, especially by adolescents. Furthermore, other concerns of ongoing steroid exposure or repeated courses of CS include suppression of linear growth and impaired development of bone strength. Consequently, CS dependence or resistance should be tolerated even less in children with UC than in adults.

5-ASA drugs have equally important roles in children as described above for adults with UC. Although numerous studies support the early introduction of thiopurines in moderate to severe Crohn's disease, there is less data in UC. However, most practitioners would consider this approach, especially in a child requiring CS to induce remission or in those with refractory disease. Further, paediatric data provide some support for tacrolimus, with less for biologic drugs at present.

Surgical intervention may have further particular considerations in children and adolescents. Firstly, colectomy should be considered with and following extensive discussion with a paediatric surgeon experienced in this procedure in young children. Close collaboration with adult colorectal surgeons will also be required. Secondly, the timing of colectomy will also need careful consideration. One important factor, for example, is the potential adverse impacts of pelvic surgery upon future fertility in young girls.

Overall, the management of refractory UC in children and adolescents requires a broad multi-disciplinary approach, with consideration of the impact of the disease and timely introduction of appropriate therapies.

Conclusions

If optimisation of standard immunosuppression fails in mild to moderate UC, then the main therapeutic options currently available are antiTNF-α therapy and colectomy. While other immunosuppressive strategies exist, they have not been demonstrated to have the same efficacy as antiTNF-α therapy. Currently the evidence for methotrexate is limited and, while there is some evidence for tacrolimus, the available studies are small.

In deciding the next therapeutic step in colitis which is refractory to standard immunosuppressive therapy, a multidisciplinary approach is essential. Discussion of what surgery involves with a colorectal surgeon and stoma-therapist will greatly aid decision making and should be endeavoured early in the process. In many cases a trial of antiTNF-α therapy will be warranted but in some situations proceeding straight to surgery may be appropriate.
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CLINICAL CORRESPONDENCE

Diabetic Charcot neuroarthropathy: The diagnosis must be considered in all diabetic neuropathic patients presenting with a hot, swollen foot

Ibrahim S Al-Busaidi, Rhett Mason, Helen Lunt

ABSTRACT

The diagnosis of diabetic Charcot neuroarthropathy (CN) is challenging. This is especially true early in the disease process, when its classical presentation of an acutely inflamed foot may masquerade as other more common lower limb conditions. Prompt diagnosis and appropriate treatment reduces the risk of CN causing permanent incapacitating foot deformity or amputation. We report two cases in which the diagnosis was delayed, resulting in long-term sequelae. These cases highlight the importance of considering CN in patients with diabetic peripheral neuropathy, who present with a red, hot, and swollen foot.

Charcot neuroarthropathy (CN) is an uncommon, but debilitating and costly complication of diabetes. Typically, it presents in patients with established diabetic peripheral neuropathy as a hot, swollen foot, either with or without pain. The diagnosis is based primarily on history and clinical examination, with no single test able to confirm or refute the diagnosis. Plain weight-bearing X-rays are used to confirm the diagnosis, but may be normal or show subtle changes in early CN. If a concomitant wound is present, advanced imaging techniques, including magnetic resonance imaging and bone scans, should be considered to differentiate between acute CN and other diagnoses, such as osteomyelitis.

It is frequently necessary to treat a foot with suspected but not confirmed acute CN by early offloading using total contact casting (a specialised casting technique) to prevent the development of irreversible complications, including ulceration, deformity, infection, and amputation.

We report two patients who were treated initially for alternate diagnoses, before a late diagnosis of CN was made.

Case reports

Case 1: A 61-year-old woman fell downstairs, injuring her left foot. Initial X-rays were unremarkable (Figure 1a); a foot sprain was diagnosed. Two months later, swelling and pain persisted. Another plain X-ray showed minor osteoarthritic changes at the first metatarsophalangeal joint. Ten months after the initial presentation, there was persistent pain and swelling. Plain X-rays now showed extensive abnormalities through the tarsometatarsal (TMT) joints. A Charcot's foot was suspected. One year after the initial fall, X-rays showed progression of the midfoot changes (Figure 1b). The patient was treated with immobilisation by total contact casting.
**Figure 1a–c:** Plain X-rays of the left foot

Panel a displays unremarkable X-ray at first presentation. Panel b was obtained at the time of Charcot left midfoot arthropathy diagnosis. Panel c demonstrates shortening of the medial column and lateral subluxation of the lesser metatarsals 6 months after initiating treatment for Charcot arthropathy.

**Figure 2a–d:** Plain X-rays of the right ankle

Panels a & b display X-rays of the ankle after an open reduction and internal fixation with tension band construct for a displaced Weber B fracture. Panels c & d show collapse of the talar dome 11 months post CN diagnosis.
then used a prefabricated walker (Moon Boot), followed by customised shoes with orthotics. Eighteen months from initial presentation, residual midfoot deformity was present on X-ray (Figure 1c). Clinical characteristics are detailed in Table 1.

**Case 2:** A 75-year-old woman sustained a displaced Weber B right ankle fracture, following a fall. Surgery was complicated by a wound infection (Figures 2a & b). A few months later, she presented with a suspected DVT. A lower leg venous Doppler ultrasound scan was normal and no specific treatment was therefore given. Signs and symptoms persisted and she was admitted to hospital for treatment of suspected cellulitis. Despite a course of oral antibiotics, signs and symptoms did not settle and she was re-admitted two weeks later with suspected osteomyelitis/septic arthritis. Investigations included a normal neutrophil count, an elevated erythrocyte sedimentation rate of 87 mm/h (N 1–30) and a modestly elevated C-reactive protein (59 mg/L). Plain X-rays were consistent with osteomyelitis of the right distal tibia and fibula and she was commenced on IV flucloxacillin. A joint aspirate grew no organisms and the clinical picture was then considered compatible with a right ankle CN. A course of offloading therapy was prescribed. There was, however, complete collapse of the talar dome 11 months post CN diagnosis (Figures 2c & d). Clinical characteristics are detailed in Table 1.

**Discussion**

The presentation of both cases, of an acutely inflamed foot or ankle in a patient with established diabetic peripheral neuropathy, is consistent with diabetic CN. Preceding foot trauma or surgery are common, but not universal, precipitants. Before reaching the diagnosis of CN, other diagnoses were considered, including foot sprain, osteoarthritis, DVT, cellulitis, septic arthritis, and osteomyelitis (see Table 1). Unfortunately, even after receiving appropriate treatment for their CN, both patients experienced residual bony deformities.

Diagnostic delays in diabetic CN are common. CN may masquerade as gout, DVT, erysipelas/cellulitis, ankle sprain, rheumatoid arthritis, osteomyelitis, and fractures. Such misdiagnoses may be partially attributed to a lack of awareness of this condition by treating professionals, and also to the lack of specific diagnostic tests, which makes a firm early diagnosis especially challenging.

In conclusion, a Charcot process should be considered in any patient with diabetes and peripheral neuropathy, who presents with an acutely inflamed foot with intact skin. Offloading of a foot with suspected CN often needs to be commenced before the diagnosis is confirmed. Locally, we are trying to increase awareness of this condition amongst at-risk patients and healthcare professionals, and would recommend other diabetes services do the same.

<table>
<thead>
<tr>
<th>Table 1: Summary of demographic and clinical characteristics of two cases with delayed diabetic CN diagnosis</th>
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<tr>
<td><strong>Case No (gender; age)</strong></td>
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<tr>
<td>Smoking status</td>
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<tr>
<td><strong>Diabetes Characteristics</strong></td>
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<td>Type</td>
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<tr>
<td>Duration (years)</td>
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<tr>
<td>Treatment</td>
</tr>
<tr>
<td>HbA1c (mmol/mol)</td>
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<tr>
<td>Peripheral neuropathy</td>
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<tr>
<td>Other diabetic complications</td>
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<tr>
<td><strong>History of trauma</strong></td>
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<tr>
<td><strong>Initial diagnoses</strong></td>
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<tr>
<td><strong>CN joint involvement</strong></td>
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<td><strong>Diagnostic delay</strong></td>
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</table>
Competing interests: Nil

Acknowledgements
We thank the patients described in this case report for giving us written permission to discuss their cases. We also thank Stephen Percival (diabetes podiatrist) for his assistance.

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REFERENCES:
A rare cause of pulmonary tuberculosis
Heidi H Y Chan, John Mpe

ABSTRACT
We present a case of bovine tuberculosis in a 50-year-old Māori female. She had worked for approximately 7 years at a local freezing works where animal organs were cleaned and packed. The diagnosis was established 4 weeks after commencement of first-line anti-TB therapy. While human zoonotic tuberculosis may be uncommon in developed countries, its diagnosis still has important public health and treatment implications.

Tuberculosis (TB) remains a devastating infectious disease worldwide. Mycobacterium bovis is an increasingly rare cause of human tuberculosis. Despite its rarity, the diagnosis of bovine TB has important public health and patient management implications. Positive tuberculin skin tests and interferon gamma release assays may be observed with Mycobacterium bovis infections. Human-to-human transmission of bovine TB has been reported, but is rare.

Case Report
A 50-year-old immunocompetent female was admitted to our hospital following a motor vehicle accident, during which she sustained an injury to her forearm. Her admission chest X-ray showed bilateral upper lobe infiltrates, suspicious for pulmonary TB.

Our patient is a New Zealand-born Māori, who grew up locally in Northland. She has been employed for the last 7 years at the local freezing works, specifically working on the offal floor where animal organs (mainly beef) were cleaned and packed. No other animal contact, overseas travel or sick contact was reported.

Her history was noteworthy for 6 months of an early morning cough with small amounts of sputum, 8 kg loss of weight over 18 months, and lethargy. Her physical examination was unremarkable.

A mycobacterium tuberculosis complex was cultured on her sputum and she was initiated on standard TB therapy (isoniazid, ethambutol, rifampicin and pyrazinamide). However, repeated smear tests returned 4+ positive, despite treatment in the following weeks. Phenotyping, including the Wayne assay, revealed resistance to pyrazinamide (susceptible however to other agents). This was confirmed with pncA gene mutation analysis which detected a mutation indicating either an M. bovis or BCG strain. The next step using molecular typing (MIRU) showed results typical with M. bovis confirming the diagnosis, so although Xpert TB polymerase chain reaction test is available, it was not performed in her case.

Pyrazinamide was withdrawn from her treatment. She went on to complete 2 months of ethambutol, rifampicin and isoniazid, and then 7 months of rifampicin and isoniazid. Her case was notified, and contact tracing involving household members and workmates was undertaken as per usual for mycobacterial TB, as there were no available guidelines on bovine TB to follow. The results of these are not known to us. On subsequent follow-up, our patient was deemed cured with no known complications from her illness.

Discussion
Tuberculosis remains a global public health threat and the most devastating human infectious disease, especially in developing countries.1 Zoonotic TB is rare in humans. Most zoonotic cases are caused
by *Mycobacterium Bovis*, with global estimates of less than 1.4% of TB cases outside of Africa attributed to *Mycobacterium bovis*. While human zoonotic TB may be uncommon in developed countries, small pockets of the disease are thought to remain, with median incidence rates of 0.03 and 0.16 per 100,000 population in Australia and New Zealand respectively. In New Zealand, 276 cases of TB were notified in 2013, and of these, *M. bovis* was identified in three cases.

The situation is different in low income countries, with crude estimates of seven cases per 100,000 population.

*M. bovis* affects a broad range of mammalian hosts, including the brush-tail possum in New Zealand. Human infections occur through consumption of infected animal products, occupational exposure to infectious aerosols from infected animals or their carcasses and less frequently through direct contact via mucus membranes and broken skin. Human-to-human transmission of bovine TB occurs, but is much rarer, with only several case reports.

There are no clinical, radiologic or pathologic features to distinguish disease caused by *M. tuberculosis* and *M. bovis*. Differentiation can only be definitively achieved by sophisticated laboratory methods involving culture, typing of isolates according to growth characteristics, biochemical properties, routine resistance to pyrazinamide and specific non-commercial nucleic acid techniques.

*M. bovis* has intrinsic resistance to pyrazinamide. Therapy for human bovine TB is extrapolated from experience with treatment of pyrazinamide-resistant *Mycobacterium tuberculosis*—with 2 months of rifampicin, ethambutol and isoniazid and 7 months of rifampicin and isoniazid.

**Figure 1:** Chest X-ray of our patient showing bilateral upper lobe infiltrates suspicious for active pulmonary TB.
CLINICAL CORRESPONDENCE

Competing interests: Nil

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A 68-year-old gentleman presented to the Emergency Department with intractable right shoulder pain following a minor trauma 3 weeks previously. His pain was worsening and had become unbearable, despite regular Paracetamol, Ibuprofen, Codeine and Nortriptyline. He had also noticed a developing weakness in the grip strength of his right hand and some altered sensation along the inner border of his hand. He had previously undergone nephrectomy and prostatectomy for renal and prostate cancer, and was an ex-smoker. On examination, he had good range of movement and minimal tenderness in his neck and shoulder with 4/5 power in extension and abduction of his fingers and hypoaesthesia in C8 to T1 dermatomes, with no hand muscle atrophy apparent. Pupils were of equal size and reactivity bilaterally. Radiographs were obtained, as shown in Figure 1a &1b.

The patient was referred for further investigation and imaging, which showed multiple bony lytic lesions, with a histological diagnosis of Multiple Myeloma. He is currently undergoing chemotherapy treatment.

Discussion

Pancoast syndrome was first described as shoulder and arm pain, atrophy of the hand muscles, and Horner’s syndrome (ptosis, miosis, and anhidrosis) caused by a carcinoma arising at the apex of the chest.1 This characteristic picture is normally associated with non-small cell lung cancer.1 Myeloma is a rare, but described, cause of the syndrome.2 Muscles, upper ribs, thoracic vertebral bodies, subclavian vessels, the inferior portion of the brachial plexus, and the upper end of the thoracic autonomic chain, including the stellate ganglion, may

Figure 1: a) Chest Radiograph showing thickened right apical cap. b) AP Radiograph of the neck showing absent first rib on the right side.
be involved to give rise to these symptoms and signs. Apart from primary lung tumours, tumours of the chest wall, lung metastases and haemopoietic malignancies have been implicated, as well as infective causes with staphylococcal, pseudomonal, tuberculous and fungal organisms. Early detection on chest X-ray is difficult in the early stages, due to overlying first rib and clavicle, but an asymmetry of apical cap of over 5mm is suspicious. CT is an important diagnostic investigation and MRI gives more accurate detail of the extent of invasion. Histological confirmation can be obtained through percutaneous transthoracic needle biopsy with ultrasound or CT guidance.

Learning points

- A history of trauma may be a red herring and intractable pain and history of previous malignancy are red flags
- Careful and systematic evaluation of Radiographs is key to ensure recognition of easily missed subtle findings

Competing interests: Nil

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Dear Editor,

We write to share our concern about a proposed change to the Code of Ethics of the Pharmacy Council of New Zealand (PCNZ), which would remove the requirement that health products sold by pharmacists have “credible evidence of efficacy”. As doctors, we have a keen interest in products and services sold to provide health benefits, and in particular their scientific plausibility and the evidence that they are safe and effective.

The pharmacist has an important role in the multi-disciplinary delivery of health care services. Every prescription leads the patient to an interaction with a pharmacist. Further, they are the first accessed health provider for many patients, and there is increasing emphasis on the pharmacist’s role in diagnosis, provision of advice and education, and more recently, prescribing.

Pharmacists, like many health providers, have a conflict of interest when they sell and give advice about health products from which they make profit. There is evidence that financial pressures impact the clinical decisions of pharmacists. The pharmacist is trusted by patients, and other members of the scientific health care team, because of their scientific training. Many patients will assume that the pharmacist endorses the health products sold in the pharmacy as scientifically supported. But many pharmacies sell products that are known to be ineffective, such as homeopathic remedies or potentially harmful, such as ear candles. Selling such products conflicts with the principles of the current Code of Ethics as it reduces patient autonomy (the patient that wrongly assumes a health product is scientifically supported is ill-prepared to make an informed decision). More broadly, it tarnishes the reputation of pharmacists as a profession.

Clause 6.9 of the Code of Ethics is important, as it specifically precludes pharmacists from selling and promoting unsupported treatments:

“Only purchase, supply or promote any medicine, complementary therapy, herbal remedy or other healthcare product where there is no reason to doubt its quality or safety and when there is credible evidence of efficacy.” (emphasis added)

Unfortunately, many health products sold in pharmacies do not meet this standard. The PCNZ has identified this breach, and should enforce their ethical code. However, the current proposal would change the code so that the sale of ineffective treatments becomes permissible. The new clause (6.9b) currently under consideration states that pharmacists must:
LETTER

“Only supply any complementary therapy or other healthcare product where there is no reason to doubt its quality or safety and when sufficient information about the product can be provided in order for the purchaser to make an informed choice with regard to the risks and benefits of all the available treatment options.”

We support the idea that adequate information on complementary therapy should be provided, and that an informed patient has the right to choose remedies that have no scientific basis. However, if such remedies belong anywhere, it is in the supermarket or health food shop—not in pharmacies where the scientific mantle is tacitly cast across all products.

The proposal that the PCNZ would no longer require that health products sold by pharmacists should have “credible evidence of efficacy” would undermine the scientific basis of health treatment in New Zealand. It also risks real harm to patients, not just in terms of wasted money, but in lost opportunities to receive effective treatment. More generally, it encourages the public to believe that treatments that are unproven or entirely implausible may be relied upon. There is substantial evidence that this causes harm.6

The Chief Scientist of the Royal Pharmaceutical Society (UK) recently wrote:

“Surely it is time for pharmacists to cast homeopathy from the shelves and focus on scientifically based treatments backed by clear clinical evidence”

Surely it is. The sale of ineffective health products as if they are effective is unethical. In this age of science, pharmacists should be outraged by the proposed change to their ethical code.

Kind Regards,
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Meeting the health needs of newly arrived refugees

Helen Saunders

The New Zealand government has responded to the Syrian refugee crisis by agreeing to take in an additional 600 emergency refugees from Syria over the next 3 years and there is a budget attached to this. The numbers of refugees arriving every 8 weeks will increase from 125 to 145 from November 2015 and from July 2016 to 165; this is a 33% increase in people that will require health screening and management at the refugee resettlement centre. As more refugees are resettled in New Zealand over the coming years, it is important that health practitioners in the community and hospitals understand what refugee health screening involves. Clearly, increasing the numbers of refugees will require additional resource at the resettlement centre and a greater investment in primary care as these people settle in the five resettlement locations around New Zealand.

New Zealand is fortunate to have a unique national reception centre, Mangere Refugee Resettlement Centre (MRRC) in Auckland, for newly arrived refugees and asylum seekers. A national reception centre confers a number of benefits for the refugees, but it must be acknowledged that the concept is not necessarily transferable to countries that receive many more refugees. The refugees come in groups to stay for a 6-week period. They have a health assessment, English language tuition and orientation to their new country. The MRRC is currently being rebuilt to accommodate more people and to incorporate the health, education and immigration services present on site.

New Zealand provides a comprehensive health screening programme for newly arrived quota refugees delivered by the Refugee Health Screening Service (RHSS), part of the Auckland Regional Public Health Service. Offshore, the refugees have a limited health assessment and the more intensive screening is done as a mandatory process on arrival in New Zealand. Health screening protects the health of the public, but it also provides essential personal health care that few refugees have had access to for some years. In addition, doing this assessment soon after arrival allows health issues to be identified and treated early and so decreases downstream costs to the New Zealand health system and the individuals.

Refugees coming to New Zealand are from a range of countries, faiths, educational backgrounds and present with a range of health needs. Most do not speak English and so interpreters are an essential part of the work. The RHSS team has built up expertise over many years; examples include awareness that Middle Eastern people may present with more hypertension and diabetes, African people with more schistosomiasis and Bhutanese with dietary Vitamin B12 deficiency. Refugees are resilient people who have often survived a long and challenging journey to New Zealand. It takes time to develop trust and understand their health needs: a 15-minute appointment is inadequate to address these. Each person is seen by a clinician for a comprehensive social, physical and psychological history and examination. Alcohol use and smoking are assessed and smoking cessation advice offered. Tuberculosis screening is undertaken with all people 11 years and older by having a chest X-ray and children less than 15 years having a Mantoux skin test. Tests are done for infectious diseases such as hepatitis B and C, HIV, faecal parasites including schistosomiasis and sexually transmitted conditions like chlamydia, gonorrhoea and syphilis. In
addition to routine laboratory tests clinicians would do in New Zealand, screening is done for haemoglobinopathies and vitamin D deficiency. Screening for diabetes and cardiovascular risk is done for men at 35 years and older and women 45 years and older. Women are offered a cervical smear and contraception is discussed and started on request. Many refugees have very poor oral health and dental work is started at MRRC. Family violence and mental health concerns are discussed and RHSS work closely with a mental health NGO, Refugees as Survivors, when issues present.

Urgent conditions may require admission to hospital for surgery or other intervention during the initial 6-week period. Respiratory and paediatric infectious disease specialists, with a knowledge of refugee health, review refugees with abnormal findings during the 6-week period at MRRC.

A critical part of the process involves assessing immunisation status and giving vaccinations; preventing diseases contracted within our country. Many have come from refugee camps and seen the devastation caused by vaccine-preventable diseases, and so are universally keen to be vaccinated. The refugees and asylum seekers are either started on the New Zealand Immunisation Schedule, or are given catch-up vaccinations if they have a record of vaccinations overseas.

At the end of their time at MRRC, refugees have a discussion about their health findings and are educated about the New Zealand health system, including how to enrol with a general practitioner. Clinical notes are sent electronically, GP2GP, so that all health screening information is available to the new clinicians. Referrals are also sent to the services in each resettlement area for health issues requiring specialist review.

New Zealand has a crucial role internationally in welcoming refugees to our land. Many refugees will contribute significantly to New Zealand in the future. Realistic support of refugees in this early phase is needed so health problems do not impede their successful resettlement in New Zealand.

Competing interests: Nil

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Claiming exercise does not solve the obesity crisis is ‘reductionism’ at its worst

Michael Hamlin, Lee Stoner


While the editorial listed above contains a number of statements we regard as misleading at best and just plain false at worse, we are also concerned that the authors have potential conflicts of interest, especially around their comments on carbohydrates. However, in this letter we wish to concentrate our reply around the suggestion made by Malholtra et al (2015) that physical activity has little effect on weight loss or obesity.

The root cause of the obesity pandemic is likely multi-dimensional in nature, including increased caloric intake, decreased caloric expenditure, as well as a myriad of socio-cultural determinants. Malholtra et al however, suggest in their editorial that there has been little change in physical activity levels (energy expenditure) in the western population over the last 30 years, and that obesity is solely due to changes in caloric consumption. Such statements ignore a substantial amount of research indicating a reduction in occupational, household and active transport energy expenditure in contemporary societies. Such a drop in physical activity (or more precisely, increased sedentariness) without a subsequent reduction in caloric intake will almost certainly result in in a positive energy balance. Indeed, when modeled, the reduction in occupational energy expenditure over the past 50 years accurately predicts the average increase in body weight in US men and women.¹

We do not disagree with the statement made by Malholtra et al that a large number of people who are shown to have a normal BMI have metabolic abnormalities typically associated with obesity, however such statements ignore the fact that BMI is not actually measuring ‘fatness’. There is an imperfect association between BMI and body fatness, particularly when lean muscle mass is altered, ie, as occurs with certain forms of exercise. Moreover, the continued focus on obesity may be obscuring the bigger picture, ie, cardio-metabolic complications. That is, obesity is a risk factor for cardio-metabolic diseases, not a guarantee.² Strong evidence has emerged to suggest that people who are ‘fat’ can still have low cardio-metabolic risk if they are ‘fit’.³,⁴ Such associations indicate just how complex the relationship between fatness and health can be, and how myopic Malholtra and associates’ arguments are.

We do not believe that the general public or the scientific community consider that obesity is entirely due to a lack of physical activity, as suggested in the Malholtra et al editorial. Most health departments in western countries promote a healthy diet in conjunction with regular exercise for maintenance of body weight and good health. Physical activity is actually good for you, something we think Malholtra et al are missing the point on. Regular physical activity, quite apart from its effects on maintaining weight loss,⁷ also decreases the risk of cardiovascular disease and diabetes,⁵ some cancers,⁶ and osteoporosis.³⁰ Just as important, regular physical activity improves self-esteem, self-confidence, and enhances overall psychological wellbeing.
LETTER

Competing interests: Nil

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LETTER

Time to move beyond industry self-regulation of food marketing in New Zealand
Stefanie Vandevijvere, Boyd Swinburn

A letter to the NZMJ by the chief executive of the New Zealand Food & Grocery Council states that our article on protecting New Zealand children against unhealthy food marketing creates the false impression that self-regulation has failed in New Zealand. It also mentions that our article on this issue is outdated.

First, what does “success of self-regulation” actually mean? From a public health perspective it does not mean compliance with a voluntary code that is very nonspecific (eg, in terms of the exact foods that cannot be marketed to children), compliance with a code not independently assessed, or the lack of complaints made by the public. Instead, “success of self-regulation” should mean that exposure of children, defined as individuals aged 18 years or younger, to the marketing of unhealthy foods, as determined by independent criteria, through all media, decreases significantly over time. A recent systematic review of the literature has shown that self-regulation by industry has not worked anywhere to reduce exposure of children to unhealthy food marketing. This concern is also clearly highlighted in the draft final report of the World Health Organization Commission on Ending Childhood Obesity published last week. While the author criticising our article correctly points out that 67% of the most prominent packaged and soft drink companies in New Zealand do have a policy to restrict food marketing to children on their websites, only 20% of fast food companies have such a policy mentioned on their website. Consequently, transparency, specificity, comprehensiveness and strength of policies to restrict junk food marketing to children by New Zealand companies could be substantially improved.

There is high-level agreement at the international level and consensus among national public health experts that comprehensive regulations to restrict junk food marketing to children are a top priority to reduce childhood obesity. In addition, 73% of the New Zealand public is supportive of tougher restrictions to reduce
junk food marketing to kids. However, in order to move beyond the current inertia due to the ongoing divide between advocates for industry self-regulation and those advocating for comprehensive government regulations to restrict unhealthy food marketing to children, let’s start exploring the feasibility and effectiveness of a quasi-regulatory approach, as proposed and explained in our viewpoint. For such an approach to have a chance to work, the Government should set clear parameters, and enforcement and monitoring mechanisms. This will also be an excellent opportunity for the New Zealand Food & Grocery Council and affiliated companies to clearly demonstrate their commitments to protecting children against unhealthy food marketing in New Zealand.

Competing interests: Nil

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Trimethoprim-sulfamethoxazole versus vancomycin for severe infections caused by methicillin resistant *Staphylococcus aureus*

This randomised trial was conducted in Israel to determine whether trimethoprim-sulfamethoxazole is non-inferior to vancomycin for the treatment of severe infections due to methicillin resistant *Staphylococcus aureus* (MRSA)? Apparently, two previous trials had provided conflicting results.

No significant difference in treatment failure was noted and the difference in 30-day mortality was also non-significant. However, the mortality rate in those with bacteraemia was significantly worse in the trimethoprim-sulfamethoxazole group.

The conclusion reached was that trimethoprim-sulfamethoxazole did not achieve non-inferiority to vancomycin in the treatment of severe MRSA infections, and the difference was particularly marked for patients with bacteraemia.

*BMJ* 2015;350:h2219

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**Pneumonia requiring hospitalisation among US adults**

Community-acquired pneumonia is a leading cause of hospitalisation and death among US adults. Incidence estimates of pneumonia confirmed radiographically and with the use of current laboratory diagnostic tests are needed. Apparently, the last similar study done in the US was in the 1990s, before the routine administration of pneumococcal conjugate vaccine in children, and the development of more sensitive laboratory tests.

Among 2,259 patients who had radiographic evidence of pneumonia and specimens available for both bacterial and viral testing, a pathogen was detected in 853 (38%): one or more viruses in 530 (23%), bacteria in 247 (11%), bacteria and viral pathogens in 59 (3%), and a fungal or mycobacterial pathogen in 17 (1%). The most common pathogens were human rhinovirus (in 9% of patients), influenza virus (in 6%), and *Streptococcus pneumoniae* (in 5%). Unsurprisingly, it was found that community-acquired pneumonia incidence correlated with age—those aged over 80 years had a six-fold incidence compared to the whole group.


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**Arthroscopic surgery for degenerative knee disease?**

What are the benefits and harms of arthroscopic knee surgery involving partial meniscectomy, debridement, or both for middle-aged or older patients with knee pain and degenerative knee disease? This is the question which this study from Denmark and Sweden examines.

The researchers identified nine relevant trials. The main outcomes were pain and physical function. Apparently, arthroscopy showed a small benefit for pain at 3 and 6 months. There were no significant benefits on physical function. Harms noted included deep venous thrombosis (4.13 events per 1,000 procedures) and its consequences.

They conclude that the small benefit seen from interventions that include arthroscopy is limited in time, absent 1 to 2 years after surgery, and associated with harms.

An editorial reviewer notes their results and his opinion is that the procedure is overused, ineffective, and potentially harmful.

*BMJ* 2015; 350:h2747 & *BMJ* 2015; 350:h2983

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**URL:**

Our King and Country need us

It is well-nigh impossible to write of the tumult and tramplings in Europe at the present time in terms of hyperbole. We may well say in the words of a contributor to this issue of the Journal, we have reached the “climax of history.” The soldier sons of this new land have emulated the example of Caesar’s Tenth Legion, of Napoleon’s Old Guard, and of Wellington’s Light Division, and while we glory in their valour, as medical men we are deeply impressed by their suffering. The Angel of Death has been abroad. As John Bright said in simple but glowing phrase, “We can almost hear the fluttering of his wings.” Even with our present numbers in the field the need for succour for the dying, the wounded and the diseased has reached a magnitude that in the peace and quietude of other days we little dreamt of. But to avoid defeat, troops and yet more troops must be sent to the field, and the need for medical officers is increasing.

Let us not neglect what is historical and sentimental. Our armies are on the road to the ancient Byzantium. On their one hand lies the Plain of Troy, and on the other the landing of another force in Macedonia at the ancient Thessalonica. We hear again the cry, “Come over into Macedonia and help up.” And in a more matter-of-fact way we have the simple belief that while New Zealand soldiers are fighting and dying, New Zealand doctors will never leave them unaided. As we go to press the Council of our Association has met urgently for the help of the Defence authorities to procure the doctors required for the New Zealand Medical Corps, and seventy at least are needed from the present time until June. A hundred have already gone. It becomes the duty, nay the privilege, of every able-bodied doctor in New Zealand to offer his services to the forces of the Crown, and we are sure the response will be a worthy one. It is true that doctors are badly required in New Zealand, and there will be hardship for the people here, but we must remember that we are not fighting alone for our honour,

A BABE JOKE. Miss Fastleigh: Good gracious! Going to discard those things called puttees the soldier wears around his limbs. They have had to bear arms up to the present: now it will be bare legs. Miss Chipin: Oh, how rude! (Observer, 09 October 1915).

but for our very existence as an Empire. We have reason to believe that as far as possible a system of reliefs will be established for medical officers whereby no medical officer against his wish will be tied down to prolonged service abroad.

We feel confident that General Henderson, who is one of ourselves, will help us in every way, and we will as loyally help him in the important and difficult task in which he is engaged. It is a time for sacrifice for all at home and abroad. When the returned wounded arrive in New Zealand there will be much medical and surgical work to be done, and both expeditionary and home service are required; but the first is the more urgent and necessary. We believe that any busy doctor’s life in practice is by no means a slight sacrifice for the public good, but we live now in a time, rare down the ages when we may make our lives significant.

Our minds are troubled and confused with the duty we owe to the State, to our families and homes, and to our patients, and withal we ought to read and study, but have little time for rest or reflection; and when peace comes, and a peace based, at whatever cost, upon the eternal principles of truth and justice for which our country and our noble allies are draining blood and treasure, may we all have the reflection that in the troubled times we did the right thing and the most and best that we could do.

Editorial, NZMJ October 1915

URL:
National Heart Foundation Grants Awarded July 2015

At the July meeting of the Scientific Advisory Group of the National Heart Foundation, a total of 29 grants were awarded. The awards included 7 Project Grants, 10 Fellowships, 7 Small Project Grants and 5 Travel Grants. A total of 5 Summer Studentships were also awarded to the Medical Schools at the University of Otago and the University of Auckland.

Project grants

**Dr Nigel Anderson**
Department of Radiology, University of Otago, Christchurch

*High resolution multi-energy CT imaging of vulnerable atherosclerotic plaque.*

$107,768 over 2 years.

**Dr Allamanda Faatoese**
Department of Medicine, University of Otago, Christchurch

*Cardiovascular and lipoprotein profiles of Pacific in Canterbury – the Pasifika Heart Study.*

$78,834 over 1 year.

**Dr Sarah Fitzsimons**
Department of Medicine, University of Auckland

*IMPERATIVE-ECHO.*

$144,640 over 2 years.

**Dr Anna Pilbrow**
Christchurch Heart Institute, University of Otago, Christchurch

*Improving cardiovascular risk prediction in the general population.*

$77,949 over 2 years.

**Associate Professor Helen Pilmore**
Department of Renal Medicine, Auckland City Hospital

*Canadian-Australasian randomised trial of screening kidney transplant recipients for coronary artery disease (CARSK study).*

$150,000 over 2 years.

**Dr Anna Rolleston**
The Cardiac Clinic, Tauranga

*The effect of a 12-week exercise and lifestyle management programme on cardiac risk reduction: A controlled trial using a kaupapa Māori philosophy.*

$150,000 over 3 years.

**Professor Ralph Stewart**
Green Lane Cardiovascular Services, Auckland City Hospital

*Oxygen therapy in acute coronary syndromes.*

$150,000 over 3 years.

Fellowships

**Dr Nikki Moreland**
A 0.3 Heart Foundation Senior Fellowship (for 2 years) was awarded to Dr Nikki Moreland, School of Biological Science, University of Auckland.

**Dr Sarah Fitzsimons**
An Overseas Training & Research Fellowship (for 1 year) was awarded to Dr Sarah Fitzsimons. Dr Fitzsimons will work in advanced heart failure management and heart transplantation at Papworth Hospital, Cambridge, UK.

**Dr Sarah Fitzsimons**
An Overseas Training & Research Fellowship (for 1 year) was awarded to Dr Sarah Fitzsimons. Dr Fitzsimons will work in advanced heart failure management and heart transplantation at Papworth Hospital, Cambridge, UK.

**Dr Kerryanne Johnson**
A 0.5 Overseas Training & Research Fellowship (for 1 year) was awarded to Dr Kerryanne Johnson. Dr Johnson will work in multimodality cardiac imaging at Leeds General Infirmary, Leeds, UK.
NOTICE

Dr Kashif Khokhar
A 0.5 Overseas Training & Research Fellowship (for 1 year) was awarded to Dr Kashif Khokhar. Dr Khokhar will work as an Electrophysiology Fellow at Royal Adelaide Hospital, Australia.

Dr Anthony (Shaw Hua) Kueh
An Overseas Training & Research Fellowship (for 1 year) was awarded to Dr Anthony (Shaw Hua) Kueh. Dr Kueh's imaging fellowship will focus on cardiac CT and cardiac MRI at St Paul's Hospital, Vancouver, Canada.

Dr Gnalini Sathananthan
An Overseas Training & Research Fellowship (for 1 year) was awarded to Gnalini Sathananthan. Dr Sathananthan will work as an ACHD (adult congenital heart disease) Fellow at Toronto General Hospital, Canada.

Dr Woo Bin (Tiffany) Voss
An Overseas Training & Research Fellowship 0.5 (for 1 year) was awarded to Dr Woo Bin (Tiffany) Voss. Dr Voss will undertake an Echocardiography Research Fellowship at Northwestern Memorial Hospital, Chicago, USA.

Dr Nikki Earle
A Research Fellowship (for 3 years) was awarded to Dr Nikki Earle, Department of Medicine, University of Auckland.

Dr Corina Grey
A Research Fellowship (for 3 years) was awarded to Dr Corina Grey, Section of Epidemiology and Biostatistics, University of Auckland.

Dr Vicky Yang Wang
A Research Fellowship (for 2 years) was awarded to Dr Vicky Yang Wang, Auckland Bioengineering Institute, University of Auckland.

Small project grants

Professor Vicky Cameron
Department of Medicine, University of Otago, Christchurch
Heart disease risk markers in Canterbury healthy volunteers.
$14,818 over 1 year.

Miss Nikki Earle
Department of Medicine, University of Auckland
Circulating microRNAs as markers of arrhythmia risk in survivors of myocardial infarction.
$15,000 over 1 year.

Ms Simone Inkrot
Department of Cardiology, Waikato Hospital
Person-centred care in the context of chronic heart failure management in the community.
$9,890 over 18 months.

Associate Professor Johanna Montgomery
Department of Physiology, University of Auckland
Examining the role of synapse function and plasticity in the little brains of the heart.
$14,900 over 1 year.

Dr John Pickering
Department of Medicine, University of Otago, Christchurch
Time course profiles of high sensitive troponin in patients at risk of acute myocardial infarction.
$15,000 over 1 year.

Dr Daryl Schwenke
Department of Physiology, University of Otago
A PILOT study – identifying the physiological relevance of acyl vs non-acyl ghrelin for modulating cardiac sympathetic nerve activity following acute myocardial infarction.
$14,805 over 9 months.
Dr Jichao Zhao
Auckland Bioengineering Institution, University of Auckland
*Structural characterisation of explanted intact human atria.*
$15,000 over 1 year.

**Travel grants**

Dr Sarah Fitzsimons
Department of Cardiology, Auckland Hospital
*European Society of Cardiology Congress, London, UK.*

Dr Rajesh Katare
Department of Physiology, University of Otago
*American Heart Association Annual Scientific Session, Orlando, USA.*

Dr Regis Lamberts
Department of Physiology, University of Otago
*European Society for Cardiology Congress, London, UK.*

Dr Pau Medrano-Gracia
School of Medical Sciences, University of Auckland
*MICCAI 18th International Conference, Munich, Germany.*

Ms Shruti Rawal
Department of Physiology, University of Otago
*American Heart Association Annual Scientific Session, Orlando, USA.*

**URL:**
**Differential effects of organic versus inorganic selenium species on BRCA1-mutated and non-mutated breast cancer cell lines**

Annie Ko\(^1\), Kirsty Mayall\(^2\), Holly Sprosen\(^3\), Linda Peters\(^4\), Michael Jameson\(^5\)

\(^1\)Laboratory of Molecular Biology, University of Waikato, Hamilton, New Zealand. \(^2\)Department of Oncology, Waikato Hospital, Hamilton, New Zealand

**Background:** Selenium (Se) is an essential non-metal trace element with anticancer chemopreventive effect through protecting healthy cells from oxidative damage. Twenty-five proteins in mammals are found to harbour Se in the form of selenocysteine, some of which are antioxidants that prevent reactive oxidative species from damaging the cell membrane and DNA, and also maintain the redox balance within cells. However, the effect of Se is dependent on the dosage and the chemical form of Se intake. High levels of Se (especially inorganic forms) can result in increased DNA damage, whereas low levels can cause decreased immunity, increased cancer incidence and mortality risk. Previous research showed that selenite supplementation reduced bleomycin-induced DNA damage in individuals carrying a BRCA1 mutation but a trend to increased breast cancer incidence was seen in a randomised trial in this population using supra-nutritional doses of selenite.

**Methods:** The aim of this research is to evaluate the interaction of Se dose and chemical form in BRCA1-mutated and non-mutated breast cancer cells in vitro. In this study we applied Se (as organic methylseleninic acid (MSA) and inorganic selenite) to four commercially-available BRCA1 or non-BRCA1 mutated breast cancer cell lines. Se sensitivity was measured by examining DNA damage and cell viability with the comet assay and the colorimetric MTT assay, respectively.

**Results:** Comparison of the comet assays between two BRCA1-mutated breast cell lines (MCF-7 and MDAMB231) and two non-BRCA1-mutated breast cancer cell lines (MCF-7 and MDAMB231) showed significantly (p=0.01) greater DNA damage in the cells with BRCA1 mutation for each Se compound. For cell viability, measured with the MTT assay, the IC50 of selenite is lower in BRCA1-mutated cells than the non-BRCA1-mutated cells.

**Conclusions:** From this study, the BRCA1-mutated breast cancer cell lines appear to be significantly more sensitive than non-BRCA1-mutated cells towards Se treatment. We will explore whether this differential sensitivity is maintained in conjunction with chemotheraphy. If so, this could potentially be exploited in patients with BRCA1-mutated metastatic breast cancer.

**General anaesthetic modulation of gene expression in the mouse brain**

Liam Stayte, Dr Linda Peters, Dr Logan Voss

General anaesthetics cause widespread neurochemical and physiological changes in the brain, however the precise mechanism of amnesic action is largely unknown. Gene expression changes in the hippocampus have been a focal point for investigation in this area, while effects on the cerebral cortex have been largely unreported.

The aim of this research was to investigate the in vitro cortical gene expression pattern of two memory-related genes; Arc and Bdnf, t=4 hour exposure to sevoflurane- or propofol-induced anaesthesia using an adult mouse model and compare that data to the in vivo results. Our in vivo research demonstrated that Bdnf was significantly down-regulated by sevoflurane at both t=2 hrs and t=4 hrs, and propofol at t=2 hrs (p<0.05). Up-regulation of Arc following t=4 hr exposure to propofol was also observed, but no change in Arc was found at the other time points or treatments. These results suggest that down-regulation of Bdnf occurs in the mature cerebral cortex in response to anaesthesia and support other studies that have indicated decreased expression of Bdnf in hippocampal, thalamic and immature cortical tissue.

**Ethnic disparity in patients who remain hypothyroid following definitive treatment for Graves’ disease**

Kelson Tu’akoi, Jade AU Tamatea, Goswin Y Meyer-Rochow, John V
Conaglen, Marianne S Elston

**Background:** Graves’ disease (GD) is the leading cause of thyrotoxicosis in New Zealand, responsible for approximately 64% of cases. Current therapeutic options for GD include anti-thyroid medication or definitive treatment (radioactive iodine [RAI] or surgery). There is no clear consensus as to whether the long-term outcome is better after surgery or RAI. Abnormal TSH levels have consistently been demonstrated in approximately half of all patients treated for primary hypothyroidism. The aim of this study was to assess long-term euthyroidism rates in patients following definitive therapy.

**Methods:** A retrospective review of all patients treated with either RAI or definitive treatment (radioactive iodine [RAI] or surgery) between 1 December, 2000, and 31 March, 2013, in Hamilton, New Zealand. TSH levels at 1, 2, 5 and 10 years after treatment were recorded.

**Results:** A total of 801 patients were included; 591 having received RAI and 210 surgery (total thyroidectomy between 1 December, 2000, and 31 March, 2013, in Hamilton, New Zealand. TSH levels at 1, 2, 5 and 10 years after treatment were recorded.

**Conclusion:** Surgery is associated with a higher short-term rate of euthyroidism (first 2 years) but there is no difference in the rates of euthyroidism by 5 and 10 years following treatment. Māori and Pacific Peoples have significantly lower euthyroidism rates than their New Zealand European counterparts, and this inequality was present at all time points. Overall, long-term euthyroidism rates were low, indicating the need for improved care of patients who have undergone definitive therapy for Graves’ disease.

**The progression of mild cognitive impairment (mci) to dementia in a specialist memory**

Galley N1, Zheng C2, Ma’u E1
1University of Auckland, New Zealand, 2Mental Health Services for Older Persons, Waikato Hospital, Hamilton, New Zealand

**Aim:** Mild cognitive impairment (MCI) refers to a transitional state between normal aging and early dementia and is thought to represent a population at increased risk of progressing on to dementia. The aim of this study is to determine factors associated with the risk of conversion from MCI to dementia.

**Method:** We retrospectively reviewed the clinical records of all patients diagnosed with MCI in the Waikato DHB memory service between January 2008–December 2014. Those who received no subsequent follow up in the service were excluded from further analysis.

**Results:** 168 patients received a diagnosis of MCI, with 109 being followed for at least 6 months, with a median of 568 days. Of the demographics investigated, only female gender was shown to be associated with progression to dementia. Lower cognitive testing scores at diagnosis as measured by the MoCA (p=0.0001) but not the MMSE (p=0.057), predicted progression to dementia. Functional assessments using either the Bristol scale (p=0.085) or Informants Questionnaire (p=0.091) did not predict progression. Compared to psychiatrists, patients initially diagnosed with MCI by geriatricians were more likely to progress to dementia (53.1% v 80%, p=0.003), even after controlling for age, gender and MoCA score (OR 3.55, p=0.036)

**Conclusion:** Only gender and cognitive testing scores at diagnosis predicted progression to dementia in this setting. The differences in progression rates between those diagnosed by geriatricians and psychiatrists highlights the need for a standardised approach to the diagnosis of MCI.

**Effect of the rate of purge of volatile gas anaesthetic (vga) on emergence from general anaesthetic according to a novel index to assess emergence quality**

Winders JD, Hight DF, Sleigh JW

**Background:** It is currently unknown whether the rate at which a volatile gas anaesthetic (VGA) is removed from a patient after surgery has an effect on the quality of emergence from anaesthesia. We developed an index to assess the quality of emergence to help answer this question.

**Methods:** Observational study of general anaesthetic patients at Waikato District Hospital between May 2013 and January 2015. EEG and VGA concentration data were recorded from forehead electrodes and the anaesthetic monitor throughout surgery. On waking, patients were assessed every 15 minutes with our index for pain using a numerical pain scale (above four out of ten considered high pain), arousal levels using the Richmond Agitation Sedation Score (RASS) and Ramsay sedation score, and content of thought (in the absence of sedation, agitation or high pain) using the Confusion Assessment Method for the ICU (CAM-ICU).

**Results:** 232 participants consented and 206 of these were eligible for data analysis. Logistic regression showed the rate of VGA removal did not have a significant effect on quality of emergence using our index. The use of an endotracheal tube (ETT) was associated
with increased disturbance of arousal (sedation or agitation) (p-value 0.0368, odds ratio (OR) 3.905), older patients and longer operations were associated with increased confusion (p-values 0.0297 and 0.0126, OR 1.006 and 1.058 respectively), while older patients were less likely to report high pain (p-value 0.0466, OR 0.0984).

Conclusion: This study suggests the rate of VGA flushing after surgery does not affect the quality of emergence from general anaesthesia, but other factors—such as use of ETT, operation length, and age—do. Our index, using pain, arousal and content of thought, appears to be useful as these three parameters had different predictors. More research needs to be done into the interactions between these variables and the use of this index.

Clinical and dermoscopic features of blue naevus
Jenny Chung, Amanda Oakley

Background: Blue naevi are mainly blue, benign skin lesions characterised by deeply pigmented dermal spindle-celled melanocytes. Blue naevi can mimic the clinical features of pigmented spindle cell melanoma, nodular melanoma and metastatic melanoma. There are overlapping dermoscopic features that can make the clinical diagnosis of blue naevi challenging. A good understanding of the epidemiology, clinical and dermoscopic features of blue naevi and melanoma helps the clinician decide whether to excise blue-coloured melanocytic lesion for histological diagnosis.

Aims: To retrospectively review patient and lesion characteristics in a cohort of patients diagnosed with blue naevi in New Zealand.

Method: Data were reviewed for patients diagnosed with blue naevi attending the Waikato Virtual Lesion Clinic between January 2010 and January 2015. Patient demographic and melanoma risk factors were recorded and compared with a cohort of patients diagnosed with nodular melanoma using univariate analysis on SPSS. Body location, clinical and dermoscopic features were collected for each lesion.

Result: Fifty-five patients with 57 blue naevi had a mean age of 47 years (range 4 to 78) with thirteen (24%) patients being male. In comparison, thirteen patients with 13 nodular melanoma were older with a mean age of 68 (range 32 to 90) and 85% were male. 78% of blue naevi patients were of European/New Zealand ethnicity (100% in nodular melanoma); and 43% had blue, green or hazel eye colour, compared to 77% in nodular melanoma patients. (p-value = 0.031) Nodular melanoma patients had a statistically significant history of sun damage, with 77% with many hours in the sun compared to 29% in BN patients (p-value = 0.05).

Most patients had Fitzpatrick photoskin type 2 (51%) and type 3 (27%), compared to NM with 92% and 8%, respectively. The most common body sites for BN were the face and neck (24%), hands (24%), shoulder (19%) and arms (17%); in NM they were the shoulders (23%), lower limbs (23%) and back (23%). One blue naevus was greater than 6 mm in diameter and 53% had regular shape. All NM were greater than 6 mm in size, with 54% having regular shape. 35% of BN were elevated, compared to 92% of NM.

Pigmentation in 98% of lesions was homogenous with 86% of lesions being blue only or blue mixed with another colour. Hypopigmentation was noted in 23% of lesions. One NM was reported as homogenous, and all but one (92%) were polychromatic or amelanotic. All NM had more than one local feature reported compared to 21% of BN. Diagnosis was confirmed for 6 of the 57 BN (10%) by biopsy. All NM were biopsied.

Discussion: The characteristics of blue naevi in patients referred to the Waikato VLC were similar to that described by Di Cesare, 2012 and other published works. A typical blue naevus is a small round macule or papule, with steel-blue homogeneous pigmentation on dermatoscopy. They arise in children and adults and remain stable. In comparison, blue-coloured nodular melanoma, or cutaneous metastatic melanoma, are common in older individuals and rapidly enlarge. They are typically raised and often present with the ABCDE features of melanoma (Asymmetry, Border irregularity, Colour variation and Diameter>6mm). On dermatoscopy they exhibit multicomponent features and are polychromatic. Rarely, a blue naevus may exhibit these features. A careful history and examination of the size and features of the lesion may help determine the need for a biopsy.

Conclusion: Study of the clinical and dermoscopic features of blue naevi help avoid the need for biopsies in typical benign lesions.

A review of pigmented skin lesions in dark-skinned patients referred to a teledermoscopy service
Liyanage PLAN1, Oakley A1, Rademaker M1

1Department of Dermatology, Waikato District Health Board

Background: Pigmented lesions in white-skinned individuals are of concern due to higher incidence of melanoma; however, limited data is available on pigmented lesions in dark-skinned individuals. General practitioners (GPs) in Waikato and Waitemata District Health Board regions can refer patients with skin lesions of concern to a teledermoscopic service, or virtual lesion clinic (VLC). History, clinical and dermoscopic images of the pigmented lesion are assessed to arrive at a teledermoscopic diagnosis. Published literature about reasons for referrals of pigmented lesions in Fitzpatrick IV/V skin phototypes is sparse.

Objectives: Objectives were to determine the reasons for...
referral, referral urgency, and teledermoscopic diagnoses in patients with Fitzpatrick skin phototypes IV and V.

**Methods:** Patients with Fitzpatrick skin phenotype IV/V seen in Waikato and Waitemata District Health Board virtual lesion clinics (VLC) from January 2010 to December 2014 were included. Referrals, patients’ demographic data and teledermoscopic diagnoses were evaluated.

**Results:** Of a total of 3,685 patients, only 224 had Fitzpatrick skin type IV/V (6%). One percent of referrals were categorised by the referrer as high suspicion of cancer, 14% urgent, 23% semi urgent and 33% were routine referrals. Referral urgency was not recorded in 27% of referrals. Most referred lesions (93%) were pigmented. There were 139 females (62%) with a mean age of 44 years (range 5–86 years). The ethnicity of 51.79% of the study group was Māori, followed by Asian (23.6%), Pacific origin (8.9%), European (7.1%), African (1.7%) and other (5.5%). Seventy percent had black hair colour and 93.3% had brown eyes. Three patients had a family history of melanoma in first degree relatives and 5 in second degree relatives, but none had a personal history of melanoma. Ninety-six percent reported no significant history of sunburn. Early life of residence was Australia/New Zealand in 71.8% of the study group. Many (48.6%) worked indoors with outdoor vacations, whereas 40% regularly worked outdoors. Of a total of 351 lesions, 328 (93%) were pigmented. The most frequent feature of concern to the referrer was morphological change in a pigmented lesion (59%), usually change in size, change in colour, and/or bleeding. One-fourth of referrals were for a new lesion, and 16% of referrals were for an existing lesion of unspecified concern to either doctor or patient. The size of the pigmented lesions varied from 1 mm² to 12 cm² (mean 123 mm²). Most pigmented lesions were diagnosed as melanocytic naevi (n=116, 33%) followed by seborrheic keratosis/solar lentigo (96, 27%) and dermatofibromas (22, 6.2%). Among the melanocytic naevi, 100 were acquired, 10 were congenital and 6 were atypical clinically. They were mainly distributed on head and neck (45%) or trunk (38.7%). There were 7 suspected melanomas (classified as definite, probable or possible), 3 basal cell carcinomas and 1 squamous cell carcinoma. However, there was only 1 histologically confirmed melanoma.

**Conclusion:** Referred skin lesions in patients with dark skin are usually benign mela-noctic naevi or seborrheic keratoses/solar lentigos. The clinical and dermoscopic characteristics of benign and few malignant lesions were similar to those observed in light-skinned individuals.

**Comparison of melanoma risk factors in confirmed melanoma patients and general cohort referred to the Waikato Virtual Lesion Clinic**

**G Harvey, A Oakley**

**Background:** The baseline risk factors for melanoma are age, gender and ethnicity. Other relative risk factors identified in the Clinical Practice Guidelines for the Management of Melanoma in Australia and New Zealand (2008) include personal history of melanoma (x10 compared to no previous melanoma) or non-melanoma skin cancer (x4 compared to no previous history), more than 100 melanocytic naevi (x7 compared to <15 naevi) and atypical naevi (x6 in patients with >5 atypical naevi compared to those with none). Light skin, hair and eye colour, and family history of melanoma are less significant risk factors.

**Aims:** To compare melanoma risk factors of the general cohort of patients referred to Waikato Virtual Lesion Clinic (VLC) to VLC patients with confirmed melanoma.

**Method:** Retrospective review of melanoma risk factors recorded in patients referred to the VLC between January 2010 and May 2015. Numbers of melanocytic naevi, atypical naevi, and presence of actinic damage were not recorded.

**Results:** There were 3,773 patients; 179 had melanoma (5%). 56% of the entire cohort and 84% of the melanoma patients were aged over 50 years. 36% of the entire cohort and 54% of the melanoma patients were male. 90% of the entire cohort and 99% of the melanoma patients were of European heritage.

Smaller differences between the control and melanoma groups were seen with personal history of melanoma (6% compared with 11%), light skin (Fitzpatrick skin type 1-2 in 73% compared with 88%), and fair or red hair colour (28% v 32%), blue eye colour (46% v 61%), history of sunburn (90% v 97%), and family history of melanoma (first-degree relative in 7% compared with 10%).

**Conclusion:** Our data confirms published risk factors are more common in melanoma patients than in the general VLC cohort.

**The effect of pharmacist medicine counselling on treatment goals for end stage renal disease patients on haemodialysis**

Singh H¹, Ragupathy R², Sizeland P³, Goddard J¹, McNabb F³

¹Pharmacy Services, Waikato District Health Board, Hamilton.
²Waikato Renal Services, Waikato District Health Board, Hamilton
³Pharmacist medicine, Waikato Renal Services, Waikato District Health Board, Hamilton

**Introduction:** Non-compliance with medications is an issue in end stage renal disease (ESRD) dialysis patients. Barriers to compliance include potential lack of understanding and poor education around complex medication regimens. Non-adherence to medications may contribute to suboptimal clinical outcomes.¹² There is a shortage of studies that evaluate
the effect pharmacist-led education programmes have on clinical outcomes in patients with ESRD. 2

Method: Twenty-four ESRD patients receiving haemodialysis at the Waikato Regional In-centre Dialysis Unit were included. A non-randomised cohort study design was used, with the intervention (n=14) and one control (n=10) group. The intervention group received fortnightly one-on-one semi-structured counselling sessions with a pharmacist over a six month period. The first session each month covered one topic, with the patient required to prove recall in the next session. A visual education tool with supplementary text was developed and used. The study was approved by the Northern B Health and Disability Ethics Committee.

Results: There was no significant difference in the proportion of patients achieving target phosphate levels - primary outcome - between intervention and control groups (0.52 v 0.38, p=0.096, Chi-Square test). The proportion of patients achieving systolic (0.49 v 0.29, p=0.014, Chi-Square test) and diastolic blood pressure targets (0.94 v 0.66, p<0.001, Fisher’s exact test) after dialysis was significantly better in the intervention group.

However, the mean ultrafiltration rate was significantly higher in the intervention group (2.8L v 2.4L, p=0.001, two tailed t-test).

Discussion: In this small cohort of patients, pharmacist-led medication counselling was not shown to definitely improve clinical outcomes in ESRD patients receiving haemodialysis. Limitations include small sample size and the effect of unmeasured confounding factors on clinical outcomes, which were not accounted for in this study.

These factors complicate the interpretation of the results. A larger study, over a longer time period may be needed to provide sufficient power for some outcomes. Further studies applying these principles to pre-dialysis patients may also be of value.

Understanding barriers to optimal medication management for those requiring long-term dialysis: rationale and design for an observational study and a quantitative description of study variables and data. BMC Nephrology 2015;16:102.


The vascular access between cost and efficacy

M Ramadan, T Pegg, N Fisher

Background: Radial artery approach (RAA) for diagnostic angiography and intervention is considered the preferred access site, however little is known about the costs of radial or femoral artery approach (FAA). We compared the two approaches in terms of cost effectiveness, hospital stay & post-operative complication in a regional New Zealand secondary care centre.

Method: Comparison of 100 consecutive patients undergoing elective and acute diagnostic cardiac catheterisation via radial approach vs 100 patients via femoral approach. Patients awaiting transfer to tertiary centres were excluded from the analysis of the hospital stay variable. Equipment and procedural data were retrospectively analysed for all cases.

Results: Mean Intra-operative cost was 141 for RAA v $150 for FAA (RR 1%, P 0.91). 63% of patients undergoing a RAA stayed < 1 day versus only 35% of FAA stayed < 1 day (P 0.003). The mean length of stay for a RAA was 0.54 days v FAA 1.2 days. In elective patients RAA mean length of stay < 0.2 days, v FAA 0.7 days (p<0.000666). Mean contrast volume in RAA was 100 ml v 120 ml with FAA (P 0.002). Fluoroscopy times were 4 mins for FFA v 5 mins for RAA (p=0.8). No patients undergoing RAA experienced a procedure-related complication v 3/100 FAA patients had major bleeding complications.

Conclusion: Radial approach is cost effective and safer than femoral in a real world secondary care regional PCI centre. These results are consistent with the international trials.

Intestinal colonisation pattern in very low birth weight preterm infants following robotic supplementation

Olivia Egan, Dr Chris Mansell, Dr Arun Nair

Gut microbiota play an important role in neonatal development with the ability to influence the physiology, immunology and biochemistry of the host. Premature very low birth weight (VLBW) infants weighing <1500 grams at birth have an increased risk of developing gastrointestinal problems such as necrotising enterocolitis (NEC) along with systemic infections. Research suggests that the colonisation of beneficial bacteria is delayed in preterm infants and this may contribute to the high incidence of inflammation, feeding intolerance and infections in this group. A baseline study conducted at Waikato Hospital also demonstrated a paucity of beneficial bacteria in VLBW infants indicating that there is a need for interventions aimed at normalising gut flora and improving long-term health outcomes in this at risk group. The aim of this study was to characterise the effects of probiotic supplementation in a cohort of VLBW infants born into the NICU at Waikato Hospital during the 10-week study period. The probiotic Inforan which contains bifidobacterium bifidum and lactobacillus acidophilus was used. Lactobacillus and Bifidobacterium are two probiotic bacteria that predominate the microflora of healthy, term neonates. Aerobic and anaerobic stool microflora were collected following probiotic supplementation and serially characterised. Conventional stool culture methods were used and colony identification was achieved via Matrix-assisted laser desorption/ionisation-time of flight mass spectrometry (MALDI-TOFMS). Results showed that beneficial
bacteria were present in stool samples from the first week of life, accounting for 12.4% of all growth. This finding supports the use of probiotic supplementation as a therapeutic treatment for VLBW preterminfants.

**Is Inguinal Hernia Repair in those under 6 months of age Safe and Ideal?**

Divya Kosuri, Jitoko Cama
Paediatric Surgery Department,
Waikato Hospital, New Zealand

Over a 3-year period, from January, 2010, to December, 2013, a total of 302 patients with inguinal hernias were operated on at our institutions who were under 6 months of age. Of these, 76 (25%) patients were born prematurely and 226 (75%) were term babies. Of these premature babies, 17 (22%) presented with strangulations requiring taxis reduction before surgery, of which 2 (11.7%) required an open reduction. Of the 76 (25%) premature babies, 7 (9%) had an associated ipsilateral undescended testis (UDT). Of the term 226 babies, 55 (24%) patients presented with strangulations and 17 (7.5%) patients had a nassociated UDT. Bilateraling uinal hernias was present in 61 (20%) patients, of which 24 (39%) were premature babies and 17 (27.9%) had a strangled hernia on presentation. Two (3%) patients later re-presented with strangulation of the contralateral hernia.

An ipsilateralundescended testis was a common association with inguinal hernias as was seen in 7 (9%) premature babies and 17 (7.5%) term babies. Orchiopexy being done at the same time of the hernia repair was performed in 4 (57%) of the premature babies and 10 (58.8%) of the term babies. Two (28.5%) premature patients needed a contralateral orchiopexy later, one got transferred and one UDT later descended into scrotum. Only one patient (14%) from the prematurity group needed to have redo-orchiopexy procedure 4-years after the initial surgery and one had recurrence of hernia. Of the 17 UDT term babies, 10 (58.8%) had orchiopexy at the same time and 5 (29%) had orchiopexy later and 1 re-do with 3 recurrent hernias. One inguinal wound infection and 2 hydroceles from under 6 months of age but difficult to assess the testicular atrophy due to the subjective findings of the assessors on follow-up. Inguinal hernia recurrence was noted in 4 babies (1%) which demonstrated a very low morbidity if these operations are done by paediatric surgeons when patients are under 6 months of age. There was no morbidity which high light the safety of the anaesthetic even at this age but long-term follows-up will be required on some of these patients due to various reasons. We believe that inguinal hernias in children under 6 months should be managed surgically on a semi-urgent basis to minimise the risk of strangulation and other long-term complications.

**Heart Failure Self-Care in Aotearoa/New Zealand: Results from the New Zealand Heart Failure Registry**

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**Purpose:** Excess in HF mortality amongst ethnic minority groups is likely to be multifactorial, including cultural and historical factors. Self-care is known to contribute outcome in heart failure (HF) patients. International comparisons indicate that self-care behaviours could be improved worldwide. HF self-care amongst Māori has not been studied. Our analysis describes HF self-care in Aotearoa/New Zealand (NZ) and aims to identify potential differences between Māori and New Zealand Europeans (NZE).

**Methods:** We added self-care assessment to the nationwide NZ HF Registry at 3-month follow-up post admission with acute or decompensated chronic HF, using the 9-item European Heart Failure Self-care Behaviour Scale (EHFScBS-9). On a scale of 0-100, higher scores indicate better self-care. A score ≥70 indicates adequate self-care. We analysed differences between Māori and NZE using bivariate analysis. We used logistic regression to assess factors predicting better than median self-carescores.

**Results:** Of n=235 who completed baseline and follow-up visits between December 2013 and September 2014, self-care data was available for n=107 [24% Māori; mean age 73.38% female, mean EF 28%]. We found no difference in mean self-care scores between Māori v NZE [64±15 vs 58±17, p=0.12]. In logistic regression including age, sex, ethnicity, symptoms, medication, and education factors, only providing patients with a target dry weight range according to which they could adjust their flexible diuretic regimen, and outpatient referral were associated with better self-care [OR 5.86, 95% CI 1.15-29.91, p=0.033; OR 6.01, 95%CI 1.71-21.11, p=0.005]. Dyspnoea and ankle oedema at baseline were associated with worse self-care at follow-up [OR 0.11, 95%CI 0.02-0.80, p=0.030;OR=0.34, 95%CI 0.14-0.84, p=0.019].

**Results:** Despite clinical differences such as having lower EF, Māori display similar self-care skills as NZE. Overall, self-care skills could be improved. Our data suggest that providing patients with the tools to self-care (e.g. providing target weight range) and ensuring outpatient follow-up are imperative.

**URL:**

Obituary

George Stewart Purvis
6 June 1926–6 December 2014
MB ChB Dip Obst FRNZCGP

S tewart Purvis will be remembered as one of Papakura's longest serving General Practitioners.

After a childhood in Masterton, Gisborne and Christchurch—followed by years in Dunedin at Otago Medical School—he loved the opportunities offered in the area of Papakura in the early 1950s. It was warm, fishing and boating were easy to access, he made good friends who took him duck shooting and it was near to Auckland for shopping, movies and shows. He and his wife, Leslie, raised five children in Papakura, and as the town grew, so did his community interests. Stewart became a member of the Rotary club, served on the foundation Board of Rosehill College and became the Chairman, enjoyed learning Morse code with the local Radio Club, had fun with the Woodturners Guild, and for over 40 years was dedicated to his patients. Thousands of times he delivered babies at Papakura's or Pukekohe's maternity hospital, and knew exactly how many minutes he needed to drive to each. House calls were taken for granted in his era. Before the morning, afternoon and evening surgery (Monday, Wednesday and Friday nights for over 40 years) he drove all over South Auckland and as far away as Orere Point. Many patients did not have transport, and often he took his children for the drive, to give Leslie a break and the children an outing, where they were entertained by the healthy members of the patient's families, as well as their animals.

Flying was something he was fascinated by. His father had trained as a pilot towards
the end of World War I, and with Ardmore being very close to Papakura, Stew became a designated Medical Examiner for Civil Aviation in 1967. He did try to learn to fly, but was plagued by airsickness, so was unsuccessful in attempts to become pilot. (Interestingly, his son Graham is a pilot.)

In 1998, he became a Fellow of the Royal College of New Zealand General Practitioners. In 1991, he was awarded the Paul Harris Fellowship by Rotary International for special and significant contributions to his Community and Rotary during 30 years of Rotary membership.

Upon retiring, he became interested in computing, joined the local Probus club and continued with his Rotary interests. Going on a trip to China with Leslie was a highlight of his early retirement. Overseas travel had always been limited by the difficulty in obtaining locums until then. He was a man with a huge range of interests, and would go to Whitcoulls or the University Bookshop regularly to buy armfuls of books on topics he found interesting. Maintaining a large property and tinkering in the toolshed kept him busy and his grandchildren entertained—they used to beg for rides with him on his ride-on mower.

Stewart and Leslie were both well known and respected in Papakura. Sadly, Leslie died six months after Stewart. They are survived by their 5 children, and numerous grand and great grandchildren.

Author information:
Janet Sweetman

URL:
Dr Maurice Matich (Snr)
19 February 1922–24 August 2015
OBE MBChB FRNZCGP

Maurice Matich (Snr) died peacefully at his Dargaville home on 24 August, 2015, in his 94th year.

He was born in Dargaville, the son of Croatian immigrants, and brought up on the shores of the Kaipara harbour at a bay now known locally as Matich’s Bay.

He often attributed his longevity to an early diet of fresh Kaipara mullet and snapper, and oysters from Beacon Point.

He trained at Otago Medical School, qualifying in 1946. He was the first graduate of Croatian heritage to come out of Otago. His ability to speak Croatian came in handy over the years, as many of the old Croatian gum-digging families settled in the Dargaville district.

He initially intended to get his Fellowship in Obstetrics in England, but having met and married Maureen, and with the Cold War worsening, he returned to Dargaville and the surrounding area to work as a GP. He remained in the Dargaville district for the next 50 years, retiring in 2000. He delivered several thousand babies during his time.

He became interested in medical politics, becoming Chairman of the Medical Association in 1974–75. He was involved in negotiating favourable GP fees for the newly developed Accident Compensation Corporation, his mantra always being, “I don’t care who pays me, so long as it is enough!!”

In 1975 he was appointed to the Royal Commission into Contraception, Sterilisation and Abortion whose 1977 report led to the Contraception, Sterilisation and Abortion Act.

In the late 60s he also set up an innovative GP Group Practice in Dargaville with the late Drs Neville Hogg and Phil Barham. The present Dargaville Medical Centre is a continuation of this.

He was held in high regard by local Māori, overseeing the transition from mud-floored huts at Kaihu and further south at Repia to proper homes in the late 50s and early 60s. He often said that health was more than medicine, and encompassed many things, such as good housing and sanitation. He was instrumental in setting up satellite clinics in the surrounding areas, including diabetes clinics to help improve Māori health.

He is considered a Rangatira of the Pouto marae and his photo will sit there alongside the other elders.

In his spare time, he enjoyed farming on the family farm at Mangatara, just outside of Dargaville, and his children recount great times spent there planting pine trees and burning swamp kauri—the value of which not being appreciated at the time.

He himself suffered life-threatening fractured ribs whilst bulldozing trees on the farm. The young doctor who assessed him at Whangarei Hospital had difficulty understanding what a GP was doing on a bulldozer!

He played bowls and golf, attaining high standards in each, but his main joy was time spent fishing and mucking around on...
the Kaipara Harbour. Children and grandchildren were taught to swim, fish, water ski, chase stingrays and dolphins, and sail. They remember with much affection the kauri launch Swanee on which many a good time was had.

He is survived by his wife Maureen, and his children Visko (England), Maurice (Western Australia), Stephanie (Wellington), Siobhan (Auckland), Michaela (Whangarei), Damian (England) and Amanda (Dargaville).

Author information:
Maureen Matich, Stephanie and Amanda Matich, Richard Harman

URL: