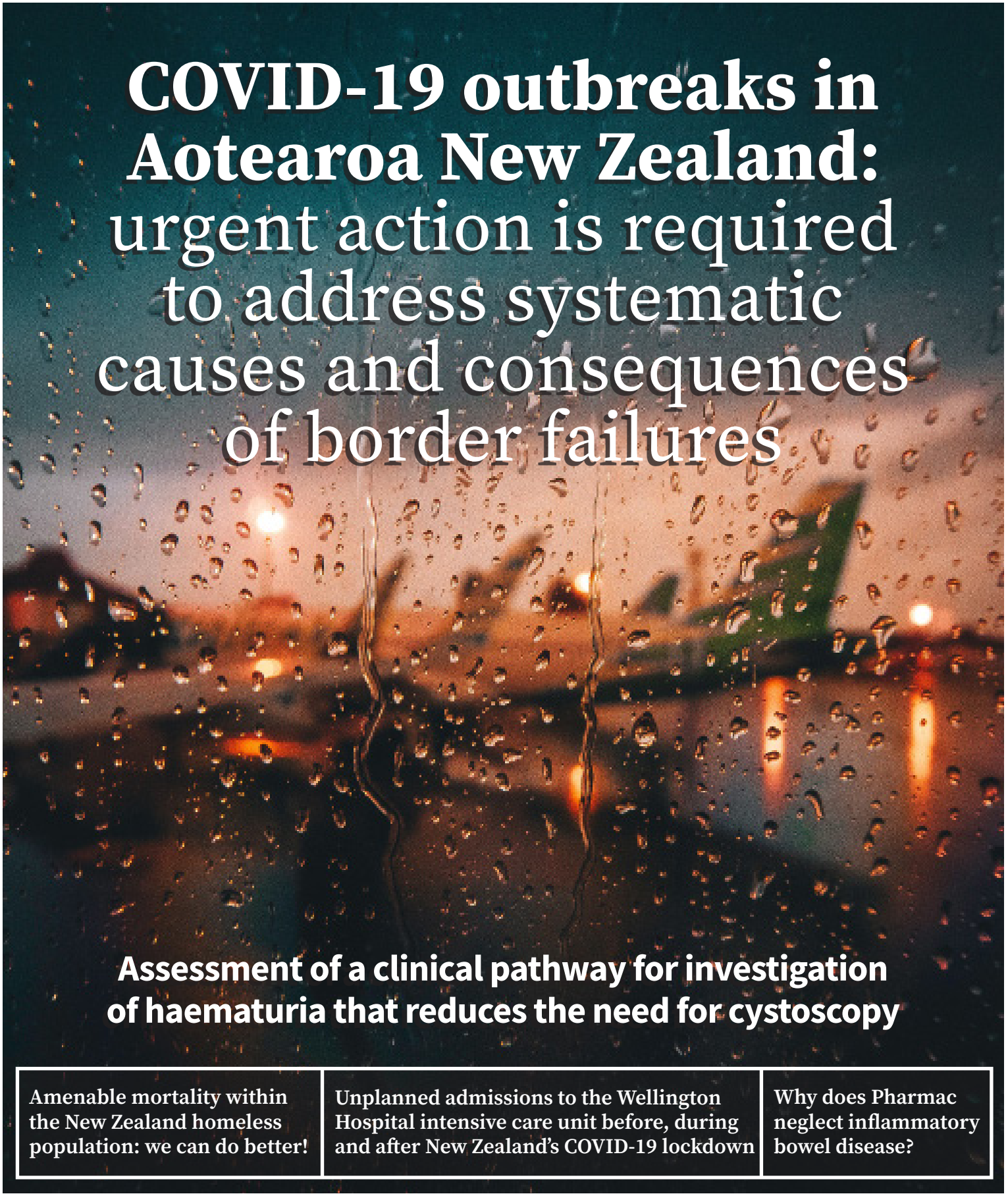
The
New Zealand
Medical Journal
Journal of the New Zealand Medical Association
Vol 133 | No 1527 | 18 December 2020



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The New Zealand
Medical Journal
Publication Information
published by the New Zealand Medical Association

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ISSN 1175-8716

ISSN 1175-8716

Faculty of Radiation Oncology 2018 workforce census: the status of the radiation oncology workforce in New Zealand

Melissa L James, Philip Munro, John Leung, Siddhartha Baxi

Radiation oncologists treat cancer with radiation treatment, which is an important cancer treatment used for up to 50% of cancer patients. This is a report of a survey of the New Zealand radiation oncology workforce. The survey shows that New Zealand is reliant on overseas trained oncologists (currently 30% of the workforce). Radiation oncologists report working long hours to make sure their direct patient responsibilities are met, with little time for research and other quality improvement activities. Over half of the radiation oncologists report a desire to retire within the next 15 years, and the numbers of trainees are too low to meet this demand. This reports raises concerns that the radiation oncology workforce is facing critical shortages which may significantly impact cancer services in the future.

Amenable mortality within the New Zealand homeless population: we can do better!

Sandrine Charvin-Fabre, Ottilie Stolte, Ross Lawrenson

The coroners' records of people identified as homeless reveal a pattern of deaths in young people, mainly males, who have died without effective intervention from the health system. Many of these are young men who have died from suicide. We believe our findings are evidence of the need to provide homeless people with better access to healthcare services that will take account of the special circumstances in which most homeless people are living.

Improved foot management of people with diabetes by primary healthcare nurses in Auckland, New Zealand

Barbara Daly, Bruce Arroll, Krishnarajah Nirantharakumar, Robert Keith Rhodes Scragg

Nurses play an important role in the management of people with diabetes. Educating patients to protect their feet and check for early signs of foot disease is essential to reduce foot ulceration and amputation. Practice nurses have significantly expanded their role in managing diabetes patients over the last decade by increasing foot examinations and providing recommended foot-care education. Almost 60% of patients had their feet checked when visiting a practice nurse in 2016 compared with 36% in the 2006–2008. Improved management was associated with nurses attending diabetes education in the past five years.

Change in health profile of refugees resettling in New Zealand, 1980–2014

Martin Reeve

New Zealand has been officially taking refugees from overseas since the end of the Second World War. Since 1980, they have all stayed at the Mangere Refugee Resettlement Centre on arrival, where they prepare of their new life in New Zealand, which has included health screening. In 1980 the doctors at Mangere reported that a lot of the refugees had infectious diseases such as gut parasites like hookworm, but very little in the way of chronic diseases such as diabetes. In recent years the amount of infectious diseases has reduced, in some cases quite markedly, but the amount of chronic disease has increased. This is probably because most refugees do not come from large refugee camps as they used to, but now mostly come from private accommodation arranged for them by the United Nations agency for refugees, where they have access to better healthcare, so the infectious diseases do not arise or are taken care of, and the chronic diseases diagnosed and treated. This is important because infectious diseases can be dealt with quickly, but chronic diseases usually take a lifetime of care. The records for mental health are not so complete, so a similar comparison cannot be made, which is unfortunate, as mental health is often the most important health issue for a resettling refugees.

Assessment of a clinical pathway for investigation of haematuria that reduces the need for cystoscopy

Peter J Davidson, Graham McGeoch, Brett Shand

The use of a bladder tumour marker, Cxbladder Triage, allows 39% of patients with the problem of blood in the urine to be assessed fully by their general practitioners. This avoids, for these patients, the need to go to a secondary-care hospital and have assessment by telescope into their bladders.

Drug-induced ocular inflammation

Priya Samalia, Joanne Sims, Rachael Niederer

Ocular inflammation induced by medications is uncommon but is important to recognise. This paper provides a description of our experience of ocular inflammation and the drugs that can cause it at our centre as well as a review of the literature. Bisphosphonate medication, commonly used for bone protection, was most frequently associated with ocular inflammation. Other newer cancer drugs can induce ocular inflammation, but in the majority of cases, inflammation can be managed without the need to stop these life preserving medications.

Unplanned admissions to the Wellington Hospital intensive care unit before, during and after New Zealand's COVID-19 lockdown

Paul J Young, Benjamin Gladwin, Alex Psirides, Alice Reid

This study reports unplanned ICU admission rates during New Zealand's initial COVID-19 lockdown. In association with the lockdown, we observed a dramatic drop in unplanned ICU admissions across almost all diagnostic categories.

Consensus statement on the treatment of transplant-eligible patients with newly diagnosed multiple myeloma in New Zealand

Nicole Chien, Ken Romeril, Bart Baker, Hugh Goodman, Henry Chan, on behalf of the Myeloma Interest Group

Multiple myeloma is the second most common blood cancer in New Zealand. The disease remains incurable, but there has been considerable advancement in treatment that has led to improved patient outcome. The current consensus statement aims to provide up-to-date recommendation for treatment of newly diagnosed transplant eligible myeloma patients in New Zealand.

Why does Pharmac neglect inflammatory bowel disease?

Andrew McCombie, Malcolm Arnold, Marian O'Connor, Richard Stein, James Fulforth, Belinda Brown, Richard Gearry

Inflammatory bowel disease (IBD) has not had a new drug funded by Pharmac since 2009 despite comparable countries in the OECD having new effective drugs funded such as vedolizumab and ustekinumab. This is also despite similar drugs being funded in recent times for patients with immune mediated inflammatory diseases in rheumatology and dermatology who, it should be noted, are less likely to be hospitalised. Funding these new drugs would be more effective and cost effective than double dosing existing biological drugs for IBD patients in New Zealand. Overall, Pharmac neglects IBD despite the high direct and indirect costs of untreated IBD relative to other diseases.

Training clinicians to lead clinical IT projects

Robyn Whittaker, Rosie Dobson, Lara Hopley,
Delwyn Armstrong, Barbara Corning-Davis, Penny Andrew

The health sector needs clinicians who can understand and lead digital and IT projects within the health service as we progressively 'digitise' systems. They are important 'translators' between the end users of systems and the developers of the systems. Waitematā District Health Board and the National Institute for Health Innovation developed a 'hands-on' training programme for a range of clinicians at the DHB. These clinicians found the week-long programme to be enjoyable and useful.

COVID-19 outbreaks in Aotearoa New Zealand: urgent action is required to address systematic causes and consequences of border failures

Amanda Kvalsvig, Jennifer Summers,
Lesley Gray, Lucy Telfar Barnard, Michael G Baker

ABSTRACT

Between August and November 2020, Aotearoa New Zealand experienced eight known failures of the COVID-19 border control system. Multiple introductions of this highly transmissible virus into New Zealand's almost completely susceptible population present a high risk of uncontrollable spread, threatening New Zealand's elimination strategy. In this editorial, we propose that, although steps are being taken reactively in response to these known breaches, systematic underestimation of risk across the pandemic response makes future failures inevitable. We present an epidemiological framework for identifying and addressing risk, giving examples of actions that can be taken to reduce the probability of further outbreaks and enable New Zealand to benefit from sustained elimination of COVID-19.

By May 2020, Aotearoa New Zealand had successfully eliminated community transmission of SARS-CoV-2 (COVID-19).[1] The only remaining source of new infections in this island nation was then by introduction through the border.[2] Managing COVID-19 transmission risk from the large numbers of returning New Zealand citizens, permanent residents and government-approved visitors has placed enormous demands on staff and systems. Although the vast majority of returning travellers have made a safe transit through the borders into their communities, system failures can and do occur.

Lapses in border security during Alert Levels 3 and 4 could not develop into sustained outbreaks, because the whole country was effectively in quarantine. But when the country returned to Alert Level 1 the risk of rapid community transmission returned. Since that initial return, the country has experienced eight occurrences of transmission to individuals outside managed isolation and quarantine (MIQ) facilities. The circumstances surrounding these high-risk events (as far as they are known) are detailed in a recent Public Health Expert blog.[3] Since publication of the blog, an additional instance of community transmission has been identified in the Defence Force worker (November) outbreak (Case F).

These known recent outbreaks have been swiftly controlled using a well-coordinated public health response supported with innovative and effective use of genomic sequencing. However, each undetected introduction of the SARS-CoV-2 virus into community spaces is an extremely high-risk

event, as illustrated by the Auckland August outbreak, New Zealand's largest to date. The origin of the index community transmission occurrence in that outbreak remains unknown as the outbreak only became visible after it was already well-established and difficult to control, and the outbreak reached 179 cases before transmission was extinguished.

COVID-19 outbreaks in Aotearoa have caused significant morbidity (including chronic severe morbidity—the 'Long COVID' syndromes) and, sadly, also fatal cases.[4] Community transmission that requires stepping up Alert Levels is highly disruptive, with consequences that include widespread hardship from loss of employment, increased mental distress, reduction in economic activity and both educational and non-educational harms to children and young people from school closures.

The COVID-19 pandemic has some characteristics that lead to a systematic underestimation of risk. We propose using the well-established epidemiological concept of false negative test results to bridge this gap and identify the key areas where additional control measures will make the most difference.

Understanding systematic border failures as a problem of false negative results

Health professionals are familiar with the concept of false negative diagnostic test results, where a true positive is erroneously identified as a negative or missed case. This situation results in lost opportunities to manage a case appropriately. In an infectious disease outbreak, this type of error also means that individuals will be unaware of the risk they pose to others.

The proportion of false negative results is a function of the sensitivity of the test (ie, the proportion of true positives testing positive).[5] Thus, because no test is perfect, a negative COVID-19 result does not rule out infection: it only means that the person is less likely to be a case than if they had tested positive. What this means in practice is that the risk of being falsely reassured by a test depends on two factors:

1. the person's chance of being infected based on their circumstances (the 'pre-test probability')
2. the test sensitivity or, equivalently, the false negative risk[6]; the latter appears more appropriate for a risk assessment format.

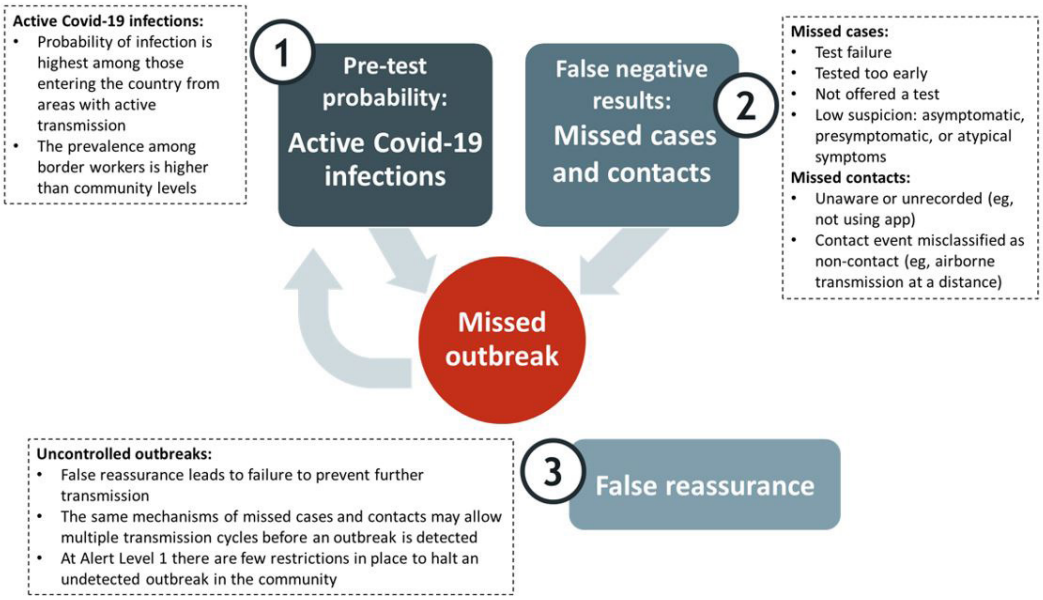
A key strategy in using this approach for a systematic assessment of risk in the border system is to think about COVID-19 testing beyond the narrow sense of diagnostic testing in individuals[7] (eg, using the RT-PCR test) and instead consider case finding as a COVID-19 test of the border system and the country as a whole. In that context, a 'positive test result' indicates detection of COVID-19 transmission from border settings into the community, while a 'false negative' is a missed transmission.

There are indications that the border system may be experiencing many false negative results in addition to the known positives. Genomic sequencing of imported cases during the first pandemic phase in 2020 demonstrated that only 19% of introduced sequences resulted in onward transmission of more than one case.[8] This phenomenon has also been described outside New Zealand and is known as overdispersion. The converse of this observation is that the number of true introductions of COVID-19 into communities is likely to be larger (and may be much larger) than the number of observed outbreaks.

How false negatives drive border failures: areas for intervention

Several factors combine to make COVID-19 outbreak prevention particularly challenging for border systems and for the pandemic response as a whole. Prevention of border failures needs a systematic approach, where risks are addressed or mitigated proactively. In particular, a full assessment of risk requires an understanding of the 'critical control points' where risk factors coincide to enhance and amplify one another. Figure 1 illustrates

Figure 1: Using a 'false negatives' approach to identify three key drivers of border failures.



false negatives as a driver of border failures and shows how they interact.

Using a 'false negatives' lens, the three drivers of border failures become more visible, indicating the three broad areas where preventive actions will make the most difference.

1. Pre-test probability is high at the borders:

- There is a *high risk of infections among persons entering New Zealand*, including returning New Zealanders and airline and shipping crew, particularly if they started their journey in a region with high levels of active transmission. Infections may be transmitted to others during travel (eg, on ships or aircraft), or in MIQ facilities after arrival in New Zealand, further increasing the pre-test probability of infection.

2. A high risk of false negatives is an intrinsic property of the COVID-19 pandemic:

- It can be *difficult to identify a case* before onward transmission has occurred. Cases can be asymptomatic or pre-symptomatic while infectious,[9] or they may present with atypical symptoms (eg, children presenting with diarrhoea). Without a basis for suspecting COVID-19 infection, individuals may not be tested. Even if tested routinely, as in the MIQ system, RT-PCR tests can return a false negative result if the timing of the test is not optimal.[10]
- COVID-19 transmission occurs not only via droplet spread during close contact, but also via airborne aerosol spread and, much less commonly, via spread from contaminated surfaces. Transmission can thus occur between individuals who are separated in space or time, making it *difficult to identify all contacts of a case*. Identifying contacts is important because contacts are the potential next cases in the transmission chain and the COVID-19 serial interval is short.[11]

3. The consequences of missing even one case through false reassurance are potentially severe:

- Border-associated workers are at a high risk of infection when they work in settings where there are infectious cases. They currently appear to experience a *high level of occupational risk* of COVID-19 infection, and this reason alone justifies stringent measures to keep them safe in their workplaces.
- However, border workers also present a *risk to their close contacts*

Table 1: Systematic approach to prevention of border failures.

	Examples of actions to:		
Populations	**1. Minimise the pre-test probability of infection**	**2. Minimise the risk of a missed case or contact**	**3. Minimise the consequences of a missed case or contact**
Incoming travellers	• Switch to a risk-based ('traffic light') system to identify travellers from jurisdictions with high and low levels of community transmission and adjust the intensity of border control measures accordingly.[3] • Pre-departure testing/quarantine for high-risk ('red zone') jurisdictions. • Review in-flight measures including mask wearing, ventilation and filtration of cabin air, physical distancing. (Despite reassurance from the airline industry,* there is convincing evidence of recent transmission on a long-haul flight to New Zealand despite in-flight precautions.)[12] • Develop a vaccine strategy for incoming travellers. • Systematically investigate all COVID-19 positive cases detected in MIQ to identify risk factors for infection that are potentially modifiable.	• Regular revision of COVID-19 diagnostic tests and testing regime to achieve optimal sensitivity of the process (eg, using frequent low-sensitivity point-of-care tests instead of less frequent high-sensitivity tests).[7,13] • Consider the use of detection dogs in airports and MIQ facilities.[14] • Involve users of the system in development of measures to increase ownership and adherence to physical distancing requirements.	• Active: Stringent infection control procedures in MIQ and port facilities to prevent incoming travellers from infecting other travellers or border-associated workers (see next row). Procedures need to include provision for emergencies (eg, media recently reported close contacts occurring during a fire alarm in an MIQ facility). • Passive: Built environment, particularly air filtration and natural or mechanical ventilation, designed to reduce airborne transmission,[15] and UV light as used in tuberculosis treatment settings may also have value for COVID-19.[15] • Development of purpose-built quarantine facilities outside main centres (eg, Ōhakea airforce base)[16]
Workers in border-associated occupations	• Supply PPE to hospital standards and institute environmental protections as above.	• Optimise timing of tests relative to transmission opportunities (ie, testing schedule linked to work schedule). • Review and optimise exemptions for some border-associated occupations. • In some settings (eg, Defence Force workers in accommodation facilities), test wastewater to 'capture' missed infections. • Use of contact tracing technology (eg, CovidCard) to track connections in time and space.[17]	• Physical distancing measures timed to their likely exposure history (eg, not to attend meetings or crowded indoor social events and to avoid settings such as aged-care facilities during set time periods). • Transmission measures timed to their likely exposure history (eg, wearing a mask in public spaces). • Workers and vulnerable whānau may need to reduce close contact during set time periods, following the model of increasing restrictions placed on Defence Force workers in this environment.[18] • Consider live-in arrangements for high-risk staff, as is being proposed in Victoria, Australia, and prohibit second jobs.[19]

Table 1: Systematic approach to prevention of border failures (continued).

Close contacts of workers in border-associated occupations	• Occupational safety protections as above to prevent infections in border workers.	• Monitor health status with a low threshold for testing (including testing children presenting with gastrointestinal symptoms and other less typical manifestations).	• Contacts of workers and vulnerable whānau may need to reduce close contact during set time periods. • Intensify contact tracing for border workers by identifying contacts prior to them commencing work.[19]
Whole population	• The whole population is protected when returning travellers and border workers are protected. • Targeted, equitable population vaccine strategy.	• Available and accessible COVID-19 testing. • Wastewater testing, particularly in areas close to border facilities. • Enhanced sentinel surveillance in selected communities.	• Additional protections at Alert Level 1 including mandatory masks in public transport, general practitioner waiting rooms, aged-care facilities, hospitals and so on, as previously recommended. • Built environment, particularly ventilation, designed to reduce airborne transmission.[15]

* https://www.iata.org/en/pressroom/pr/2020-09-08-012/

because these workers then mix with others (co-workers, household contacts and the general public) with few restrictions when away from border settings, as if their level of risk was the same as the general population. Some border-associated occupations involve workers travelling between regions in the course of their jobs, with potential for viral spread between regions.

- The default response setting of *Alert Level 1* includes minimal measures to prevent undetected transmission in public spaces; New Zealanders mix freely in crowded indoor settings and few wear masks unless required to do so.
- Virtually the whole country is *susceptible to COVID-19 infection*.

Given these inherent risks, it is unsurprising that Aotearoa is experiencing a high frequency of infection transmission from the border into the community despite the large amount of effort and resource deployed in the system.

Risk assessment: reviewing the border response in a systematic way

Agencies reviewing the border response using a risk assessment approach can prevent systematic underestimation of risk by aiming to understand and address the problem of false negative results. Such a review would consider measures to:

1. Minimise incoming infections to reduce the pre-test probability of infection.
2. Minimise the risk of a missed case or contact.
3. Minimise the consequences of a missed case or contact by increasing infection control measures in settings where infected and susceptible individuals mix in time or space. The stringency of measures needs to be adjusted proportionately to recognise the pre-test probability and risk of false negatives for each setting and population.

Ideally, a multi-agency review would invite users of the system (eg, border workers and guests in MIQ facilities) to contribute their day-to-day experiences and insights about how systems work 'on the ground' and to identify points where there may be potential for undetected transmission.

Table 1 shows examples of actions that could be taken across these three areas.

Summary and recommendations

There is an urgent need for a review of the border system to prevent ongoing border failures that incur high wellbeing and economic costs. Multiple potential actions are listed in Table 1, and this table could be further populated during the course of the review as vulnerable points in the border system are identified.

Prioritisation would be needed and could be based on considerations such as effectiveness, acceptability and cost. High priorities are likely to include switching to a risk-based approach with additional measures, particularly pre-travel quarantine and testing, for travellers from high incidence countries, to prevent them arriving in New Zealand while infected. Quantitative assessment of false negative risks can be used to compare the likely effectiveness of proposed control measures.

Although COVID-19 is a new infection, it has been eliminated in Aotearoa New Zealand using well-established infection control measures such as border restrictions and quarantine. Similarly, sustained elimination will require the application of epidemiological principles in a systematic way to guide appropriate action, as shown in this editorial by the use of false negative results as a framework for management of risk at the borders. A high standard of strategic risk management is required because impacts on population wellbeing from breaches in control of this highly transmissible infection are substantial and should never be underestimated.

Competing interests:
Dr Telfar-Barnard reports other from New Zealand Ministry of Health, outside the submitted work.

Acknowledgements:
This work was supported by funding from the Health Research Council of New Zealand (20/1066).

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URL:
www.nzma.org.nz/journal-articles/covid-19-outbreaks-in-aotearoa-new-zealand-urgent-action-is-required-to-address-systematic-causes-and-consequences-of-border-failures

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Faculty of Radiation Oncology 2018 workforce census: the status of the radiation oncology workforce in New Zealand

Melissa L James, Philip Munro, John Leung, Siddhartha Baxi

ABSTRACT

AIM: This paper outlines the results of the Royal Australian and New Zealand College of Radiologists (RANZCR) Faculty of Radiation Oncology (FRO) 2018 workforce census. Here we report the responses of New Zealand radiation oncologists and trainees in order to understand characteristics of the New Zealand radiation oncology workforce.

METHOD: The workforce census was conducted online during July–September 2018. Distribution was by Survey Monkey to all radiation oncologists (fellows, life members, educational affiliates, retired) and trainees on the RANZCR membership database, including members from Australia, New Zealand and Singapore. All responses were aggregated for analysis. This paper addresses only responses from New Zealand members. The census was designed to explore issues relevant to the New Zealand workforce, and questions from previous workforce censuses were repeated in order to monitor trends.

RESULTS: The response rate for New Zealand radiation oncologists was 73.3% (44/60). The majority (67%) were male. The average age was 50.8 years. Three-fifths (59.5%) reported New Zealand ethnicity. One-third obtained their specialist qualifications outside of Australia and New Zealand. Most worked in the public sector only (63.4%), with only two in exclusive private practice. Most radiation oncologists attained a consultant post immediately on completion of training, but there were 26 who pursued an overseas fellowship. Most worked one full-time equivalent or greater (FTE), with 17.5% working less than 1.0 FTE. Radiation oncologists reported working a median of 50.0 hours per week, with half working over 10 hours above their contracted hours. Most time was spent on clinical duties with minimal time spent on research. Radiation oncologists reported seeing an average of 235 new patients per year (median: 230). Leadership positions were held by 21/43 respondents. Within 15 years, 55% of the current workforce reported an intention to retire, including 30% of those currently practising highly specialised brachytherapy. Females in the workforce were less likely to work fulltime and spent less time in research and management activities. All trainees reported full-time work, although 50% expressed a desire for part-time training. Half of the trainees reported working 6–10 hours on call, and 60% reported two or less hours of protected teaching per week. Despite this, 90% of trainees were satisfied with their career choice.

CONCLUSIONS: Radiation oncology is a small specialty in New Zealand, with a significant reliance on overseas-trained specialists. The specialty continues to work significant overtime hours while time spent on research and non-clinical duties remains low. The growth in staffing between the 2014 and 2018 census has been low. Trainee numbers do not appear sufficient to meet the demand for replacing staff, due to retirements and the reduction of hours. Radiation intervention rates are low in New Zealand, but growth would be reliant on an expansion of the workforce beyond simply replacing staff losses. The radiation oncology workforce in New Zealand remains vulnerable, and careful consideration must be given to expansion and retention to ensure a viable workforce for the future.

Health workforce planning requires a complex interplay of factors: changing workforce demographics, the education required for the appropriate skill set (a time lag for training means the workforce cannot rapidly adapt to increases in the number of skilled personnel required), recruitment and retention, organisational culture and the demand (again, a complex interplay of incidence, changes in population demographics and other treatment options). Radiation oncology is integral to cancer care, with one in two cancer patients estimated to benefit from radiation treatment.[3] Thus, workforce planning is vital to ensure this crucial service is able to meet future needs. This article presents the results of the sixth Royal Australian and New Zealand College of Radiologists (RANZCR) radiation oncologist and trainee workforce census, surveying the Australian, New Zealand and Singaporean membership (see Appendix 1).[1] Here we concentrate on the New Zealand responses, which provide a self-reported snapshot of the current radiation oncology medical workforce in New Zealand and inform us of workforce demographics, patterns of work, potential changes in retention, organisational structure and the thoughts of those who are in training and who may be recruited to positions in the future.

Previous RANZCR workforce surveys were performed in 1996, 2000, 2006, 2010 and 2014. In 2014, for the first time, analysing results by country was possible.[2] This analysis indicated some unique issues facing the New Zealand workforce and provides a basis to analyse trends and inform future planning.

International radiation oncology workforce studies have indicated a number of themes, including demographics of the work force (including diversity), work (hours, type and context) and trainee needs.[4,5] This survey enables us to explore those themes in the New Zealand radiation oncology workforce and compare with international trends and, also, with data reported for other specialties within New Zealand.

Methods

The Faculty of Radiation Oncology workforce census ran from July to September 2018 and was hosted on Survey Monkey. A link inviting participation was sent to all active radiation oncologists and registrars in the RANZCR membership database. Weekly reminders were sent until closure.

Census questions were designed by the Faculty of Radiation Oncology Economics and Workforce Committee. Questions from previous censuses were repeated to monitor trends, and additional questions were added to explore current issues, such as time spent in multidisciplinary clinics and involvement in leadership and issues relevant to New Zealand, such as brachytherapy specialisation.

Questions in the survey followed logical rules guided by previous responses. For example, a person who identified as retired would not be asked questions regarding work hours.

Statistical analyses, including independent samples t-tests, Chi-squared, and Mann–Whitney U tests, were performed where appropriate using IBM SPSS Statistics v19 software (Armonk, NY: IBM Corp).

Results

Eligible study sample

The census was sent to 654 members and 457 responded (69.9%). In New Zealand, the survey was sent to 86 with 63 responses (73.3%) (Table 1).

This table indicates the proportions within the membership categories were similar, indicating a low likelihood of non-responder bias. The ratio in the retired member category is lower at 50%, but as these were excluded from subsequent analyses, the effect on outcomes was not thought to be significant. For further analyses, the term radiation oncologists included all those eligible to practise as a specialist in radiation oncology in New Zealand (including fellows, life members and educational affiliates).

Radiation oncologists

Demographics

The RANZCR membership database identified 60 radiation oncologists in New Zealand, 44 (73.3%) of whom responded to the census (Table 2). There were 19 radiation oncologists in New Zealand who obtained their specialist qualifications outside of Australia and New Zealand. There were 42 responses to the question about year of graduation, with 29 (69.1%) graduating between

Table 1: Population of radiation oncologists/trainees in New Zealand.

Category	N (population)	N (respondents)	Response rate (%)
Fellows	54	40	74%
Retired members	4	1	25%
Students	22	18	81%
Educational affiliates	4	2	50%
Life members	2	2	100%
Total	86	63	73%

Table 2: Demographics of New Zealand radiation oncologists and radiation oncology trainees.

Variable		
Gender	**Radiation oncologist N (%)**	**Trainee**
Male	40 (67%)	14
Female	20 (33%)	8
Total	60*	22
Male to female ratio	2:1	1.75:1
Age	**Radiation oncologist N (%)**	**Trainee**
25–29	0	2 (9)
30–39	7 (11.7%)	19 (86.4)
40–49	23 (38.3%)	1 (4.6)
50–59	17 (28.3%)	0
>60	13 (21.7%)	0
Total	60*	22*
Average (years)	50.8	32.8
Median (years)	49.5	33
Ethnicity	**Radiation oncologist N (%)**	**Trainee**
New Zealand	25 (59.5%)	6 (33.3)
Asian	7 (16.7%)	9 (50%)
European	3 (7.1%)	2 (11.1)
Other	7 (16.7%)	1 (5.6)
Total	42 (100)**	18 (100)**
FTE	**Radiation oncologist N (%)**	**Trainee**
<1.0	7 (17.5%)	0
1.0	20 (50%)	22 (100)
>1.0	13 (32.5%)	0

*Survey data supplemented with membership data.
**Numbers vary with number responding to each question.

1975 and 1995, 10 (23.8%) between 1996 and 2005 and only three (7.1%) between 2006 and 2018. Eight reported holding a higher degree, including five with a doctorate (MD, PhD).

Immediately after graduation, three reported acting in a locum position, 18 reported working as a fellow and 26 reported becoming a consultant immediately. Most fellowship positions were undertaken overseas.

Work

Members were asked their full-time equivalent (FTE) status, with 0.1 FTE being four hours and 1.0 FTE five days (see Table 2). The reported average actual hours worked was 47.4 (range: 2.0 to 64.0 hours; median: 50.0). There were 22/41 (53.6%) who reported working over 50 hours per week, with 15/41 (48.4%) working over 10 overtime hours. There were significant differences when work times were compared with Australian data (Table 3).

Most of the work time was spent on clinical duties (attendance at multidisciplinary team meetings, consultations, simulation, dosimetry and contouring) (average: 31.5 hours; median: 27.0). Respondents also reported non-clinical tasks. Between 1 and 10 hours per week (average: 2.8) were spent supervising trainees, and 1 to 20 hours (average: 4.1) was spent on management. Of the 24 respondents to the question, 17 (70.1%) reported doing one hour or less per week of research (average: 2.3 hours). Australian colleagues reported a 30% higher average of 3.3 hours per week.[1]

There were 26 (63.4%) respondents working exclusively in the public sector, 13 (31.7%) in a public/private mix and two (4.9%) exclusively in the private sector.

On average, respondents saw 234.8 new patients per year (range:30-400; median:230.0).

There were 33 (82.5%) who reported having hospital admitting rights, with the majority (85.0%) seeing this as valuable.

Two-thirds of respondents (67.5%) reported some specialist areas of practice (Figure 1). Stereotactic radiation and breast were the most common specialist areas.

Brachytherapy is a specialised radiation technique using radioactive sources placed directly into the patient, most often for prostate and gynaecological cancers. Of those 19 working in brachytherapy, 13 practice gynaecological brachytherapy and three intended to cease practice. Interrogation of this data finds that 30% of those practicing gynaecological brachytherapy were 60 years old and over.

There were 21 respondents who practise stereotactic radiation treatment (high-dose radiation given to small tumours), with 18/21 using this technique for lung cancer and 15/21 for brain tumours.

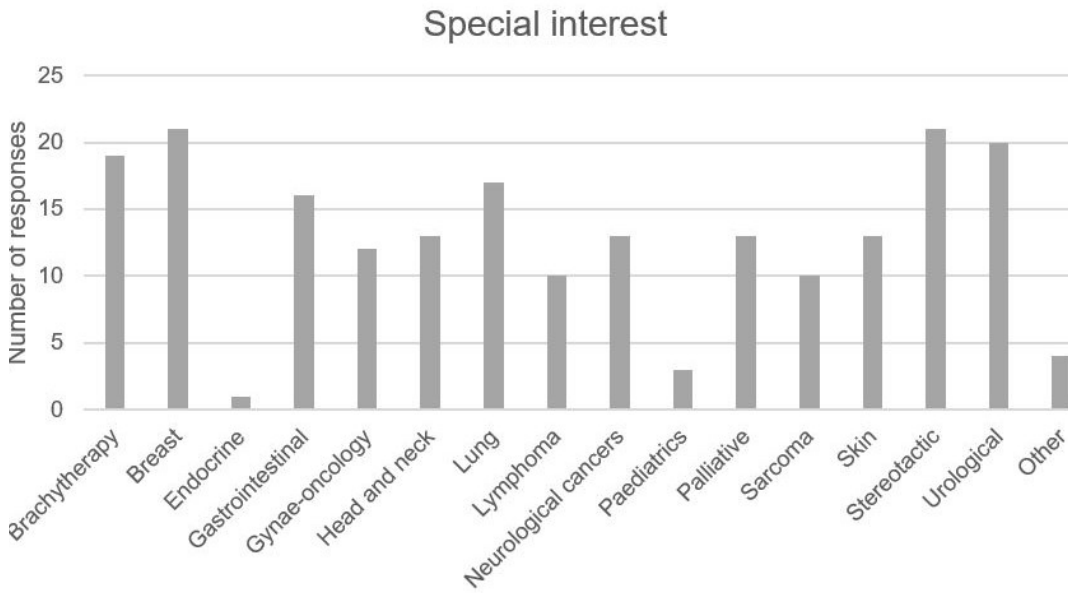
Of the 43 respondents, 21 held at least one leadership position, including leadership at the hospital level, network, college and in the national arena.

Table 3: Reported clinical activity hours.

Activity	New Zealand	Australia	P-value (t-test)
Total clinical hours	31.5 (3.0–94.0)	35.6 (2.0–532.0)	0.211
Multidisciplinary meetings	5.6 (1.5–57.0)	4.1 (0.5–55.0)	0.325
New cases	6.1 (1.0–12.0)	6.5 (1.0–20.0)	0.330
Follow-ups	6.9 (1.0–25.0)	8.6 (1.0–30.0)	0.025*
On treatment cases	2.7 (1.0–8.0)	4.5 (1.0–30.0)	0.000**
Simulation	2.3 (1.0–5.0)	2.3 (1.0–10.0)	0.944
Dosimetry	2.7 (1.0–5.0)	2.7 (1.0–15.0)	0.871
Contouring	6.0 (1.0–15.0)	8.3 (1.0–460.0)	0.285

*Significant at p<0.05.
**Significant at p<0.01.

Figure 1: Areas of specialty interest.



Future plans

Nearly two-thirds of respondents (62.5%; n=25) reported no plans to change their hours within the next three years and one-quarter (25%; n=12) intended to decrease hours, whereas only three (7.5%) indicated they planned to increase their hours (Table 4).

Table 4: Retirement plans.

Retirement plans	N (%)
No plans for retirement	18 (45)
Intention to retire in the next 5 years	7 (17.5)
Intention to retire in the next 6–10 years	5 (12.5)
Intention to retire in the next 11–15 years	10 (25)
Total	40 (100%)

Female radiation oncologists

Data indicated that more female radiation oncologists worked less than 1.0 FTE than males (1.3:1). A similar number of new patients per year were seen, with females reporting seeing an average of 229.8, and males 240.4.

Work-type differences were noted. Females reported lower research hours, with a range of 1–2 hours per week (average of 0.5 hours), compared with males who reported a range of 1–24 hours (average of 2.1 hours). Of the 21 involved in leadership positions, eight were female (38.1%) and 13 were male (61.9%), which would correlate to the slightly lower time spent in management activities (females averaged 3.1 hours, compared to 3.6 hours reported by males), and males reported spending more time per week on jurisdictional activities (2.1 hours vs 1.1 hours, $p<0.05$). Statistically significant differences in clinical work were found with female radiation oncologists spending more hours per week on dosimetry and simulation than their male colleagues (2.9 hours vs 1.9 hours, $p<0.05$; 3.5 hours vs 2.3 hours, $p<0.05$, respectively).

Radiation oncology registrars

Demographics

There were 24 radiation oncology trainees in six training centres in New Zealand. There were 18 trainees who responded to the survey, with respondents from across the five years of training (Table 2).

Prior to entering radiation oncology training, seven (38.9%) had other degrees (five in the sciences and two in nursing). One had a further specialist qualification. Common reasons for choosing a career in radiation oncology included an interest in oncology patients (83.3%; n=1), lifestyle (72.2%; n=13), work hours (61.1%; n=11) and family considerations (55.6%; n=10).

Work

The trainees all reported working full time. Nearly half (44.4%; n=8) indicated a desire to train part time, while 38.9% (n=7) wished to have a part-time specialist post. The reasons included maternity leave, family commitments and lifestyle.

Three-quarters of trainee respondents (77.8%; n=14) reported spending more than 36 hours per week discharging clinical duties and 83.3% (n=15) reported more than six hours per week on after hours on call (half reported working between 6 and 10 hours per week).

Time in radiation planning is important for a trainee to learn the technical aspect of radiation oncology. Trainees most commonly have five hours or less in planning a week (83.3%; n=15), with only three (16.7%) reporting between 6 and 10 hours. Despite being in training, 61.1% (n=11) of the trainees reported two or less hours of protected time for teaching, with three reporting no time.

Only half (n=9) reported that they had enough time to pursue interests outside of work.

Future plans

Most trainee respondents (88.9%; n=16) were satisfied with their career choice, with one unsure and one unsatisfied. Trainees reported multiple concerns for the future. The most common were job availability (88.9%; n=16), fellowship opportunities (38.9%; n=7), concerns with declining government resources (27.8%; n=5) and being ”forced” to work in a rural area (11.1%; n=2). When reporting causes of stress, three-quarters (n=14) had concerns with training demand, two-thirds (n=12) reported concerns with either balancing responsibilities or with job demands, 61.1% (n=11) with training in remote centres and 44.4% (n=8) were concerned with future job prospects. The mandatory rotation within the training programme was reported as a significant cause of stress.

Although one-third of trainee respondents (n=6) had considered leaving the specialty, all reported their intention was to continue at the time of the census.

A significant proportion intended to complete a fellowship after training (66.7%; n=12), with three being undecided). Three-quarters of trainee respondents (77.8%; n=14) intended to have a mix of private and public work and the majority (94.4%; n=17) also hoped to have an academic component.

Discussion

The first thing we note is that the workforce in radiation oncology is small. At the time of the census, there were 60 practicing radiation oncologists with 22 oncologists in training. The small size of the workforce renders it vulnerable to fluctuations in supply and demand.

Radiation oncologists

Demographics

To explore trends over time and internationally, the demographic data from the survey was compared with data from the 2014 census and national and international data.

The number of fellows in the 2014 census was 56, indicating only minimal growth of four radiation oncologists over the four years.[2] The 2014 data reported 23% (14/60) of radiation oncologists were greater than 60 years of age, with 12% (7/60) under than 40.[2] The current survey indicates very similar proportions in these age brackets, with no recent influx of younger practitioners. This contrasts with the Canadian data and American data, which reported a greater proportion in the younger age brackets. In 2018 the Canadian radiation workforce consisted of 30% under 40 years of age (171/567), and in 2017 the American workforce, 20.1%.[4,5]

One-third of the radiation oncologists on the membership database were female, unchanged from 2014. The percentage of females in the medical workforce in New Zealand overall in 2018 was 45.1%. This data includes resident and prevocational doctors.[6] The data for medical specialists in New Zealand indicates the proportion of females in 2018 was 39.2%, slightly higher than the proportion of females in radiation oncology.[7] The higher ratio of female participation in the radiation oncology workforce for those under 40 may suggest that the trend is following the general medical workforce figures, and that higher rates of female participation may be seen in the future, reflecting international trends. The Canadian workforce report indicates

that from 1990 to 2018 the proportions of females in the workforce rose from 18% to 38% for the radiation oncology workforce overall and from 28% to 50% for trainees.[5]

In both the 2014 and 2018 censuses, three-quarters of respondents reported exclusively public practice.[2] This contrasts markedly with the Australian data, where there has been a substantial increase in the private sector, with the census overall revealing nearly one-third working solely in the private sector.[1]

The proportion of radiation oncologists receiving their specialist qualifications outside of Australia and New Zealand was high at 32% (19/60), similar to 2014 data. This brings a breadth of experience, but a continued reliance on the overseas market increases vulnerability as international supply and demand fluctuates and international regulations change. Interestingly, this is not a challenge unique to radiation oncology, as the 2018 national medical workforce survey indicates 40.1% of the New Zealand national medical workforce are international medical graduates.[6]

There was 58% of the radiation oncology workforce reporting New Zealand ethnicity and the next largest reporting Asian ethnicity (16%). When compared with the national medical workforce in 2018, 54.5% reported New Zealand ethnicity and 11.2% Asian.[6] It would be essential in future surveys to explore more detailed breakdown of New Zealand ethnicity, in order to ascertain the proportions of Māori and Pasifika within the workforce. Within the general medical workforce in New Zealand, Māori make up 3.5% of doctors compared with 14.7% of the population, and Pasifika less than 2% compared with 7% in the general population.[6] It is a RANZCR priority to explore and address this imbalance.

The concerning trends highlighted by the demographic data are that the workforce is small, is only slowly growing, remains heavily reliant on overseas trained doctors and faces the potential challenge of clinicians moving into the private system and putting further pressure on services in the public health system. Ministry of Health consideration of increasing the funding for training posts in radiation oncology is urgently required. Programmes addressing recruitment must also consider increasing diversity within the profession, particularly with regards to Māori, Pacific Island and female participation. Considerations to increase diversity would include provisions for part-time training, scholarships and radiation oncology information sessions and house surgeon and medical student teaching programmes and "career fares".

Work

The median contracted hours was 40, and actual hours worked was 50, in both the 2014 and 2018 surveys.[2] Of concern, however, was a higher proportion working over 10 overtime hours per week. (35.1% in 2014 and 48.4% in 2018),[3] once more higher than our Australian counterparts.[1] Thus, the trend to work significantly longer hours than contracted at least continues and may have worsened.

The median contracted hours and the median clinical hours worked was similar, indicating that time must be made outside of this for administration, teaching and research. This was reflected in the fact that 82% of respondents reported doing one hour or less of research a week, similar to the 2014 report.[2] International research concludes that involvement in clinical trials provides benefits to patients, even for those patients not directly enrolled themselves.[9] Because of this, a draft New Zealand National Oncology and Haematology National research strategy process document has recommended that clinical trials be "incorporated as standard clinical practice", but this document also reports that "across New Zealand, enrolment in clinical trials is lower than international recommendations and benchmarks, even in large metropolitan centres".[10] A study from the UK found that "dedicated time and funding were the biggest barriers for doctors becoming involved in research".[11] This challenge of dedicated time would appear to be a problematic barrier to research in radiation oncology within New Zealand.

For clinical tasks, the reported median number of new patients seen per week of 6.1 was similar to 2014 responses (6.0).[3] The median new patient numbers also remained similar (245 in 2014, 235 in 2018).[3] The time spent on contouring was not reported in the previous censuses; however, this census reported it was a significant component of the work undertaken, with a median of 6 hours (range: 1–15 hours). This is a

change over the last decades of radiation treatment, as we moved away from simple x-ray simulation, and is in line with international data. The German Society of Radiation Oncology reported on time measurements for the process of radiation and found that the technical processes (contouring and assessing and approving a plan) was the most time consuming, requiring on average 3 hours and 54 minutes per patient for intensity modulated radiation treatment (IMRT).[12] The increased time taken for this has been "absorbed" into existing staffing levels and may be reflected in the increased out-of-contracted hours work. This would be consistent with the RANZCR survey of trainees, which found 80% spent time "out of hours" contouring.[13]

Specialist radiation techniques require consideration, as only a proportion of the workforce possess these skills. A potential area of vulnerability is in gynaecological brachytherapy, where 30% of the 10 practising are over 60 years of age.

The workforce census highlighted an involved and engaged workforce, with almost 50% reporting they held at least one leadership position. The fact that many held more than one points to the problem of a small number of clinicians attempting to hold posts across many domains.

On reflection of the work trends for radiation oncologists, increasing overtime hours indicates a need for modern job sizing activities to be performed. The historical measure of numbers of patients does not account for complexity of treatments, and this must be considered to ensure adequate radiation oncology resource. Job sizing must also reflect the need to move the essential contouring hours to within working hours, as well as allowances for time to perform research, leadership, administration and teaching as essential facets of a radiation oncologist role. Recruitment must ensure that New Zealand maintains the ability to perform specialist radiation oncology treatments.

Future plans

Over half (55%) of the current workforce reported an intention to retire within 15 years. This compares to around 46% for the Australian data.[2] This is clearly an area of concern. Membership data indicate that, between 2013 and 2018, 12 new fellows graduated the training programme.[8] Should this rate continue without increase, it will be insufficient to make up for losses through retirement and reduction of hours, let alone allow any growth in capacity.

Radiation oncology trainees

Radiation oncology trainees all reported working full time; however, 40% wanted to be able to work part time. Overtime workload was significant, with half of the trainees reporting 6–10 hours overtime per week and only half having time to pursue interests outside of work. Although most report an interest in oncology as the driver for career choice, almost three-quarters chose the career as it offered a lifestyle they wanted, and 55.6% chose radiation oncology as it was "family friendly".

We need to be mindful that, although they were a committed group, the trainees make clear that lifestyle and outside of work are priorities and overwork is likely to be to destructive to morale and potentially to retention. In a specialty dependent on sustained growth in numbers of new fellows, it is concerning that one-third of trainee respondents reported intending to leave the specialty and two-thirds had concerns with balancing responsibilities. These findings are consistent with reports of a 2012 trainee survey by the RANZCR. In this survey, trainees across Australia and New Zealand indicated lifestyle was an important reason for choosing radiation oncology as a career, and only 40% in this survey had time to pursue interests outside of work.[14]

The quality of training is also important in securing the future of the speciality. Trainees report a relatively low training versus service time. Contouring time was less than five hours a week for 83%, and protected time for teaching for the majority was less than two hours per week. Limited time in planning is not unique to New Zealand, with 60% of USA residents reporting insufficient exposure to treatment planning.[13,15]

Retention in New Zealand after gaining the fellowship may be influenced by the fact that the majority of trainees wish to have an academic component to their career, but opportunities for this with current fellow staffing levels are low. It was interesting that 42% of radiation oncology

respondents embarked on a fellowship post after obtaining the Fellowship of the Australian and New Zealand College of Radiologists (FRANZCR), the majority being undertaken overseas. Limited fellowship opportunities exist in New Zealand. The international fellowship has much to offer, with experience brought back to New Zealand. However, not all trainees are able to move overseas, and hence this decreases employment opportunities, and historical figures reveal some never return to New Zealand after an overseas fellowship, with a further loss of potential workforce.[8] The development of fellowship positions within New Zealand has been identified by the RANZCR as a priority, but funding these remains challenging.

The future of the specialty is reliant on training registrars to become skilled and engaged radiation oncologists. Recruitment may be increased by the option of part time training, adequate job sizing, more flexible rotation programs and accreditation programs ensuing adequate protected training time. Investment in training increased numbers of registrars is urgently required.

Current initiatives

The New Zealand National Radiation Oncology Plan predicted that a further 28 oncologists would be required between 2017 and 2021 to maintain current demand for radiation services. This plan acknowledged that this prediction was based on current workloads and that "if overtime is used extensively now, then that would continue into the future".[16] This projection also did not take into account loss from the workforce due to part-time work or retirement, or did it allow for an increase in capacity to potentially improve the current low proportion of patients in New Zealand who receive radiation. This intervention rate is 37.4%,[16] well below the 48%–52% recommended in the literature.[1]

The RANZCR has identified a need to increase recruitment and retention and has been exploring initiatives. Cancer workforce has also been identified in the Ministry of Health cancer plan as a priority focus area, as has the need to grow the Māori and Pacific workforce.[17]

Conclusion

The radiation oncology workforce in New Zealand is small, with minimal growth in staffing numbers in recent years. The workforce continues to be reliant on radiation oncologists trained overseas, who comprise a third of current fellow numbers. The workforce has an older demographic with a high rate of intention to retire in the next decade. Overtime work is significant and contracted hours do not routinely allow for time in research and other non-clinical duties. Trainee numbers do not seem sufficient to meet the potential demand for replacements due to decreasing hours and retirements. There is some evidence that work conditions may not be well adjusted to the priorities of the trainees, and this may adversely affect retention. Workforce planning is vital and must include consideration of modern radiation work components, diversity and skill mix. These factors must be not only considered but addressed, to ensure a viable radiation oncology workforce for the future.

Competing interests:
Nil.
Acknowledgements:
The authors would like to acknowledge all members of the RANZCR Economic and Workforce Committee for advice with the preparation of this manuscript. We also acknowledge Shristi Shrestha (Analyst, Economics and Analytics RANZCR) for assistance with data analysis.
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Amenable mortality within the New Zealand homeless population: we can do better!

Sandrine Charvin-Fabre, Ottilie Stolte, Ross Lawrenson

ABSTRACT

AIM: To describe the context surrounding the deaths of homeless people in New Zealand and to determine the proportion of deaths that could be considered amenable to healthcare.

METHOD: We used coroners' findings related to 171 deaths of persons with "no fixed abode" at the time of death, from 2008 to 2019. Recent lists of amenable mortality from the New Zealand Ministry of Health and the Office of National Statistics in the UK were combined to determine the rate of amenable mortality.

RESULTS: The life expectancy of homeless persons identified in this sample was 30 years shorter than in the housed population, with a mean age of death of 45.7 years. Deaths occurred mainly alone, in public spaces (56.1%) or in private vehicles (14%). Three-quarters (75.8%) of homeless persons died from conditions amenable to timely and effective healthcare interventions, mostly from natural causes (45.7%) and suicide (41.5%).

CONCLUSION: Homeless people experience considerable challenges when accessing the healthcare system, as uncovered by the dramatic rate of amenable mortality. Our findings highlight the urgent need to implement specific models of care that are designed to meet the social and healthcare needs of homeless persons and address the significant health inequalities they experience.

Homelessness is an increasing and complex worldwide issue. New Zealand, like other higher-income countries, faces a growing prevalence of homelessness. Estimates indicate that between the 2006 and 2013 censuses, the absolute number of homeless persons increased from 33,000 to 41,000 (an increase of 24.2%), compared to the population growth during the same period of 5.3%.[1–2] Definitions of homelessness vary across countries depending on the social, cultural and legal context in which they operate.[3] The New Zealand Coalition to End Homelessness adopted a broad definition of homelessness based on a gradation of housing insecurity, ranging from those living rough or in their cars to those living in uninhabitable dwellings, in temporary accommodation or in overcrowded households.[4] Widening the definition of homelessness means that "hidden homelessness" is accounted for and better illustrates the health inequalities that impact mainly Māori and Pasifika peoples among this population.[4]

Health inequalities that affect the homeless population worldwide contribute disproportionately to a dramatic premature mortality rate compared to the housed population. Although the mortality rate varies between studies, typically homeless people die 15 to 30 years younger than their housed counterparts.[5–7] A New Zealand hospital-based study looked at risk factors for mortality in a cohort of homeless patients, which included 126 deaths with a median age of death of 52.6 years.[8] Many of the patients had a record of cardiovascular disease and diabetes as well as mental health issues and substance misuse.

Premature mortality results from a complex combination of medical conditions often related to severe and chronic comorbidities and the consequences of social exclusion shaped by homelessness—that is, marginalisation and stigma, loneliness, violence and adverse living conditions. Consequently, homeless people experience poor and irregular access to healthcare, unmet care needs, delays in clinical presen-

tations and a high use of emergency departments.[9–12] Yet, access to high-quality healthcare improves many health outcomes and can reduce the number of premature deaths.[13] The concept of amenable mortality as an indicator of performance (eg, weakness or strength) of the health system has been debated for decades as a way to determine the boundaries of health interventions.[14] The New Zealand approach has been to develop a measure of amenable mortality that reflects the performance of the healthcare system, excluding a wider and intersectoral approach based on the social determinants of health.[15] Amenable mortality is an important indicator of healthcare access and quality, which serves to identify areas of healthcare concern and support specific healthcare initiatives for diseases where effective intervention exist.[16] The classification of causes of death amenable to clinical interventions is based on expert reviews of medical knowledge and technologies and the causal epidemiology of diseases. To improve health outcomes within the population and reduce health inequalities, the New Zealand amenable mortality list was updated in 2016 as part of the System Level Measures and the refreshed New Zealand Health Strategy.[16]

The objectives of this present study are to use coroners' reports to describe the context surrounding the deaths of homeless people in New Zealand and to determine the proportion of deaths that could be considered amenable to healthcare intervention.

Method

Data collection

A critical challenge in reporting the deaths of homeless people is the lack of a systematised source of statistics for this population. The Mortality Collection classifies all causes of death registered in New Zealand using the International Classification of Diseases, Tenth Edition (ICD-10). The inclusion of the ICD-10 coding for homelessness (Z.590) has only recently begun to be used for identifying or registering the deaths of homeless people. These data are incomplete, and so the Mortality Collection is not a viable source of homeless mortality data.

Further, within District Health Boards (DHBs), the use of the Z.590 code has not been generally adopted. How DHBs record "no fixed abode" is unclear and varies between different hospitals.

Instead, the utility of medico-legal databases is recognised worldwide as a valid source of data for public health endeavours, especially for accessing data on populations that are difficult to reach (such as homeless people or prisoners) or to determine the nature, distribution and determinants of amenable deaths such as suicide.[17–19] Under the New Zealand Coroners Act 2006, deaths must be reported to the coroner if the death appears to (a) be without known cause, self-inflicted, unnatural or violent, (b) have occurred as a potential result of a medical procedure, (c) have occurred while someone was in official custody or care or (d) have been in relation to which no death certificate was issued.[20] The Case Management System is the New Zealand database systematically recording all deaths reported to coroners since 2007. The Information Advisor of the Coronial Office of Wellington provided data on all coronial deaths with the "no fixed abode" criterion at the time of death. One hundred and seventy six full-text coroners' findings reports were identified and released to SCF (first researcher). This included all the deaths of people with no fixed abode that were reviewed by the coronial service between January 2008 to June 2019.

Data analysis

Five cases did not meet the criteria for homelessness. The study sample is thus based on 171 coroners' reports. Demographic information was extracted from each report. Since ethnicity was not reported individually in the coroners' reports, this information is not available. The circumstances surrounding the deaths were obtained from the elements of information accompanying the coroners' findings: extracts of police and toxicology reports, forensic examination, witnesses' statements and elements of medical history provided by DHBs, community services or general practitioners. The majority of deaths due to natural causes were not followed up by a coroner's inquiry. Only a few inquiries into patients who died from natural causes (n=10) were considered necessary by the

coroners. Detailed medical information for all the deaths included due to natural causes was therefore not available for analysis. Conversely, deaths by suicide were assessed and ascertained after a long and detailed coroner's inquiry, enabling a detailed analysis. Underlying causes of death, based on forensic examination findings, were coded using ICD-10 classification. For the purposes of this study, drug- and alcohol-related deaths were coded using the proposal from Randall et al.[21] All deaths directly related to drug or alcohol use were coded as accidental poisoning (X40-X45) or related to mental and behavioural disorders (F10-F16, F19, F55). The causes of amenable mortality were revisited, combining the lists published recently by the New Zealand Ministry of Health (2016)[16] and by the Office of National Statistics in the UK.[22] This latter list was the main basis used to develop the amenable mortality list common to all the OECD countries.[23] It is based on a previous definition of amenable mortality that was developed for use in the Australian and New Zealand context.[24] Given this common background, and that aetiologies of diseases, risk factors and the healthcare standards are likely to be similar, the combination of the two lists was regarded as applicable. Variations across amenable mortality lists rely on different subcategories within groups of diseases and depend on the local epidemiology of diseases and the evidence of effectiveness of the intervention, as well as the quality of the cause-of-death coding procedure. For example, pneumonia not related to pneumococcal infection was removed from the New Zealand list because the quality of coding was deemed inadequate by the expert panel.[15] Health inequalities are extreme for the homeless population since they are marginalised in terms of accessibility to healthcare. Hence, the list that we have used was enlarged accordingly to capture all relevant amenable conditions. The threshold is set at 75 years of age for amenable deaths other than by accident or suicide, due to the frequent difficulty of assigning a single cause to deaths beyond this age in the general population.

Ethics approval

Ethics approval was obtained from the Human and Research Ethics Committee from the University of Waikato.

Results

Sociodemographic characteristics

Of the 171 homeless people's deaths reported to the coronial office, the majority were males (n=145, 84.7%), with females accounting for 15.2% (n=26). The mean age of death regardless of cause or gender was 45.7 years: 46.7 years for females and 44.8 years for males. The average age of death by accident and suicide was dramatically younger: 36.5 years and 38.2 years, respectively (Table 1). At the time of death, a small minority (n=25) of homeless people were employed (14.6%). The majority of people were unemployed (n=91, 53.2%), with a small number receiving a benefit (10.5%). Eleven homeless people were retired (6.43%). The information was unavailable for nine individuals (5.2%) and not specified in 17 cases (9.94%).

Underlying causes of death (Table 1)

The main cause of death was from natural causes (42.6%). Among these, deaths from cardiovascular diseases were the most frequent (n=33), followed by infectious diseases (n=9) and acute alcohol toxicity (n=7). Three cases of death by hypothermia were also reported. Suicide, ascertained by clear evidence of an intention to end one's life, accounted for nearly one third of all deaths (n=49). Thirty-three deaths (19.2%) were classified as accidental and mainly attributed to a vehicle crash or a pedestrian struck by a vehicle or a train (n=12), a fall from a height (n=7), a fire (n=4) or a drug overdose (n=4). Deaths from an unascertained nature due to an advanced decomposition of the body or the impossibility of precisely determining the cause of death accounted for 5.2% of all deaths. Seven deaths were the consequence of criminal homicides.

Circumstances of death and amenable mortality (Table 2)

Information on the location of death was available for 168 deaths. The most common place where death occurred, regardless of the cause of death, was public spaces such as streets, doorways, parks and reserves, forests, beaches, harbours or rivers (56.1%), followed by private cars or campervans (14%), private housing, but mainly garages (12.8%), hospitals (8.7%) and temporary

Table 1: Underlying causes of death and amenable mortality by age group (n=171).

Age group	Suicide N=49 (28.6%)	Accident N=33 (19.2%)	Natural N=73 (42.6%)	Homicide N=7 (4.09%)	Unascer-tained N=9 (5.2%)	Total cause N=171	Amenable N=118/153 (75.8%)
Mean age (SD)	38.2 (14–61)	36.5 (13–57)	54.5 (17–78)	44.2 (27–64)	44.7 (25–57)	45.7 (13–78)	45.4 (13–71)
10–14	1	1	0	0	0	2	2
15–19	1	0	1	0	0	2	2
20–24	7	5	0	0	0	12	12
25–29	4	3	1	1	1	10	5
30–34	4	5	1	1	4	15	5
35–39	9	5	3	0	2	19	13
40–44	7	5	4	3	0	19	12
45–49	6	3	12	0	0	21	15
50–54	6	2	14	0	1	23	18
55–59	3	4	15	0	1	23	16
60–64	1	0	9	2	0	12	7
65–69	0	0	6	0	0	6	6
70–74	0	0	5	0	0	5	5
75+	0	0	2	0	0	2	0

accommodation such as motels, hostels and backpacker accommodation (5.26%).

Information included in the coroners' findings reports was sufficient for assessing amenable mortality in 153 cases of death. According to the amenable mortality list, the categories of death from unascertained and criminal nature were excluded (n=16), as well as death from natural causes that occurred beyond 75 years old (n=2). The contribution of amenable death to the overall mortality of homeless people was extreme, with 75.8% of deaths (n=118) considered as amenable to timely and effective healthcare intervention. The mean age of amenable death was 45.4 years old (Table 1). In the group aged up to 24 years, the prevalence of amenable mortality was 100%, due to suicide and accidents (Table 1). Among amenable deaths, 45.7 % (n=54) resulted from a natural cause, particularly cardiovascular disease (n=33), alcohol-related death (n=7) and pneumonia (n=6). A single case was cancer related; however, the post-mortem forensic examination diagnosed four cases of cancers at an advanced stage. Suicide represented 41.5% of the amenable deaths (n=49), and accidents related to a vehicle crash or pedestrians struck (n=12) or resulting from fire effects (n=3) accounted for 12.7% of all amenable deaths (Table 2).

Nearly half of the amenable deaths from natural causes occurred in public spaces (46.1%), followed by deaths in private dwellings (21.1%), in cars or campervans (17.3%), in hospital (15.38%) and, lastly, in temporary accommodation (7.6%). Most of the homeless persons who died from an amenable death were alone at the time of death and were found deceased by witnesses sometimes several months after that death occurred.

Suicide (Table 3)

One of the main causes of death was suicide, accounting for 28.6% of all deaths (Table 1). In those under 44 years of age, over two-thirds of deaths were due to suicide (67.3%). Homeless persons who self-harmed were found mainly in public spaces (67.3%) or in their private vehicles

Table 2: Amenable mortality within the homeless population (modified from Otalunde et al and New Zealand Ministry of Health, 2016).

Group	Condition	Age	ONS UK-2016	NZ-MOH-2016	Amenable mortality (N=118)
Infections	Tuberculosis	0–74	A15-A19, B90	A15-A16	0
	Meningococcal disease	0–74	n/a	n/a	0
	Pneumococcal disease	0–74	A40.3, G.001, J.13	A40.3, G.001, J.13	n/a
	HCV	0–74	B17.1, B18.2	B17.1, B18.2	0
	HIV/AIDS	All	B20-B24	B20-B24	0
	Other selected bacterial infections	0–74	A.38-A41, A46, A48.1, B50-B54, G00, G03, J02, L03	n/a	n/a
Neoplasms	Stomach	0–74	C16	C16	0
	Colon	0–74	C18	n/a	1
	Rectal	0–74	C19-C21	C19-C21	0
	Bone and cartilage	0–74	n/a	C40-C41	0
	Melanoma	0–74	C43	C43	0
	Female breast cancer	0–74	C50	C50	0
	Cervical	0–74	C53	C53	0
	Uterus	0–74	C54-C55	C54-C55	0
	Prostate	0–74	n/a	C61	0
	Testis	0–74	C62	C62	0
	Thyroid	0–74	C73	C73	0
	Hodgkin	0–44	C81	C81	0
	Acute lymphoblastic leukaemia	0–74	C91, C92.0	C 91	0
	Liver	0–74	C22	n/a	0
	Mesothelioma	0–74	C45	n/a	0
	Bladder	0–74	C67	n/a	0
	Benign neoplasms	0–74	D10-D36	n/a	0
	Lip, oral cavity, pharynx	0–74	C00-C14	n/a	0
	Oesophagus	0–74	C15	n/a	0
	Trachea, bronchus, lung	0–74	C33-C34	n/a	0

Table 2: Amenable mortality within the homeless population (modified from Otalunde et al and New Zealand Ministry of Health, 2016) (continued).

Endocrine and metabolic	Diabetes mellitus	0–74	E10-E14	E10-E14	2
	Disease of thyroid	0–74	E00-E07	n/a	0
	Addison's disease	0–74	E27.1	n/a	0
Drug use disorders	Alcohol-related disease	0–74	F10, G31.2, G62.1, I42.6, K29.2, K70, K73, K74 9excl. K74.3-K74.5), K86	n/a	7
	Illicit-drug disorders	0–74	F11-F16, F18-F19	n/a	0
Neurological	Epilepsy	0–74	G40-G47	n/a	0
Cardiovascular	Rheumatic and other valvular heart diseases	0–74	I01-I09	I01, I05-I09, I33-I37	0
	Hypertensive disease	0–74	I10-I15	I10-I13	1
	Ischaemic heart disease	0–74	I20-I25	I20-I25	19
	DVT with pulmonary embolism	0–74	I26, I80.1-I80.3, I80.9, I82.9	I26	3
	Atrial fibrillation and flutter	0–74	n/a	I48	0
	Heart failure	0–74	n/a	I50	6
	Cerebrovascular disease	0–74	I60-I69	I60-I69	1
	Aortic aneurysm and dissection	0–74	I71	n/a	3
Respiratory	Influenza	0–74	J09-J11	n/a	0
	Pneumonia	0–74	J12-J18	n/a	6
	COPD	0–74	J40-J44	J40-J44	0
	Asthma	0–74	J45-J46	J45-J46	2

Table 2: Amenable mortality within the homeless population (modified from Otalunde et al and New Zealand Ministry of Health, 2016) (continued).

Digestive disorders	Gastric and duodenal ulcer	0–74	K25-K28	K25-K27	3
	Acute abdomen, appendicitis, intestinal obstruction, pancreatitis, hernia	0–74	K35-K38, K40-K46, K83, K85, K86.1-K86.9, K91.5	n/a	0
	Cholelithiasis	0–74	K80	K80	0
Genitourinary disorders	Renal failure	0–74	N17-N19	N17-N19	0
	Nephritis and nephrosis	0–74	N00-N07, N25-N27	n/a	0
	Obstructive uropathy and prostatic hyperplasia	0–74	N13, N20-N21, N35, N40, N99.1	n/a	0
Injuries	Transport accidents	All	V01-V99	V01-V99 (excluded trains)	12
	Accidental falls on same level	All	W00-X59	W00-W008, W18	0
	Suicide	All	X60-X84, Y10-Y34	X60-X84	49
	Fire (burns)	All		X00-X09	3
	Homicide/ assault X85-Y09, U50.9	**All**	X85-Y09, U50.9	n/a	0

Table 3: Circumstances of death by suicide.

	N=49	%
Sociodemographic		
Age in years (median range)	38.2 (14–61)	
Male gender	41	85.7
Clinical diagnosis		
Psychosis	5	10.2
Bipolar disorder	5	10.2
Depressive illness	23	46.9
Problematic alcohol use	18	36.7
Drug use (casual/regular)	19	38.7
No history of mental health issues	8	16.3
Other	2	4
Unknown	3	6.1
Current or past treatment for mental health issues	23	46.9
Past expression of suicide thoughts and behaviours		
Communicated suicide intent (lifetime)	34	69.3
Communicated suicide intent (last year)	10	20.4
Suicide attempt (lifetime)	14	28.5
Suicide attempt (last year)	6	12.2
Suicide notes	2	4
Contact with health professionals		
Contact up to one year	6	12.2
Contact last month	12	24.4
Contact last year	14	28.5
No contact at all	11	22.4
Unknown	5	10.2
Suicide method		
Hanging	30	61.2
Self-poisoning	10	20.4
Jump/fall	5	10.2
Other methods	4	8.1

Table 3: Circumstances of death by suicide (continued).

Suicide location		
Public space	33	67.3
Vehicle	6	12.2
Temporary accommodation	5	10.2
Private dwelling	4	8.1
Hospital	1	2
Stressful life events		
Any events	34	69.3
Relationships breakdown	12	24.4
Financial problems	12	24.4
History of legal issues	7	14.2
Conflict with other persons	7	14.2
Bereavement	5	10.2

(12.2%), while 10.2% died in temporary accommodations and 8.16% in private garages. One person died in hospital from the direct consequences of suicide. Hanging was the most common method used (61.2%). The coroners' inquiries have revealed that 73.4% of homeless persons who committed suicide were diagnosed with mental health issues, mainly from alcohol or drug misuse and depressive mood disorders. However, the proportion of homeless persons treated for psychiatric disorders was less than half (46.9%). In addition, there was only evidence of recent contact with health professionals in just under a quarter of cases (24.4%). In the majority of cases (40.8%), the final contact was up to one year or more prior to death, and 22.4% of homeless persons had no contact at all with health professionals. References to lifetime suicide ideation and past suicide attempts were drawn from statements from relatives and health professionals. Nearly 70% of homeless persons had communicated suicide intent in their lifetime (69.3%), and 28.5% had evidence of prior self-harm. In nearly 70% of cases, homeless people had experienced significant and multiple stressful and traumatic life events.

Discussion

The main findings of this study are the devastating and dehumanising consequences of homelessness that result in premature and preventable deaths. The mean age of death of homeless persons identified in the sample as having "no fixed abode" at the time of death was over 30 years younger than in the New Zealand housed population, with an overall mean age of death of 45 years, reduced further to 38 years in cases of suicide.[25] The vast majority of deaths occurred in public spaces or in private vehicles. Just over three-quarters of homeless persons died from conditions amenable to timely and effective healthcare interventions, mainly from natural causes of death and suicide.

Our findings are consistent with previous results showing that premature and amenable mortality associated with homelessness is considerable, although exact comparisons cannot be made due to the variety of data sources and definitions of homelessness.[7,26–27] However, congruent to our results, prior homeless coronial samples indicate an average age of death of 46 years for all causes[26] and from nearly 36 to 39

years by suicide.[19,28] Cross-sectional studies of homeless deaths identified by linking hospital admissions and mortality data in England and New Zealand found a mean age of death of 52 years, which remains extremely young.[7–8] These studies included homeless patient samples who had been hospitalised and therefore may have benefited from medical follow-up.

The amenable mortality burden uncovered in our study is significantly higher than in a UK study that assessed this proportion to be approximatively one-third.[7] The UK study focused on the deaths of homeless patients admitted to hospitals that provided links with community healthcare services. Further, our findings were based on an extended list of amenable causes of death in a way that more clearly reflects the medical conditions associated with homeless deaths. The difference between the two amenable mortality lists was relevant in 23 cases and was mainly related to alcohol diseases, acute and treatable pneumonias and specific cardiovascular diseases (eg, heart failure and aortic dissection). We reported minimal rates of diabetes and cancers, which contradicts previous international and New Zealand hospital-based studies.[7–8] It is likely that many such cases would not be reported to the coroner, thus illustrating the differences in sampling. The magnitude of social isolation and disconnection from the health system, combined with chronic psychological distress and unstable life conditions, negatively affects the health-seeking behaviours of homeless people.[29–30] For homeless people, the difficulties of accessing basic human needs compete with the drive to access health and operate as significant additional stressors to receiving care.[29] Further, it is likely that the patients with "no fixed abode" cannot be registered with a general practitioner, because of a lack of address and that the cost for the co-payment within primary care is a further barrier to accessing regular care. Our findings are sadly aligned with extant literature and reiterate the pressing need for improving the accessibility to healthcare for homeless people.[30]

Of particular concern, and in line with other findings, suicide was prevalent among homeless youth and young adults.[28] In addition, the prevalence of lifetime suicide ideation (69.3%) was significantly higher than those of depressive disorders (46.9%). Yet, in the context of homelessness, research identifies that suicide ideation is a more sensitive indicator of acute risk of suicide than depressive symptomatology, in comparison to the general population.[31–33] Abuse and trauma especially are recognised as being major pathways to homelessness and strong predictors of suicide ideation among homeless adults and youth, which is intensified by different sources of emotional distress when living on the streets.[32–35] We found that nearly 70% of cases had evidence of stressful and traumatic life events that reverberate through the rate of suicide ideation we uncovered. Hence, we would argue that assessing suicide ideation should be part of routine screening provided by health providers in contact with homeless patients.

The strengths of this study include detailed data on the deaths of a group of patients who are often hard to identify from routine data sources. Our sample included homeless persons who did not receive regular healthcare, and this reflects the considerable challenges of meeting the healthcare needs among this population. It has been argued that the concept of amenable mortality suffers from a lack of accurate determination of the underlying cause of death.[13] By using findings from forensic examinations, this pitfall has been avoided. The study has some limitations. The study focused on a specific subset of homeless people identified as having "no fixed abode" at the time of death. People living in transitional housing, motels or private dwellings are provided with an address and have not been identified. Thus, our findings are relevant to those who were the most isolated and deprived in terms of support and access to healthcare, as is suggested by the extremely low rate of deaths in hospital settings for a population without a home. It is also conceivable that some relevant coroners' reports could have been missed. The proportion of natural causes differs significantly from previous hospital-based studies in England and New Zealand that evidenced cardiovascular diseases, cancers and respiratory diseases as being the main underlying causes of deaths.[7–8] Our sample framing relied on deaths that must be legally

reported to coroners due to their violent or undetermined causes, and which represented nearly half of all deaths. This has likely led us to underestimate the contribution of natural causes of deaths to the overall mortality. Ethnicity was not individually reported on the coroners' findings, meaning that data regarding Māori and Pasifika people, who are mainly impacted by homelessness within New Zealand, were not available.[1]

Implications and need for future research

Our findings carry important implications for the development of health policy to enable earlier identification of homeless patients at high risk of premature mortality. This involves enhancing access to care, as well as providing the continuity and quality of care for homeless people with life-limiting conditions. Considering cardiovascular disease and suicide are leading causes of amenable mortality, regular access to a source of care is an imperative for this population. Within primary care, access to homeless-tailored services that emphasise outreach programmes and free care delivery has shown positive outcomes in terms of accessibility and continuity of care, and should therefore be facilitated.[36] Components of an effective response should also promote a holistic and patient-centred approach (or whānau-centred approach if appropriate) to support self-esteem recovery.[29] Treatment plans that actively encourage the participation of the homeless patients are needed to ensure adherence to care and follow-up. A first step in this direction could be to implement homeless-sensitive care training programmes for health providers within primary care and emergency departments, with special attention given to suicide ideation identification. For homeless patients with mental health issues or dual diagnoses, assertive community treatment seems the most encouraging response regarding regularity of health contacts and housing stability.[37]

That said, many homeless people are not mentally ill or substance users. Future research should assess more specifically healthcare utilisation and access barriers in various settings and for different subgroups of the homeless population. Lastly, this study has also provided the opportunity to highlight the lack of systematic capture of homelessness through different administrative data sets, other than by using a reductive identification of homeless persons by the "no fixed abode" criterion. Equally important, the use of the Z.590 code should be encouraged within DHBs, including during the completion of the Medical Certificate of Cause of Death, if we are to understand how to adequately and effectively improve the healthcare of the homeless population. This would be facilitated if the Law Commission's recommendations for modernising the legislation relating to death, burial, cremation and funerals in New Zealand became the responsibility of the Ministry of Health.[38] This should allow for a better recording of homeless deaths and would also ensure better recording of ethnicity data.

Conclusion

Homeless people experience considerable challenges when accessing the healthcare system, as uncovered by the dramatic rate of amenable mortality. Our findings outline the pressing necessity to implement specific models of care that are designed to meet the social and healthcare needs of homeless persons and address the significant health inequalities they face. This research highlighted an extreme situation of social isolation and disengagement from the healthcare system that point out the challenges of accessing regular sources of care and receiving comprehensive and culturally sensitive care. Future work should provide a more comprehensive picture of healthcare utilisation for the diverse groups of homeless patients, to assist policy decisions as part of comprehensive and effective response to homelessness.

Competing interests:
Nil.

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Improved foot management of people with diabetes by primary healthcare nurses in Auckland, New Zealand

Barbara Daly, Bruce Arroll, Krishnarajah Nirantharakumar, Robert Keith Rhodes Scragg

ABSTRACT

AIMS: Evaluate trends in foot examinations for people with diabetes by primary healthcare nurses between 2006–2008 and 2016 in Auckland, New Zealand.

METHODS: All primary care nurses in 2006–2008 and 2016 were identified and 26% and 24% were randomly sampled and surveyed, respectively. Nurse participants completed a self-administered questionnaire and telephone interview about the care provided for people with diabetes.

RESULTS: Significantly more patients consulted by practice nurses received foot examinations in 2016 (58%) compared with 2006–2008 (36%), and foot-care education (66% versus 26%). Of the 43% of patients who had no foot examination in 2016, 23% had no previous examination documented. Significantly more nurses in 2016 than in 2006–2008 self-reported routinely examining patients' feet (45% versus 31%) and giving foot-care education (28% versus 13%). These practices were associated with nurses undertaking >5 hours of diabetes education within the past five years.

CONCLUSIONS: Practice nurses have significantly expanded their role in managing people with diabetes over the last decade by increasing the number of foot examinations and providing recommended foot-care education. Improved management was associated with nurses attending diabetes education in the past five years. Gaps were identified in conducting the recommended number of foot examinations, categorising patients' risk of foot disease and recording previous examinations.

Foot disease is a common complication of diabetes with a lifetime risk of up to 15% to 25%,[1] and it is the leading cause of lower-limb amputation.[2] Peripheral neuropathy, peripheral arterial disease (PAD) and infection are the most common pathological conditions that underpin diabetes-related foot ulceration or disease.[2,3] Foot ulceration takes on average three months to heal and impairs an individual's productivity[4] and quality of life.[3] The probability of a further foot ulceration within 12 months after the onset of foot disease is 40%,[2] and mortality within this period is 14%,[5] which increases to over 70% by five years.[2]

There are few reports on diabetic foot disease in New Zealand. One study of 2,192 people with diabetes who attended eye screening in a semi-rural region classified 13% of patients as high risk of developing foot disease.[6] A survey of 53 Māori primary care patients in Auckland with long-term diabetes found 53% had developed pre-ulcerative foot lesions and 8% had current lesions, despite over 85% having a good knowledge of foot care.[7] A cohort study linking primary health and hospital records identified additional risk factors for lower-limb amputation as male gender, Māori ethnicity, economic deprivation, elevated HbA1c

ISSN 1175-8716

and dyslipidaemia.[8] A national cohort study that followed most people diagnosed with diabetes in New Zealand (n=217, 207) between 2010 and 2013 reported that 0.92% had at least one lower-limb amputation.[9] Similar risk factors were identified as in the previous studies, plus comorbidities and a previous amputation.[9]

Despite the high prevalence of diabetes in New Zealand's non-European populations,[10] a review of 12 European and Australasian countries reported that New Zealand had one of the lowest annual rates of minor and major amputations in people with PAD (55% of whom have diabetes), reporting 9.3 and 7.2 per 100,000 people, respectively.[11] This may reflect a lower proportion of active smokers (14%), younger Māori and Pacific populations with diabetes[10] and mostly free treatment for lower-leg ulceration and disease compared with the other countries surveyed.[11] Despite this, there are regional differences in lower-limb amputations for people with diabetes with higher rates in the Waikato and Hutt Valley regions.[12] Lower rates of diabetes-related foot disease have been reported for Asian populations in New Zealand[8] and the UK, which is attributed to lower rates of neuropathy compared with the European population.[13]

Although the incidence of lower-limb amputation has decreased in many developed countries, including New Zealand,[3,11,14] the prevalence of diabetes-related foot disease will continue to rise due to the increasing number of people developing type 2 diabetes[15] and the increased survival rate.[16] This will increase the future costs of managing diabetes, as the estimated cost per wound episode is $30,000 in New Zealand,[17] while in the US, over half the total diabetes budget is spent on peripheral vascular and neurologic complications (mostly related to lower-limb ulceration).[18]

Nurses providing community-based care are ideally placed to reduce the risk of people with diabetes developing foot disease. Comprehensive foot examinations are essential for identifying patients with reduced sensation, peripheral vascular disease and early skin changes,[19] and to arrange appropriate follow-up referral to reduce the risk of amputations.[19] Nurses are also able to identify and intensify interventions for patients with risk factors for foot disease—elevated HbA1c, hypertension, dyslipidaemia,[7,19] tobacco use, obesity and lack of physical activity.[6,7,20]

Given the increasing importance of diabetes foot disease, the aims of this report are to determine (1) whether there have been changes in foot examinations and education for people with diabetes by primary healthcare (PHC) nurses between an initial survey carried out in 2006–2008 [21] and a similar survey in 2016, and (2) whether the diabetes education of nurses is related to their management of foot disease in people with diabetes.

Methods

Study design and population

Two cross-sectional surveys of PHC nurses were carried out in 2006–2008 and in 2016 in Auckland, New Zealand. The same methodology was used for both surveys and has been described.[22,23] All practice nurses (PNs) based in the Auckland region were identified by updating and utilising a list of all general practitioners and PNs held in the Department of General Practice and Primary Health Care at the University of Auckland in 2006. In 2016, all PNs were identified by lists provided by all seven PHOs. For both time periods, lists of all district nurses (DNs) and specialist nurses (SNs) were provided by the three district health boards (DHBs) in Auckland. Of the total number of nurses, 287 (26%) in 2006 and 336 (24%) in 2016 were randomly selected and participated. Response rates were 86% and 73% for each survey, respectively. Figure 1 outlines the sampling frame for the numbers of PNs, DNs and SNs, including 19 and 25 diabetes nurse specialists, respectively, in each survey. Nurses completed a self-administered questionnaire providing biographical and work-related information and a telephone interview to ascertain information about the care provided for people with diabetes. A total of 308 people with diabetes were consulted in 2006–2008 and 447 in 2016 by the nurse participants on a randomly selected day each nurse had worked in the week prior to the telephone interview. Nurses were able to provide information for 265 (86% of the total) patients in 2006–2008. In 2016, because of the larger number of people with diabetes that were consulted, information was collected from 166 (37%)

randomly selected patients, depending on the time each nurse had available for the interview.

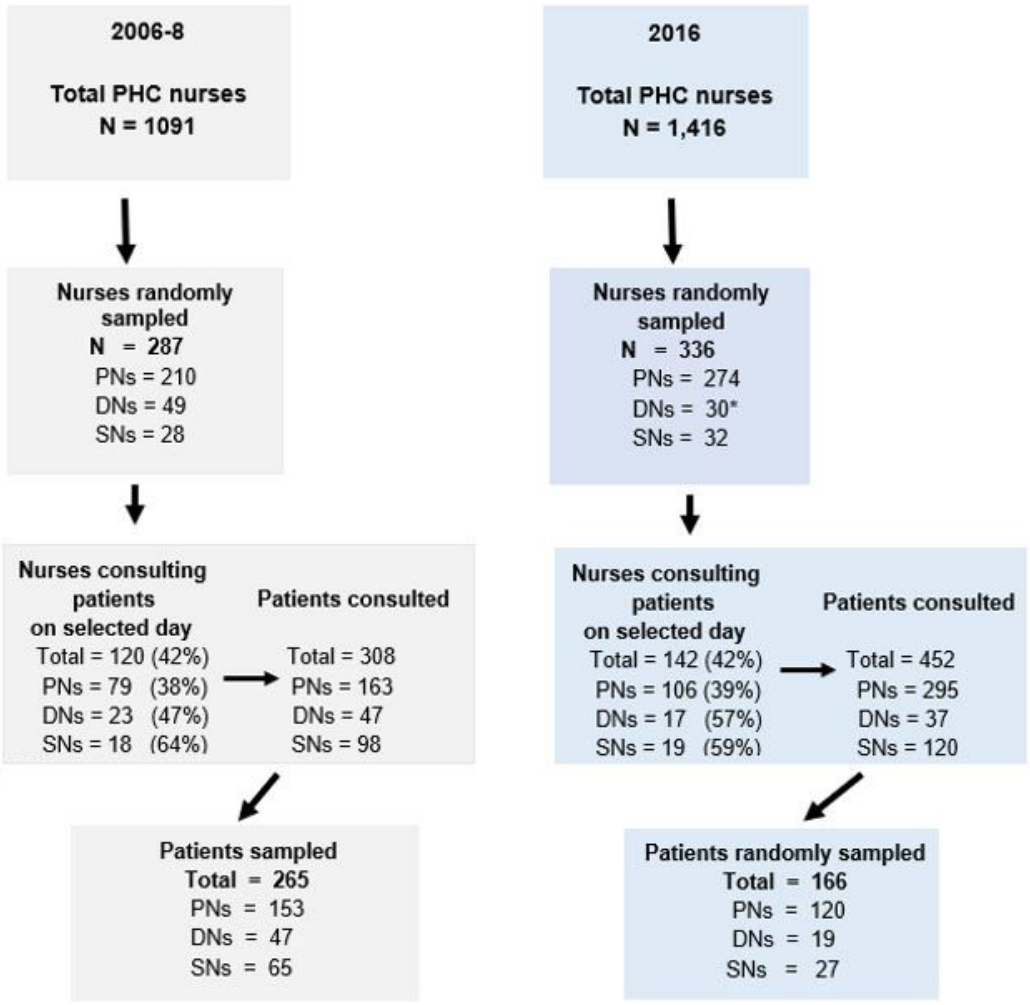
People with diabetes consulted

For both surveys, all nurses were asked during the telephone interview, and without prompting, what activities and assessments they routinely perform during a diabetes consultation. Nurses who had consulted at least one person with diabetes on the randomly selected day were also asked about the actual assessments and care provided for each patient. Specifically, nurses were asked whether they had checked each patient's feet. Nurses who responded positively were asked to state what they had checked without prompting. An additional question in the 2016 survey asked nurses who had not examined patients' feet for the "date of the patient's last foot exam". Ethical approvals were granted by the University of Auckland Human Participants Ethics Committee (014713) and Northern Regional Ethics Committee (NTX/05/10/128) for the 2016 and 2006–2008 surveys, respectively.

Statistical analysis

All patient analyses were weighted by the proportion of people with diabetes consulted by all nurse groups on any given day in Auckland during the survey period, along with weighting for the sampling of nurses.

Figure 1: Sampling frame for the total number of primary healthcare (PHC) nurses surveyed and the number of people with diabetes consulted by practice nurses (PNs), district nurses (DNs) and specialist nurses (SNs) on a randomly selected day.



*From two out of three district health boards.

SUDAAN (version 11.0 Research Triangle Institute, 2012) was used to correct standard errors for any design effects from clustering (for nurses who consulted and provided information for more than one patient) and the Mantel-Haenszel method was used to adjust for confounding variables.

Analyses of the nurse data were weighted for the proportion of nurses sampled by nurse group, to reflect all nurses providing community-based care at the time of the surveys, using SAS 9.4 (version SAS Institute, Cary, NC, 2013). Multivariate prevalence ratios from log binomial regression models using SAS (GENMOD) were used to examine any associations that provision of self-reported routine foot and wound care had with attendance of specific diabetes education over the past five years and years since graduation (as a proxy for age and experience).

Results

Numbers of nurses and patient details

Between surveys there was an 45% increase in the total number of PNs (813 to 1,181), a 46% decrease for SNs (98 to 53) and DNs remained similar (180 and 182). The proportion of PNs and SNs who consulted people with diabetes on the randomly selected day remained the same and was not significantly changed ($p>0.05$) for DNs (Figure 1). The proportions of patients consulted by the nurses in 2016 were: 56% male, 71% aged over 50 years, 72% non-European New Zealanders and 95% had type 2 diabetes; and were similar to the patients surveyed in 2006–2008.

Foot examinations and education in 2016

Fifty-seven percent of all patients consulted by 142 nurses in 2016 had their feet examined, and DNs were more likely to do this than PNs and SNs (Table 1). However, PNs were significantly more likely than DNs and SNs to test sensation ($p=0.0005$). Of the 43% of patients who did not have their feet examined during the consultation, 43% and 72% had had a foot examination within the previous 3 and 12 months, respectively. Overall, 15% of the total patient cohort had no previous record of a foot examination. Foot-care education was received by 65% of all patients consulted by the nurses, mostly relating to suitable footwear (43%), self-examination (41%) and moisturising feet and heels (24%). Twelve percent of patients received advice regarding toe and nail care, foot-related complications (including calluses), using orthotics and sensory awareness (Table 1).

Comparison of the two surveys

Table 2 compares the proportion of all patients between the two surveys who received foot examinations, foot-care education and wound care during the nurse consultation. Overall, there was a substantial (but not significant) increase in the proportion of patients who had foot examinations in 2016 (57%) compared with 45% in 2006–2008. For patients consulted by PNs, significantly more had foot examinations in 2016 (58%) compared with 2006–2008 (36%, p-value=0.03). In contrast, patients consulted by SNs had fewer foot examinations in 2016 (26%) compared with 2006–2008 (46%), although this comparison was not significant, because of the small number of patients in 2016. Overall, there was also a large increase in the proportion of patients who received foot-care education in 2016 (65%) compared with 2006–2008 (26%). In contrast, significantly fewer patients in 2016 received wound care or 'other' additional care, such as medication management, compared with patients in 2006–2008 (Table 2).

Self-reported routine foot care by nurses

Table 3 shows significantly more nurses in 2016 self-reported routinely conducting foot examinations (45%) and providing foot-care education (28%) during diabetes consultations compared with nurses in the 2006–2008 survey, who reported 31% and 13%, respectively. There was no difference in the proportion of nurses between surveys who reported routinely providing wound care.

Table 4 shows that nurses who had attended over 20 hours of diabetes education in the past five years were significantly more likely to self-report routinely examining patients' feet and providing foot-care education during consultations, but less likely to provide wound care, compared with nurses who had attended

Table 1: People with diabetes (n=166) who received foot examinations, foot-care education and wound care by 142 nurses by nurse group, after weighting for the proportion of nurses (weighted) and patients sampled (weighted=1,291) in 2016.

Variable and level	Total surveyed N=166 N	Weighted by total sampling probability				
		Total sample weighted N=1,291[a] %	Total patients by nurse group			Wald P-value[b]
			Practice nurses n=120 %	District nurses n=19 %	Specialist nurses n=27 %	
Feet examined	87	57	58	79	26	0.03
Characteristic examined						
Colour	87	57	58	79	26	0.03
Skin integrity	87	57	58	79	26	0.03
Nails	86	57	58	72	26	0.06
Oedema	81	55	55	78	26	0.04
Pedal pulses	62	45	48	25	26	0.20
Sensation	66	48	55	8	26	0.005
Microfilament	29	25	30	0	6	0.06
If no foot exam, when was last exam	79	100	(55)	(3)	(21)	0.19
<3 months	27	43	45	86	16	
4–6 months	9	12	12	0	14	
7–12 months	12	17	20	0	6	
>12 months	6	5	4	0	13	
Not known	25	23	19	14	51	
Foot care education	96	65	66	75	43	0.21
Specific education given						
Suitable footwear	58	43	45	42	25	0.34
Self-examination	59	41	44	22	30	0.30
Moisturising feet and heels	27	24	26	9	19	0.43
Consult podiatrist	13	6	5	3	16	0.36
Other (n=20)	20	12	8	51	7	0.14
Received wound care	28[c]	14	5	91	2	0.002

[a]The total weighted sample is used to estimate the total number of people with diabetes consulted by all nurses in Auckland during the study period.
[b]P-value showing the significance of variation in percentages in subgroups, from the Wald chi-square value.
[c]n=165 patients.

Table 2: Comparison between surveys of foot examinations and foot-care education received by people with diabetes and consulted by nurses on the randomly selected day, after weighting for the proportions of nurses and patients sampled in each survey and adjusting for sex, age, ethnicity and nurse group.

Variable	**Survey 2006–2008**	**Survey 2016**	**Wald P-value[a]**
Total patients sampled	265	166	
Categorical variables	**Weighted % (number sampled)**	**Weighted % (number sampled)**	
Foot examinations	45 (119)	57 (86)[b]	0.13
Nurse groups			
Practice	36 (55)	58 (64)	0.03
District	74 (34)	79 (16)	0.72
Specialist	46 (30)	26 (6)	0.21
Specific foot assessments			
Colour	45 (119)	57 (86)[b]	0.13
Skin integrity	45 (119)	57 (86)	0.13
Nails	44 (117)	57 (85)	0.13
Pedal pulses	31 (82)	44 (61)	0.13
Oedema/swelling	32 (84)	55 (80)	0.007
Sensation	30 (78)	48 (65)	0.04
Microfilament test	24 (64)	25 (28)	0.97
Ipswich (touch test)[c]	(0)	(0)	-
Other foot assessments[d]	19 (51)	2 (5)	<0.0001
Foot-care education	26 (68)	65 (94)[b]	<0.0001
Nurse groups			
Practice	26 (41)	66 (71)	<0.0001
District	30 (14)	75 (12)	0.006
Specialist	20 (13)	43 (11)	0.14
Patient to self-examine feet	8 (23)	39 (56)[b]	0.0006
Suitable footwear	7 (18)	43 (57)	<0.0001
Moisturise feet and heels	5 (13)	24 (27)	0.04
Consult podiatrist	3 (7)	5 (12)[b]	0.21
Other foot-care education[e]	3 (7)	12 (19)[b]	0.009
Follow-up podiatrist	8 (21)	13 (24)	0.15
Wound care	29 (78)	14 (28)	0.006
Nurse groups			
Practice	17 (26)	5 (10)	0.005
District	94 (43)	91 (17)	0.75
Specialist	14 (9)	2 (1)	0.08
Other care provided	50 (133)	16 (30)	<0.0001

[a]P-value showing the significance of variation in percentages in subgroups, from the Wald chi-square value.
[b]Numbers differ slightly from those in Table 1 due to adjusting for sex, age, ethnicity and nurse group.
[c]The Ipswich test, developed to encourage foot examinations, is positively predictive of at-risk feet.[24]
[d]Other foot assessments in 2006–2008 related to wounds and injuries (73%), temperature and skin (19%) and footwear and referrals (8%), and in 2016 for corns calluses, gout and capillary filling (n=5).
[e]Other foot-care education included toe and nail care, wounds, pain, foot complications, orthotics and sensation.

Table 3: Comparisons between the proportions of nurses in 2006–2008 and 2016 who self-reported routinely performing foot examinations and providing foot and wound care during diabetes consultations.

Variable and level	Survey 2006–2008	Survey 2016	Wald P-value[a]
	Weighted % (number sampled)	Weighted % (number sampled)	
Total nurses sampled	287	336	
Routine assessments and education delivered by nurses			
Foot examinations	31 (91)	45 (158)	0.0004
Foot-care education	13 (37)	28 (103)	<0.0001
Providing wound care	20 (57)	19 (64)	0.83

[a]P-value showing the significance of variation in percentages, from the Wald chi-square value.

Table 4: Multivariate prevalence ratios of self-reported routine foot and wound care by nurses in the 2016 survey, after weighting for the proportions of nurses sampled and adjusting for hours of diabetes education and years since graduation (n=336)—from log binomial regression.

Routine care	Prevalence ratios (95% CI)					
	Diabetes education (hours)			Year of graduation		
	<5 (n=108)	5–20 (n=117)	>20 (n=106)	2003–2015 (n=109)	1985–2002 (n=108)	1964–1984 (n=109)
Foot examinations	1.00	1.14 (0.98–1.33)	1.51 (1.31–1.75)[c]	1.00	0.87 (0.76–1.00)	0.93 (0.81–1.07)
Foot care education	1.00	1.30 (1.03–1.64)[a]	1.84 (1.48–2.30)[c]	1.00	0.79 (0.64–0.97)[a]	0.88 (0.72–1.07)
Wound care	1.00	0.54 (0.42–0.70)[c]	0.33 (0.23–0.45)[c]	1.00	1.63 (1.26–2.10)[c]	1.00 (0.74–1.33)

[a]p-value <0.05; [b]p-value <0.01; [c]p-value <0.001.

less than five hours' education. In contrast, the nurses' year of graduation (a proxy for experience) was not consistently related to foot-care education or wound care.

Discussion

There has been an upward trend in nurses conducting foot examinations for people with diabetes (from 45% to 57%) between 2006–2008 and 2016. This increase has been largely driven by PNs increasing examinations from 36% to 58%, offsetting the trend for SNs, where there has been a decrease from 46% to 26%. This has been accompanied by an increase in the proportion of patients receiving foot-care education and advice (from 26% to 65%) over the same period, which occurred uniformly in all three nurse groups. The trends are unlikely to be due to differences in patients between the two surveys, as demographic characteristics were similar except for an increase in non-European patients in 2016.[23] These findings are consistent with an upward trend for foot examinations in people with diabetes in North America,[25] which is associated with a new nurse-led model of care in a family practice[26] and in Hispanic people with diabetes.[27]

The significant increase in the number of PNs between 2006–2008 and 2016 [22], and in the proportion who conducted foot examinations and gave recommended foot-care education,[28,29] indicates an increased capability in their management of people with diabetes. In contrast, the decrease in the proportion of SNs conducting foot examinations in the latter survey is possibly due to their decreased numbers[22] and

increased workloads (based on the number of patients consulted).[23] This trend for a higher proportion of foot examinations in patients consulted on the randomly selected day (Table 2) is backed up by the surveyed nurses reporting that they were more likely to routinely conduct foot examinations and provide foot-care education in 2016 compared with nurses surveyed in 2006–2008 (Table 3).

The increased foot care management by nurses in 2016 may be due to an increase in nurses' knowledge of foot disease in the 2016 survey compared with nurses in 2006–2008,[30] as nurses undertaking diabetes education were more likely to routinely conduct foot examinations and provide foot-care education in 2016 (Table 4). Similar associations with increased foot examinations have been reported for NPs (although not for PNs) in Slovenia attending general family practice education,[31] and similarly for hospital-based nurses in relation to managing patients with foot ulcerations in Sri Lanka[32] and Pakistan.[33]

Previous findings from the 2006–2008 survey highlighted that few PNs were able to state all the major risk factors for diabetes complications.[30] This may reduce their ability to classify a patient's risk of foot disease. Age, being male or Māori, duration of diabetes, economic deprivation,[8] being rural-based,[6,7] obesity, retinopathy[7] and renal disease[20] all increase the risk of foot disease, in addition to being major risk factors for all diabetes-related complications. Patients with foot deformities, neuropathy, PAD and a previous or current foot ulcers are at an even higher risk[19,20,29] of non-healing wounds that result in lower-limb amputation.[34] Thus, further education for PNs could result in more people with diabetes receiving appropriate foot care.

Although international guidelines on foot management differ,[35] it is recommend that all people with diabetes have an annual foot examination and are classified by their risk of developing foot ulceration or disease.[19] Classification is based on low risk (normal sensation and palpable pulses), moderate risk (neuropathy or absent pulses) or high risk (moderate with a foot deformity, skin changes or precious ulcer),[19] with corresponding annual, 3–6 monthly or 1–2 monthly foot examinations based on risk level,[29] and specialist service follow-ups for those at high risk.[19,36] The national guideline recommends annual and 3–6 monthly foot examinations for people with diabetes with low- and high-risk feet, respectively.[28] Despite this, 43% of patients in 2016 did not have their feet examined during the nurse consultation, and of those patients, 23% had no available record of their last foot examination (including 51% of patients consulted by SNs). The latter may be due to the different patient electronic management system used in secondary care, which is where most SNs are based, compared with that used in primary care. A similar proportion of people with diabetes in primary care in the UK had records of foot examinations, although fewer patients had records in Ireland (65%), in comparison with 79% and 83% in Scotland and England, respectively.[37]

Despite a 9% increase in the population of Auckland to 1.5 million[38] and a 35% increase in people diagnosed with diabetes[39] between 2006 and 2017, significantly fewer people with diabetes received wound care (14%) in 2016 compared with 29% in 2006–2008 (Table 2). The introduction of multidisciplinary podiatry outpatient clinics in Auckland, which is associated with improved footcare,[40] may have contributed to the reduction in wound care in general practice and district nursing services, enabling the latter to reserve care for the elderly, Pacific and Māori populations[41] and the housebound.[42] However, there is a paucity of reports quantifying each service's contribution to the provision of wound care.

In addition to risk-factor management, patient education is the hallmark of best practice in reducing the development and recurrence of diabetes-related foot disease.[19] Patient awareness is reportedly poor.[19] Health literacy has been identified as an important barrier to good foot care,[43] and patient education interventions are only weakly associated with primary prevention.[3,44] A New Zealand study reported that 85% of Māori people with diabetes displayed a good knowledge of foot care, but despite this, over half developed pre-ulcerative foot lesions.[7]

Despite the global cost of diabetes-related foot disease, there continues to be a lack of interest and funding to test quality

interventions for primary prevention and for treatment to reduce lower-leg amputations, with the exception for off-loading for pre-ulcerative areas.[3,45] The lack of evidence for preventative educational interventions (particularly for patients with neuropathy),[36] and for access to quality foot-care services, contribute to the wide variation in lower-leg amputations globally,[46] including a four-fold difference in major amputations in New Zealand[12] and a 10-fold variation across primary care trusts in England.[14]

Primary care nurses are well placed to screen and classify people with diabetes who are at risk of developing diabetes-related foot disease and organise specialist referrals for patients at high risk or with a current ulceration.[19] Despite the lack of good evidence for preventative interventions, foot examinations, foot-care education, early referrals and treatment are associated with a reduction in foot ulceration.[47] An increase in nurses conducting foot examinations was associated with fewer lower-leg amputations for people with diabetes in Germany,[48] and a new referral service for patients with foot ulcers reduced the incidence of amputation in the UK and Germany.[3]

Limitations of the 2016 study include the inability to sample one-third of DNs in the Auckland region, potentially causing underrepresentation of this group of nurses. Despite this, results are expected to be fully representative of PNs and SNs and for all nurse-groups in 2006–2008 and for the patients consulted during both study periods, because of the random sampling of nurses and patients and high response rates. The three district nursing services also follow a similar model of care and criteria for accepting patients for home-based care.[41] Weighting the sampled patients potentially under- or over-inflates differences between patient survey groups, as this is based on the assumptions that the same nurse provides the same care to all patients consulted, and that patients not surveyed to have similar demographic and biophysical characteristics to those surveyed by the same nurse. It is acknowledged that patients may have differed, although DNs and SNs typically consult patients who have more diabetes-related complications and comorbidities than patients consulted by PNs.[49]

Over the past 10 years, an increasing trend in improved foot management by PNs was evident. Nurses attending diabetes education was positively associated with conducting foot examinations and providing recommended foot-care education. However, patient records of previous examinations were incomplete and not all patients had a foot examination over the past year. In addition, foot-disease risk assessments and the recommended frequency of examinations were lacking.

Competing interests:
Nil.
Acknowledgements:
We thank the primary healthcare nurses for their participation, and the primary health organisations and district health boards in Auckland for supporting these surveys.
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Change in health profile of refugees resettling in New Zealand, 1980–2014

Martin Reeve

ABSTRACT

AIM: To update data previously published on the health profile of the refugees resettling in New Zealand, and to draw attention to the change in health profile over time, with a decline of infectious disease/deficiencies, and a rise of non-communicable diseases, a worldwide phenomenon.

METHOD: Comparative data was extracted from (1) written annual reports prepared by medical officers at the Mangere Refugee Resettlement Centre (1978–1991), (2) a Microsoft ACCESS patient management system between 1995 and 1999 and (3) a MEDTECH patient management system between 2010 and 2014.

RESULTS: Over the period 1979–2014, the rate of infectious diseases has declined markedly in resettling refugees, and the rate of non-communicable diseases has increased. For example, the incidence of tuberculosis has decreased from 4% to 0.2%, gut parasites from more than 40% to, in some intakes, 15% and iron deficiency from 22% to 10%, while the diabetes rate has gone from 0.1% to 2.7%.

CONCLUSION: While management of unfamiliar infectious diseases and deficiencies (especially vitamin D) still remains an important part of the management of refugee health, their management usually involves limited time and expense, and their burden is much less than before. However, refugees now resettling in New Zealand and the rest of the world often present with familiar non-communicable diseases that require long-term management.

A note on terminology: A person who is forced to leave their home but remains within their own country is called 'an internally displaced person'. If they are then forced to leave their own country and seek refuge in a second country, they then become 'an asylum seeker'. After a determination process, they then become a 'mandate refugee' or, in New Zealand, a 'convention refugee'. Less than 1% of mandate refugees are resettled in a third country. Many countries, including New Zealand, take an annual quota of mandate refugees, 'quota refugees', and it is to this group which this paper is addressed; asylum seekers are not included. However, once a person is accepted into the New Zealand quota refugee programme, they become a permanent resident; strictly speaking, quota refugees in New Zealand should be called 'former refugees', but for simplicity they will be referred to as refugees. The whole process referred to above comes under the aegis of the United Nations High Commissioner for Refugees (UNHCR).

*

New Zealand's refugee resettlement programme started officially in 1944 with the arrival of 800 Polish people. Following that, different groups of varying size and nationality arrived each year. In 1987, the New Zealand government decided on a fixed quota of 750 per year, which was increased to 1,000 in 2015 and 1,500 in 2020. New Zealand thus follows 34 other countries in taking an annual quota of refugees for resettlement.[1]

Accommodation on arrival in New Zealand before 1979 was under the care of an interdenominational church group, the Inter-church Refugee Committee, and was ad hoc. For example, in former army barracks and immigration and workers' hostels.[2]

In 1979 the Mangere Refugee Resettlement Centre (MRRC) opened in a former army barracks built for the US Army in 1942 and used, since the war, as an immigration and workers' hostel.[3,4] Since 1979, all refugees being resettled in New Zealand stay in MRRC on arrival. In 2016 a new dedicated refugee resettlement centre was opened on the old site, and the original buildings were demolished. MRRC is under the care of the New Zealand Immigration Service (NZIS) and is a 'one-stop shop' with all the services needed for the resettling refugees on the one site, which includes medical, dental, psychological, educational and social.

Between 1979 and early 2020, the refugees arrived in intake groups every eight weeks and stayed for six weeks. Between 1979 and 2015 the intakes were approximately 125 in size, and from 2015 to 2020 they were approximately 170 in size. From 2020 it is planned that the intakes will be approximately 220 and the refugees will stay for only five weeks.

Before 2013, the refugees received little or no overseas medical screening. Since 2013 they have received limited medical screening carried out by the International Organisation for Migration (IOM). The screening includes a chest x-ray, an HIV test for adults and a clinical examination. The screening results are sent to MRRC.

During their stay at MRRC, the refugees are prepared for resettlement in New Zealand, and before early 2020 this included a comprehensive medical screening carried out by the on-site medical clinic, Refugee Health Screening Service (RHSC). The medical clinic was a government-run organisation, independent of NZIS; from 2000 until 2020, the clinic was part of the Auckland Regional Public Health Service (ARPHS).

Health data collected at MRRC from 1979 until 2020 is unique in the world. As far as is known, in no other country do all resettling refugees stay in the one site and receive medical screening. Data from other countries may be larger than that from MRRC, but it is always only a sample of the resettling population.

The increased number of refugees planned for in late 2020 has led to a radical change in health screening and management. It is planned that all refugees will receive comprehensive screening overseas and a limited assessment on arrival, and ARPHS will withdraw from providing services, which will be taken over by a general practice service whose configuration is unknown at the time of writing.[5] Thus, comprehensive on-shore screening data will no longer be obtainable for the first time in 40 years.

Obviously there have been many other changes at MRRC since 1979. One of the most important, and one not confined to refugees in general and New Zealand resettling refugees in particular, is a major change in the health profile.

From its opening in 1979 until relatively recently, the health profile was one of deficiency and infectious diseases, particularly gut parasites. Now the major burden, and one felt in all countries receiving refugees, is the classical non-communicable diseases (NCD), such as diabetes and hypertension.

A paper published by the author (in collaboration with another author) in 2005 analysed the health profile of resettling refugees passing through MRRC between 1995 and 1999 inclusive.[6] To explore the change in health profile, and other changes, the health of refugees resettling between 2010 and 2014 (before the increase in numbers) was analysed. For the purposes of this paper, the population of the 2005 paper will be called the original group (OG) and that of 2010–2014 the later group (LG). As noted below, some data from medical officers' written annual reports from the opening of the refugee centre in 1979 to 1991 is used, and this group is called the historical group (HG).

Method

The medical screening the refugees received consisted of a battery of tests and a standardised clinical examination with the assistance of trained medical interpreters.

The battery of tests consisted of core tests, such as full blood count, and conditional

tests determined by the person's age and sex. For example, children up to their 15th birthday received a Mantoux test as part of screening for tuberculosis.

While the core and conditional tests were mandatory, others were voluntary. For example, sexually active women were offered cervical smear screenings and microbiological screenings for sexually transmitted infections (STI) and other genital infections, which were purely voluntary.

Where indicated, further testing might be done. For example, those found with macrocytosis on their full blood count would receive testing for vitamin B12 and folic acid.

All results were entered on a computerised patient management system (PMS): the OG on a purpose-built Microsoft ACCESS programme, and the LG on a commercially available PMS, Medtech32.

In addition, written annual records produced by medical officers at MRRC between 1979 and 1991 were examined for historical data which was used in the original paper, and some has been included in the present paper, the historical group (HG).

The author had access to the data from the OG and, in some cases, was able to re-work the data to make it comparable with the LG. For example, the referrals to secondary services.

Those refugees found to have problems were either treated during their stay, if necessary referred urgently to hospital for inpatient or outpatient management, or referred to a primary care doctor or outpatient clinic in their city of resettlement after they had left MRRC.

Results

Demography

The total number of refugees in each of the 'Christmas tree' graphs above are similar—2,992 for the original group and 3,530 for the later group. This is to be expected, as the planned annual intake was 750 from 1979 until 2015. Hence, over five years, 3,750 refugees would expect to be resettled, though in both groups that target was never reached.

The graphs show that in general the population is a young one—though the 'tip' of the graph is in fact higher in the later group, with the presence of those of advanced age in later group, a phenomenon familiar to those working with refugees.

The graphs also show a balance between males and females: 47% female and 53% male in the original group, and 49% female

Figure 1: Age/sex distribution of OG, 1995–1999.[6]

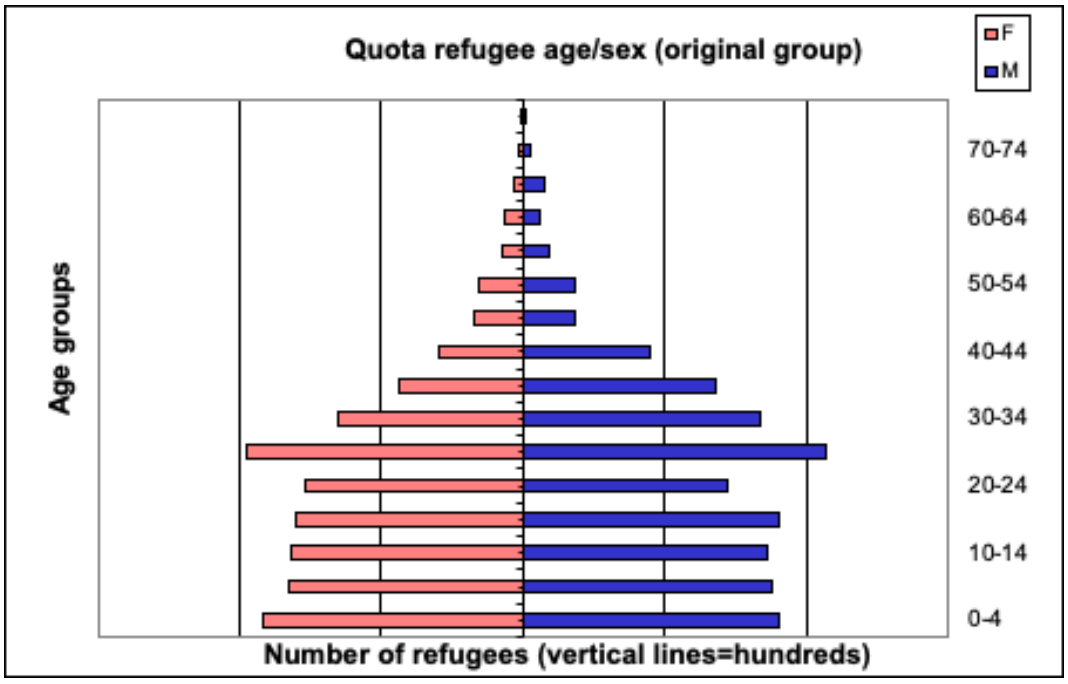
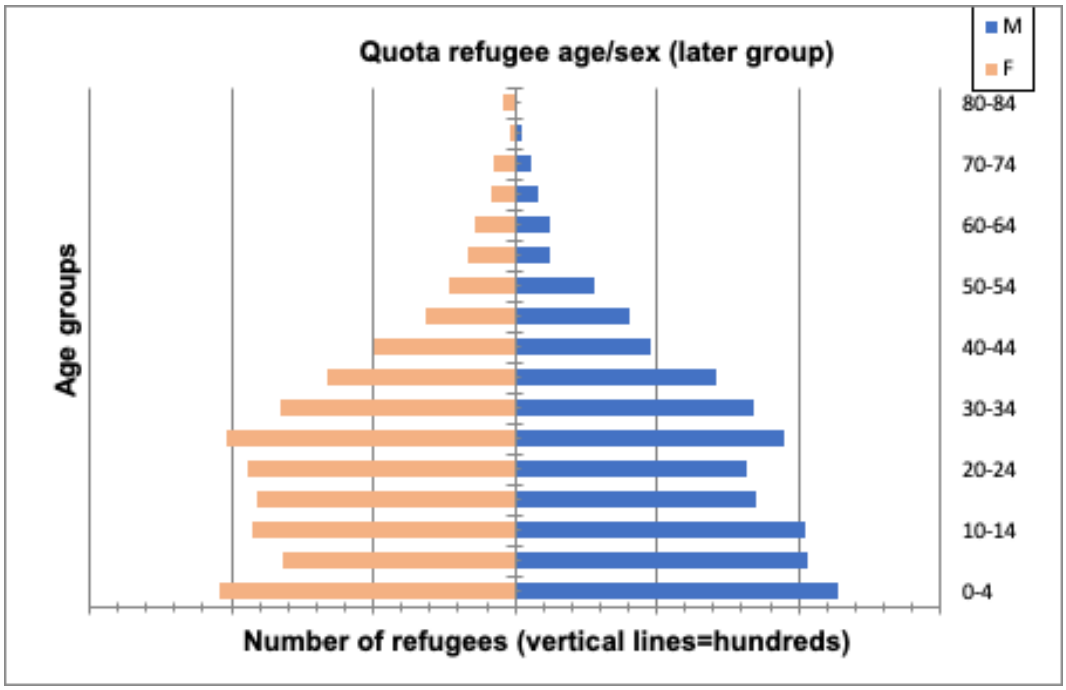


Figure 2: Age/sex distribution of LG, 2010–2014.



and 51% male in the later group. This is a consequence of the New Zealand policy of accepting predominantly family groups.

What the graphs do not show is the marked change in the origins of the refugees between the two groups.

In the original group, the top two nationalities were Iraqi and Ethiopian, making up 52.3% of the group, while in the later group, the top two nationalities were Burmese and Bhutanese, making up 50.9% of the group. In the later group, Iraqi make up 10% of the intake and Ethiopian only 0.2%. There were no Burmese or Bhutanese in the original group. The reasons for these changes will be discussed.

Infectious diseases

Tuberculosis

Tuberculosis (TB) control has always been the main focus for infectious disease control in quota refugees and shows considerable success over the years. The results will be presented as (1) overall results, (2) a focus on TB in childhood and (3) a note on abnormal chest x-rays.

Overall outcome of tuberculosis testing

The graph from the original paper has been left in its original form. The differences between the graphs shows not just the marked reduction in TB disease from a point prevalence rate of 2% to 0.18%, but it also demonstrates (1) different management in TB testing, (2) improved access to the final outcome of TB testing in refugees and (3) diagnosis and treatment of TB disease before arrival in New Zealand, which was present in the later group but not the original group.

In the original group, only 65% were assigned as discharged from testing, while in the later group, 93% were discharged. This is because:

1. Nine percent of refugees in the original group were enrolled for serial chest x-rays after leaving (see the 'CXR 9%' section of the original group graph). No refugees in the later group were enrolled for serial chest x-rays.
2. In the original group, the whole group received Mantoux testing, while in the later group, Mantoux testing was done only up to the 15th birthday. Further, the level of Mantoux was lower in the original group for the starting of treatment for latent TB infection (LTBI). Hence the 'prophylaxis 13%" includes treatment for LTBI in adults and children. The 'LTBI 6.76%' in the later group refers only to children. The changes were brought about mostly after consideration of a paper that outlined the cost/benefits

Figure 3: Outcome of tuberculosis testing in refugee screened OG, 1995–1999.[6]

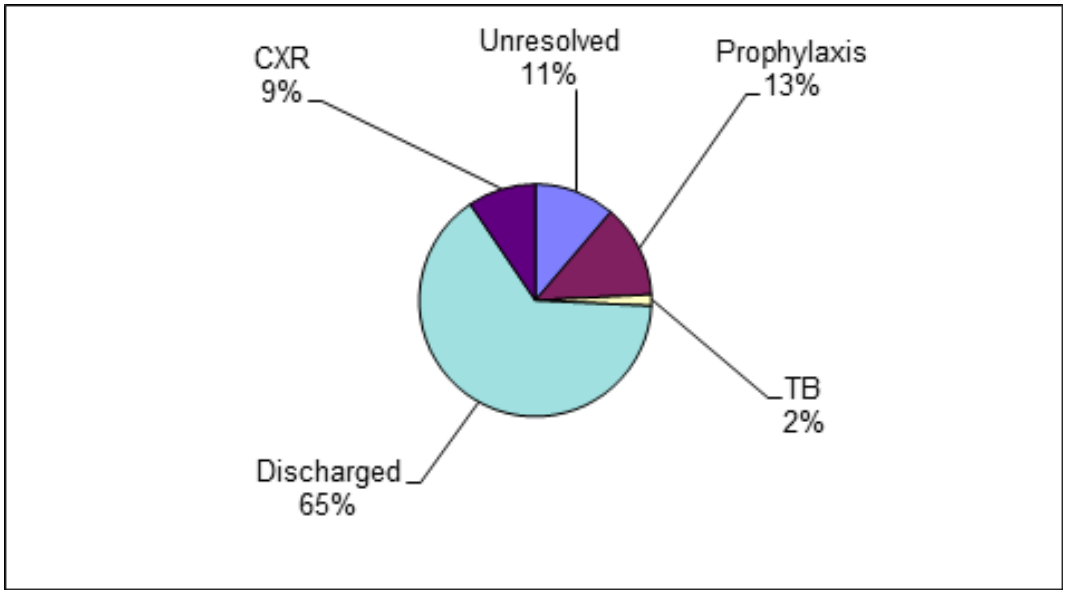
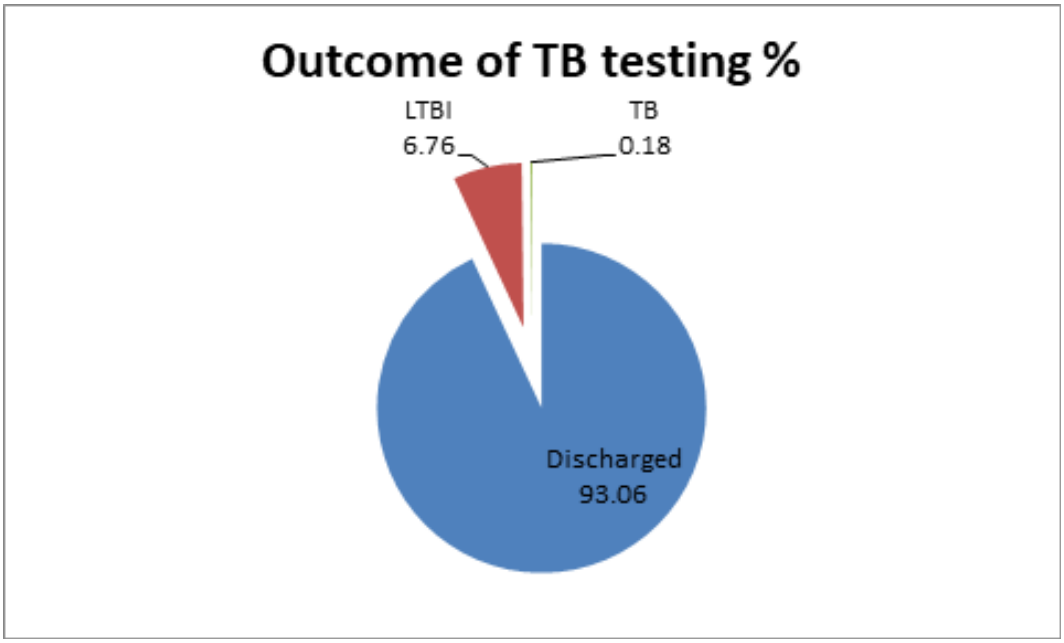


Figure 4: Outcome of tuberculosis testing in refugee screened LG, 2010–2014.



NZMJ 18 December 2020, Vol 133 No 1527
ISSN 1175-8716
www.nzma.org.nz/journal

of different methods of screening refugees and immigrants.[7]

3. At the time of the publication of the original group data, it was very difficult to track the final outcome of TB testing, hence the 'Unresolved 11%'. In the later group, due to improvements in national data collection, it was possible to track the outcome of all TB testing, hence there is no "Unresolved' section. So, the point prevalence of 2% TB disease in the Original Group is a minimum, as some of the 'Unresolved' group would have been found to have TB disease.

In summary, point prevalence of TB disease in resettling refugees:

Table 1: Summary of TB prevalence, 1980–2014.

	HG, 1979–1991	OG, 1995–1999	LG, 2010–2014
Point prevalence (%)	4.2	2.0	0.18

TB testing in refugee children

The changes in outcome and management are even more marked in children.

Overall, the proportion of children referred for assessment at the paediatric TB clinic between the OG and the LG is about the same, but the outcomes are very different. TB in refugee children is now virtually unknown, and the much higher proportion of those receiving treatment for LTBI in the LG represents a change in policy where treatment for latent TB infection was started at a lower level of Mantoux result, probably because of the high rates of TB disease in children.

The way in which data from the historical group are presented does not allow for analysis in children. But in one report, the medical officer reported that there were six children with TB disease in one intake of 125 people. As can be seen, TB disease in refugee children is now a rare event.

Abnormal chest x-rays

This section is included to remind practitioners that 'Old TB' recorded on a chest x-ray report does not exclude infectious TB disease. While signs of active TB may

Table 2: TB testing and results in children.

	OG, 1995–1999	LG, 2010–2014
Children receiving Mantoux	1,132	1,236
Referred to paediatric TB clinic for assessment (%)	334 (29.5)	266 (21.5)
Discharged, no follow up needed (% of those referred)	93 (27.8)	22 (8.3)
Further assessment needed (% of those referred)	25 (7.5)	12 (4.5)
Prescribed treatment for LTBI (% of those referred)	165 (49.4)	232 (87.2)
Prescribed treatment for TB disease (% of those referred)	16 (4.8)	0 (0)
Outcome not known (% of those referred)	35 (10.5)	0 (0)

be present on a chest x-ray, their absence does not mean that there is no infectious TB present, which can be diagnosed only by such methods of PCR, microscopy and culture of induced sputum.

All refugees 12 years and over received a chest x-ray on arrival in New Zealand, in addition to having a chest x-ray overseas. The table below summarises the situation.

The outcome of the follow up for the abnormal chest x-rays cannot be ascertained for the historical and original groups; but for the later group, all abnormal chest x-rays were referred to respiratory service specialists for their opinion, and 70% needed some form of follow-up, usually induced sputum testing.

HIV and other infectious diseases

The rate of HIV infection shows another difference between OG and LG. In the LG, HIV testing was undertaken before arrival in New Zealand. A positive diagnosis does not prevent resettlement in New Zealand, but only 20 refugees with HIV can be taken each year.[20] No pre-arrival testing was done for HIV in the HG.

In the LG, 16 refugees were confirmed to have HIV; all but two were known to have HIV before arrival and most were on medication. In the original group, none were known to have HIV before arrival, and hence none were on medication.

There is no data for the historical group; the first case of HIV infection was diagnosed

Table 3: Abnormal CXR in resettling refugees.

	HG, 1979–1991	**OG, 1995–1999**	**LG, 2010–2014**
Number of CXR taken in New Zealand	3,847	2,574	2,549
Abnormal CXR of those taken in New Zealand (%)	10.6	15.4	9.5

Table 4: Results of HIV testing in New Zealand.

	OG, 1995–1999	**LG, 2010–2014**
	% with +ve HIV test	% with +ve HIV test
Sub-Saharan Africa	3.9	2.9
Southeast Asia	1.6	0.6
Neither of the above	0.1	0.1 (all Colombian)
All quota refugees	2.0	0.5
Colombian	----	0.1

Table 5: Serology of selected infectious diseases, 1980–2014.

	HG, 1979–1991	OG, 1995–1999	LG, 2010–2014
Serological test	% positive of group	% positive of group	% positive of group
Schistosomal antibody	---	21.9	3.2
HBsAg	9.6	4.7	2.1
Anti-HCV antibodies	---	2.3	1.2
HCV RNA present	---	47.5% of those with +ve antibodies; 1.0% of group	43.9% of those with +ve antibodies; 0.6% of group
Treponemal test	4.9	4.0	1.7

in New Zealand in 1984, but routine testing of refugees after arrival did not start until 1993.

Serology of infectious diseases other than HIV infection

- Hepatitis B: The screening test is hepatitis B surface antibody and surface antigen, with the antigen being the priority if insufficient blood is taken. If the person is found to be surface antigen positive, Hbe antigen, Anti Hbcore and antiHbcore (IGM) are also tested. (Those found to be carriers have further testing and are managed according to local protocol.)
- Hepatitis C: Screening test was hepatitis C antibodies. Those found with any level of antibody were tested for hepatitis C PCR.
- Treponemal disease: Screening—electrochemiluminescence-based assay. Reactive (ie, abnormal) screens tested by TPPA and RPR.

Alimentary tract infections

Intestinal parasites

Data is available for HG, OG and LG and again show a reduction in rates of infection in the historic group. It is not possible to give exact numbers, but the medical officers recorded rates of at least 30% in each intake of refugees, and some intakes with rates of 45% infection.

Note that in Table 10, the percentage figures do not equal the total number affected, because (1) some people may have up to four parasites and (2) only the common parasites are recorded.

Table 6: Refugees affected by gut parasites 1980–2014.

Group (number)	HG, 1979–1991 (n=7,278)	OG, 1995–1999 (n=2,992)	LG, 2010–2014 (n=3,530)
% affected (number)	>>30 (?3,000)	31.0 (930)	17.7 (530)

Table 7: % of each group affected by four commonest parasites, 1980–2014.

	HG, 1979–1991	OG, 1995–1999	LG, 2010–2014
Ascaris Lumbricoides	7.5	3.0	2.9
Giardia Lamblia	12.5	12.8	6.1
Hookworm	30.5	4.3	4.0
Trichuris trichiura	16.0	5.5	4.1

Burmese refugees and the effect of type of residence before arrival on gut parasite infection

Most refugees do not now come from refugee camps but have lived in some form of housing subsidised by UNHCR before coming to New Zealand.

The LG study had refugees from Burma, some of whom had a traditional origin from refugee camps in Burma, and some had been living in Malaysia and adjacent areas in subsidised housing. This gave an opportunity to study the effect of residence on prevalence.

In total, there were 1,113 Burmese refugees; 697 were from Malaysia, of which 95 people (13.6%) were affected by gut parasites. By contrast, 416 were from Thai refugee camps, of which 107 (25.7%) were affected by gut parasites.

Helicobacter pylori

At the time of the original paper, helicobacter pylori (H. pylori) infection was recognised, but simple testing became available only late in the study group.

There are now two tests available: (1) the stool antigen test and (2) the blood EIA antibody test.

Testing for H. pylori in the OG and LG group was triggered by the presentation at screening of dyspepsia and/or gastro-oesophageal reflux. This was done only for those 18 years and over. Those who were younger were usually referred for assessment by paediatric services. It is known that proton pump inhibitors (PPI) can affect the reliability of the stool antigen test, so when the person was found to have been taking PPI up to one month before screening, the antibody test was requested, sometimes together with the antigen test when the history of PPI intake was not clear.

In the OG, only 11 EIA tests were requested, of which eight (72%) were positive.

In the LG, 405 tests were requested: 364 stool antigen, of which 238 (65.4%) were positive, and 41 blood antibody tests, of which 16 (39%) were positive.

Included in the above results are five people who had both antigen and antibody tests requested, of which both were negative in four people and positive in one person. There were no discordant results.

Hereditary haemolytic blood disorders

All refugees have been routinely tested for haemoglobinopathies and other disorders (eg, G6PD deficiency when indicated). Counselling was offered for all affected families, and specialist referral where indicated. Note that in these series, there were no transfusion dependent disorders.

Table 8: % of refugee population affected by hereditary blood disorders.

Condition	HG, 1979–1991	OG 1995–1999	LG, 2020–2014
alpha thalassaemia trait	1.4	8.1	2.3
beta thalassamia trait	1.0	1.4	1.5
HbE(heterozygous)	9.3	0.7	2.6
HbS (heterozygous)	Not done	0.3	0.9
Overall % of group affected by above and other congenital blood disorders	NA	14.9	8.5

ISSN 1175-8716

Micronutrients

Micronutrients are substances ingested or otherwise assimilated in small quantities that are essential to health.

Results

No data are available from the historic group. In both OG and LG, all refugees were routinely tested for iron, and both groups were also tested for B12 and folate deficiency when indicated, usually the presence of macrocytosis or on dietary history.

Table 9: Refugees affected by lack of micronutrients.

Micronutrient	OG, 1995–1999	LG, 2010–2014
Iron (number deficient) (%)	646 (22.3%)	368 (10.4%)
B12 (number deficient/number tested) (%)	5/39 (5.4%)	51/293 (17.4%)
Folate (number deficient/number tested) (%)	13/39 (33.3%)	0/293 (0%)

Vitamin D

Only the later group was routinely tested. For this group, a total of 1,405 people were diagnosed as having reduced vitamin D levels, a prevalence of 39.8%. Prevalence by gender: female 47.4%, male 32.4%.

Table 10: % vitamin D deficiency by ethnicity, later group.

Ethnicity	% prevalence
Afghani	69.4
Bhutanese	33.8
Columbian	13.3
Iraqi	73.8
Sri Lankan	60.1
Burmese	30.9

Vitamin D and iron

Two hundred and forty-three people had both iron and vitamin D deficiency, so one can be seen as a risk factor for the other.

Lifestyle

BMI

Table 11: BMI of OG and LG.

	OG, 1995–1999	LG, 2010–2014
Mean	23.0	24.5
Standard deviation	4.6	4.9
Underweight: BMI 18.5 or less	14.5%	6.8%
Overweight: BMI 25 or more	28.1%	39.3%

Tobacco use

Table 12: % of refugees using tobacco, 18 years and over, by gender OG and LG.

	OG, 1995–1999	LG, 2010–2014
Female	5.6	1.4
Male	32.3	20.5

Gender-related issues

Sexually transmitted infections

Table 13: Sexually transmitted infections by group and gender. Overall = % of total population, male:female ratio of those affected, OG and LG.

	OG, 1995–1999	LG, 2010–2014
Syphilis overall Male:female	4.0 1:0.6	1.7 1:0.9
Gonorrhoea overall Male: female	0.32 1:0.6	0.2 1:0.5
Chlamydia overall Male:female	Not available	1.1 1:0.9

Female specific

Contraception

Table 14: Contraceptive methods recorded on arrival, % of women interviewed, OG and LG.

	OG, 1995–1999	LG, 2010–2014
Oral	14.0	4.5
Depot	6.4	7.9
IUCD	17.0	3.6
Surgical (tubal ligation or hysterectomy)	8.8	9.7
Implant	0	1.6
Condom	17.5	15.7
Natural	12.3	2.0

These data should be interpreted with caution: for the OG only 171 women were recorded, and for assessment for contraception and for the LG, 554.

Pregnancy

Pregnancy testing was not routinely offered. Women known to be pregnant were made known to MRRC before arrival, by IOM. Shortly after arrival, all women who knew or thought they might be pregnant were invited to attend the clinic for confirmation, and if pregnancy was confirmed, further routine testing was done and they were followed up by a visiting midwife.

Table 15: % of women >12 years of age, pregnant, OG and LG.

	OG, 1995–1999	LG, 2010–2014
% of women >12 years of age pregnant	7.9	4.8
Youngest	15	17
Oldest	44	42
Mean age	27	28

Cervical smear screening

All sexually active women of the appropriate age were offered cervical smear screening. The test was voluntary. In all cases, whether the test was done or not, subsequent healthcare providers were alerted, and the women were put on the national register, unless they opted out.

Records were available for the OG and LG. No screening was done for the HG.

Table 16: Results of cervical smear screening OG and LG.

	OG, 1995–1999	LG, 2010–2014
Number tested	437	739
% abnormal overall	6.6	12.0
ASCUS, % of abnormalities	----	59.8
LSIL, % of abnormalities	----	34.8
HSIL, % of abnormalities	----	5.4

Psychological health

Psychosocial trauma is experienced by most refugees. For some it is what affects them most and is the priority for their care.

The need for a specialised psychological service for refugees was raised by the doctors at the medical clinic at MRRC from its opening in 1979, but such a specialised service, Refugees as Survivors New Zealand (RAS), did not open until 1995.

Paradoxically, this has meant that data about the psychological diagnoses for the refugees is not available from the medical-clinic records. This is because RAS is an autonomous organisation and is responsible for the ongoing psychological care of the refugees, independent of the medical clinic. It had close relations with the medical clinic and fed clinical information back to the clinic, but diagnostic categories were not always entered into the medical clinic's PMS. Referrals to RAS were the single largest referral to secondary services (see Table 19), but other organisations could refer refugees to RAS, and the refugees could refer themselves. For example, in 2015 RAS reported that approximately 50% of the intake

for the year were seen by RAS at MRRC. Ninety percent of those referred received psychological or counselling support and 10% of referrals were seen by the RASNZ psychiatrist.[8]

As part of the clinical assessment, a simple assessment of mental health was made by the clinic of the LG to assist in deciding whether to refer someone to RAS. This simple assessment was also part of the screening process for the OG. A previous study related to that OG found that about 20% of refugees had been subjected to significant mistreatment, 14% had reported some form of significant psychological symptoms and 7% were diagnosed with post-traumatic stress disorder.[6]

For the HG, the written records refer to psychological illness and some referrals made to psychological services, but no consistent data is available.

There is published information available about the mental health of refugees.[9]

Chronic illness and its effect upon service delivery

The effect of chronic illness will be explored under the three areas:

1. prevalence of certain chronic illnesses, where comparison can be made
2. prescribing patterns
3. intervention patterns of primary care doctors.

Prevalence of chronic diseases

Table 17: NCD, 1980–2014.

Chronic disease	HG, 1979–1991 N=8,195	OG, 1995–1999 N=2,995	LG, 2010–2014 N=3,530
Diabetes	12 (all found on arrival)	24 (eight diagnosed after arrival)	91 (33 diagnosed after arrival)
Hypertension*	1	74	244

*Elevated blood pressure found on routine examination, either treated or noted for follow-up, or those known to have hypertension before arrival.

Two typical and important chronic diseases are diabetes and hypertension, which will be used as exemplars. Because the numbers of the OG and LG are similar (2,995 vs 3,530), absolute numbers will be given to show the impact. HG figures are included and will be commented on in the conclusion.

While it could be argued that the diagnosis of diabetes is skewed because routine testing by HbA1c was done in the LG, this is not true for the diagnosis of hypertension.

Prescribing patterns

The change in the pattern of disease has obviously led to changes in prescribing patterns. For the HG, no data is available. For the OG, some data can be compared with the LG.

For the LG, 9,878 items were prescribed for 2,937 refugees, giving an average of 3.36 items per refugee.

Figure 5 shows the distribution of the number of items per person. The vertical axis is the number of refugees, and the horizontal axis is the number of items (ie, 830 refugees received one item, 630 two items and so on).

Table 18: Comparison of some medications prescribed, between OG and LG, absolute numbers.

	OG, 1995–1999, 2,992 people	LG, 2010–2014, 3,050 people
Anti-hypertensive agents	41	286
Hypoglycaemic agents	30	165
Oral bacterial antibiotics	812	804
Special antihelmintics*	255	116
Iron preparations	674	380
Vitamin D	0	1290

*Ivermectin, Praziquantel, Yomesan. The commonest antihelminitic, Mebendazole, was dispensed in bulk in the OG, and while noted in each person's record, it is not easily captured.

Figure 5: Prescribing patterns, LG, 2010–2014.

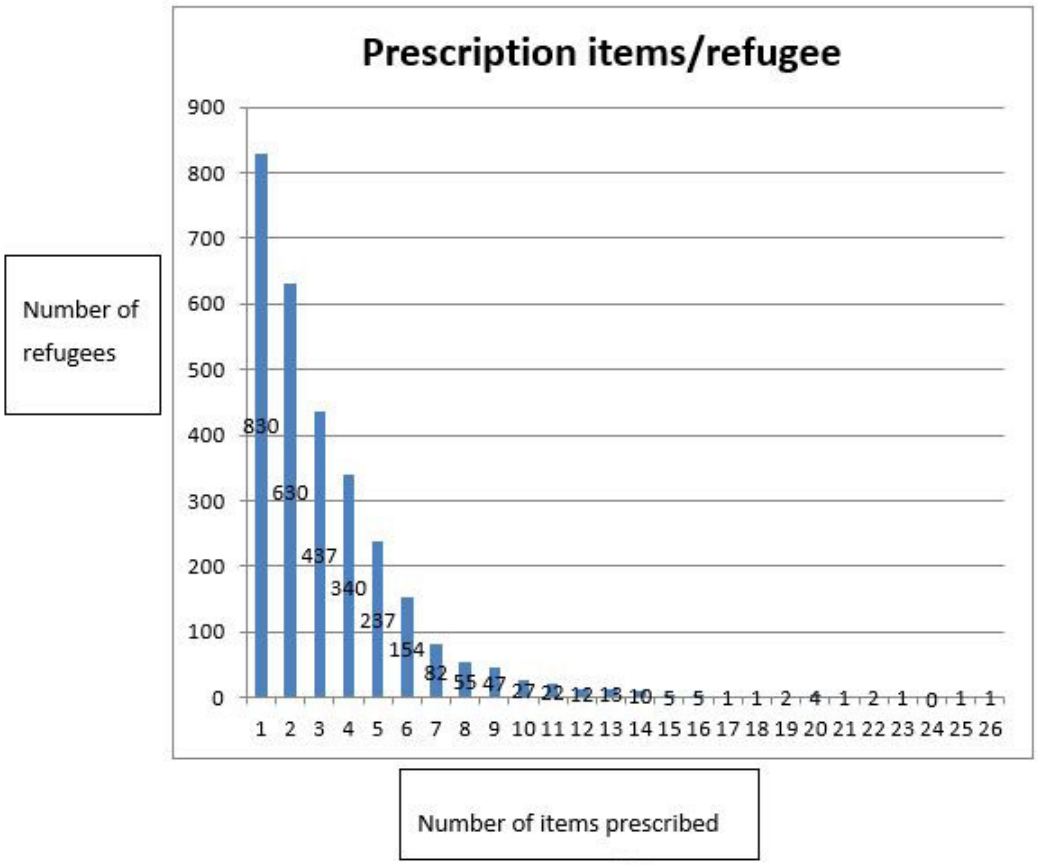
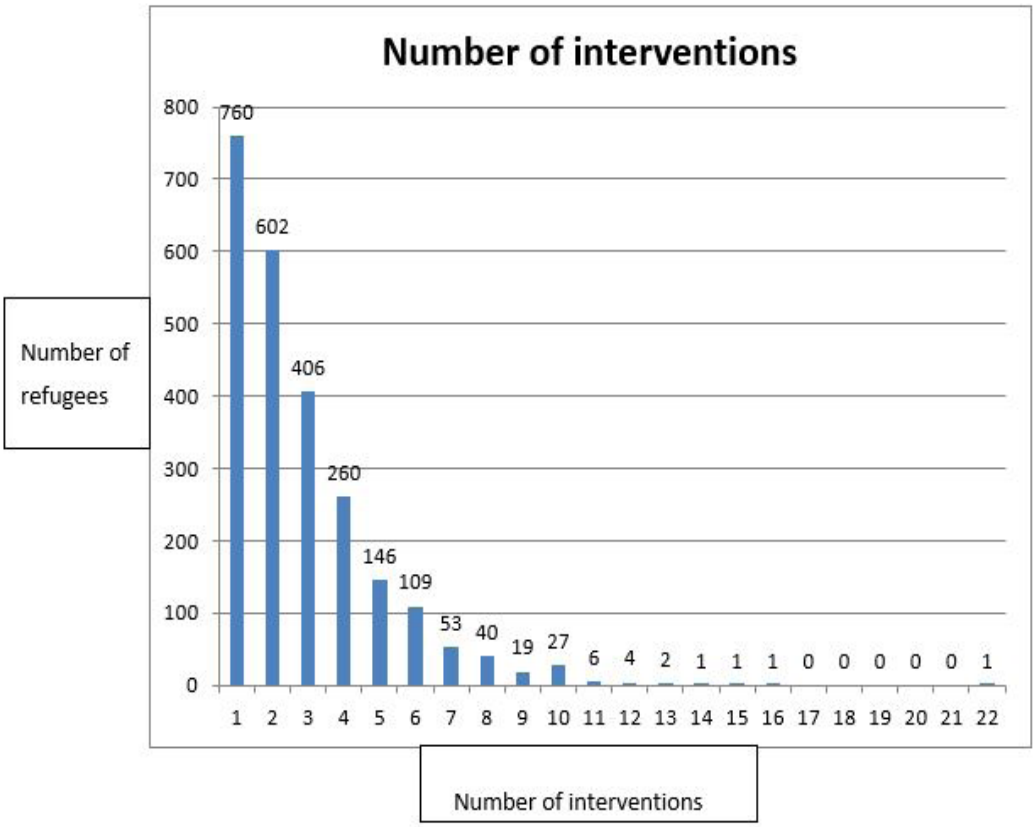


Figure 6: Interventions per refugee, LG.



Interventions by primary care doctors

As well as a screening service, MRRC provided a separate primary care service provided by primary care doctors from 2006. A screening clinician might provide some minor primary care (eg, prescribing for iron deficiency), but ongoing or more complex matters would be followed up by a primary care doctor at the clinic.

Data for HG and OG was not available. For LG, each primary care doctor recorded any intervention for the refugee on their appointment timetable in the patient management system. This may have been an actual face-to-face consultation, or a phone call to a specialist, or prescribing, and so on. For the purpose of this analysis, each entry is called an 'intervention'.

The appointment books of the primary care doctors were analysed. In all, 2,438 refugees received 6,945 interventions, an average of 2.85 interventions per refugee recorded. Given that the group analysed was 3,530 in number, this means that 70% of refugees received some form of intervention from the primary care doctors, as well as receiving routine screening.

Figure 6 shows the interventions by numbers, similar to the chart for medicines above (ie, 760 refugees received one intervention and so on).

Secondary services referrals

In many ways, comparisons between the original and later groups are difficult, as the populations are different and some ways of working were very different between the two times.

However, the figures give a broad-brush picture. The data from the original group has been re-worked to enable comparisons to be made, and to correct an error, where the referral number for paediatrics was ascribed to general medicine.

Conclusions and discussion

In November 1979, not long after MRRC had opened, the medical officer in his annual report wrote, "The refugees in our first few intakes were…infested with external and internal parasites and bacteria to an alarming degree…Exempting (sic) the normal run of coughs, colds and other minor ailments, the refugees…have been singularly free from any illnesses requiring specific treatment…."

In the 40 years since that was written, there has been a major change in the health profile of refugees resettling in New Zealand, especially in the last few years. This is a global phenomenon that has had and will have implications for staffing and the management of medical issues in resettling refugees.

Refugees are no longer "infested" with internal parasites, though there is still a significant number with gut parasites, especially those from refugee camps (see

Table 19: Referral to secondary services, original group and later group.

Service referred to	Number referred (% of referrals)—OG, 1995–1999	Number referred (% of referrals)—LG, 2010–2014
Infectious diseases	480 (19.4)	377 (11.6)
Imaging	261 (10.5)	155 (4.8)
Mental health	163 (6.6)	865 (26.7)
Respiratory medicine	146 (5.9)	103 (3.2)
ENT	139 (5.6)	182 (5.6)
Ophthalmology	129 (5.2)	129 (4.0)
Cardiology	124 (5.0)	139 (4.3)
Orthopaedics	117 (4.7)	124 (3.8)
Sexual health	114 (4.6)	74 (2.3)
General surgery	96 (3.8)	140 (4.3)
General medicine	19 (0.8)	20 (0.6)
Paediatric medicine	70 (2.8)	98 (3.0)
Gastroenterology	54 (2.2)	45 (1.4)
Endocrinology	42 (1.7)	21 ((0.6)
Urology	47 (1.9)	47 (1.5)
Obstetrics	38 (1.5)	2 (0.1)
Gynaecology	36 (1.5)	90 (2.8)
Diabetic	26 (1.1)	11 (0.3)*
Other	375 (15.1)	615 (19.0)
Total	2,476	3,237

Table 20: Quick comparison of certain diseases, 1980–2014.

Infectious disease	HG, 1979–1991 (n=8,195)	OG, 1995–1999 (n =2,992)	LG, 2010–2014 (n=3,530)
TB disease	4%	2%	0.2%
HIV	----	2.0%	0.45%
Schistosomiasis	-----	21.9%	3.2%
Gut parasites	>>30% (up to 45% some groups)	31%	14.9%
HBV carriage	9.6%	4.7%	2.1%

Micronutrient	OG, 1995–1999	LG, 2010–2014
Iron	22.3%	10.4%
B12	5.4% of those tested	17.4% of those tested
Folate	33% of those tested	0% of those tested
Vitamin D	Not tested	39.8%

Chronic disease	HG, 1979–1991 number	OG, 1995–1999 number	LG, 2010–2014 number
Diabetes	12	24 (8 new)	91 (33 new)
Hypertension	1	74	244

Table 21: % of refugee population affected by diabetes.

	HG, 1980–1991	OG, 1995–1999	LG, 2010–2014	2019
% affected	0.1	0.8	2.6	2.7

ISSN 1175-8716

the section on Burmese refugees above). Refugees now have significant rates of non-communicable diseases (NCD), of which hypertension and diabetes are exemplars explored in this paper (Table 20). The latest data from the calendar year 2019 show that this trend is stable (Table 21). There are of course other NCD, such as coronary artery disease and cerebrovascular accidents, but their analysis is more complex and does not add to the main message. Note on cancer: cancer is not a common disease found in arriving refugees, and their short stay of only six weeks makes diagnosis during their stay unlikely, so cancer in refugees is beyond the scope of this paper.

Non-communicable diseases usually require greater management issues than parasites. Putting it simply, the usual geohelminths such as hookworm can be treated with a single course of a cheap antiparasitic. They do not self-replicate internally, and have a limited life span, so continuation of infection requires periodic re-infection. This being so, in a country with good water and sewage, even if treatment is not successful, the infection will die out of its own accord.

By contrast, an NCD such as diabetes requires a lifetime of commitment by patient and therapist. Figure 6 shows the number of interventions per refugee needed by a primary care doctor in addition to routine screening, and it confirms that a high proportion of refugees need additional interventions and those with complex problems require a large numbers of interventions.

The NCD in the historical group, 1979–1991, were extraordinarily low. Was this because the medical officers failed to detect or record them? In their annual reports, they were meticulous about recording demography, notifiable and non-notifiable illnesses and other general medical problems. In preparation for another publication,[2] the author had access to the early paper records and can confirm that the medical officers completed the then-standard NZIS medical immigration form, which of course included measurement of blood pressure and the usual health screening questions.

The burden of NCD in refugees in modern times has been well recognised in New Zealand and elsewhere.[10,11] It has been pointed out that the focus of refugee health has been on infectious diseases,[12] and that addressing NCD in refugees in a timely manner is ultimately less expensive than deferring or trying to restrict treatment for them.[13]

Deficiency diseases have tended to decrease, as seen in iron deficiency, but still need follow-up—particularly vitamin D and B12 deficiency in some groups (see Table 9 and Table 10). These deficiencies in refugees are well recognised.[14–16] The absence of folic acid deficiency in the LG compared with the OG is difficult to explain and there seems to be no explanation in the literature.

Perhaps the most successful reduction is that of tuberculosis. In the historical group, the overall prevalence was 4%, which represents a point prevalence of 4,000/100,000. The medical officers reported prevalence of up to 12% in some exceptional intakes. In the original group, the prevalence had fallen to 2%, which is still 2,000/100,000. This fall must represent improved health in the refugees overseas, and in the later group, the prevalence had fallen to 0.18%. By this time refugees were being x-rayed and treated overseas for tuberculosis. This is a point prevalence of 18/100,000. The average annual incidence of tuberculosis in New Zealand was reported as 6/100,000 in 2016. The highest rates were found in the Asian ethnic group (32.7/100,000), and in the Middle Eastern, Latin American and African (MELAA) it was 17.2/100,000, which is comparable to that found in the refugees.[17]

Another success is the reduction of intestinal parasites, from rates reported as greater than 45% by the medical officers in some intakes in the historical group, to 30% in the original group and 17.4% in the later group. The section considering Burmese refugees shows that some of this reduction may be due to accommodation outside refugee camps. An unknown number of refugees have also been treated for parasites before departure, which can be very effective in reducing the burden of parasites in re-settling refugees.18

Why has there been such a change in the origin of the refugees, and what effect has it had?

The change is due to (1) a changing world situation and (2) political decisions in New Zealand.

The variation in origin of the refugees resettling in New Zealand is described in certain publications[22] and is a history of the conflicts of the world, writ small. Many of the refugees in the historical group came from Vietnam, an area in which conflict seemed to be without end at the time, but which is now a desirable tourist destination.

A political decision was made in New Zealand to restrict refugees from Africa and the Middle East,[20] but this was relaxed in 2015, to allow an emergency intake of refugees from Syria, and abolished in 2019.[21]

The change in the origin of refugees had an effect on the prevalence of such conditions as HIV, schistosomiasis, strongyloidiasis, hepatitis C and vitamin B12 deficiency.

Another variation which is not revealed by this study, but with which any worker with refugees will be familiar, is the variation in health literacy and previous access to care in a single intake. On the one hand, there may be refugees with very limited health literacy, for whom the explanation of hereditary haemolytic disorder is difficult; and on the other hand, a refugee may present their CD of their whole-body CT scan and request that it be repeated.

Also, on the one hand, there may be a refugee from a refugee camp with one or two small plastic packets of individual medicines, enough for a week or so, and on the other, a refugee with a large plastic bag full of medicines in their original containers, often bought over the counter and not prescribed.

The higher prevalence of abnormal cervical smears in the later group is probably multifactorial. For example, improved screening methods, a change in population and so on. Its analysis is beyond the scope of this paper. One study found the percentage of abnormal smears in refugee women varied from a low of 3% to a high of 10%, depending on ethnicity.[23]

Referrals to secondary services (Table 24) show many similarities between the original group and later group. The high rates of referral to secondary services should not be taken to show that refugees are necessarily an unhealthy group, but rather that their healthcare has been 'frozen', often for many years, and the number of referrals can be seen as a catchup phenomenon.

For most services, the numbers are much the same between the original and later groups.

Notable differences exist between:

1. infectious diseases: greater in the original group
2. imaging: greater in the original group
3. mental health: less in the original group
4. sexual health: greater in the original group
5. gynaecology: less in the original group
6. diabetes clinic: less in the original group.

(1) Infectious diseases can be explained by the different populations. Most striking are referrals to paediatric infectious disease services. The majority in both groups are to the paediatric TB service as the result of Mantoux testing. In the original group, almost six times as many children were referred for non-TB related infectious diseases, the majority of these being for active schistosomiasis, which does not exist in the populations of the later group.

(3) Mental health can be explained by the increased availability and expertise of the counselling service, Refugees as Survivors New Zealand. In the later group, all referrals were to this service and none to outside psychological services. In the original group, 20 referrals were to outside psychological services and the remainder to Refugees as Survivor, which started operating in 1995.

(5) Gynaecology: The difference is mostly related to the increased rate of abnormal cervical smears in the later group, with referral for colposcopy. Why there is an increased rate of cervical smears in the later group is not clear, but it does seem to be a gradual trend over the years.

(6) Diabetic clinic can be explained by the completely different structure of the clinical team and modern management of diabetes. The clinical team for the original group had no dedicated general practitioners, and diabetes management was the preserve of outpatient clinics; with its increased prevalence, diabetes management is now the stock in trade of general practice services; dedicated general practitioners were appointed to the clinical team for that reason, and the management of other chronic diseases.

This again raises the question of the impact on service provision of the different health profile of modern refugees with their increased rate of NCD; the changes in the staffing at the medical clinic between 1979 and 2014 is instructive in this regard.

When the clinic opened in 1979, and the annual intake was 750 refugees, the clinic was staffed by:

- two part-time doctors, 0.9 full-time equivalent (FTE)
- one full-time nurse, 1.0 FTE
- one full-time clerk/administrator, 1.0 FTE.

Dental services were provided by a dental unit of the territorial army. By 2020, when the Auckland District Health Board relinquished running the clinic and the annual intake was 1,000 refugees, the staffing was:

- two part-time doctors for screening, 1.2 FTE
- three nurses, two screening, all three sharing nursing duties, 2.6 FTE
- three admin staff, 2.5 FTE
- four visiting doctors, providing mostly general practice services and a little screening, 0.8 FTE
- dentist and dental assistant, 0.2 FTE each, from hospital dental department.

At the time it was felt that the general practice service FTE was less than was needed for optimal care.

The impact of the change in health profile is documented in this study by Tables 21 and 22, showing the rates of prescribing and the kinds of medication, and in particular Table 23, which shows the 'interventions' where it should be re-affirmed that this is over a six-week timetable.

The causes for the increase in NCD are probably multiple. This study shows, on the one hand, an encouraging reduction in the use of tobacco, but on the other hand, a general increase in BMI.

The new way of caring for refugees aims to screen them overseas rather than in New Zealand, provide care for any NCD found at the time of screening overseas, continue that care on arrival at MRRC and pass such care seamlessly onto the general practitioners in the receiving towns and cities, some of whom will not have dealt with refugees in the past. The exact configuration of the new medical clinic is not known, but aims to substantially increase general practice care.[5]

This study does have its limitations. In particular, a lack of analysis of mental health issues, which represent a substantial burden for many refugees. The provision of mental health care for resettling refugees would be regarded as being vital.

Other limitations include social/lifestyle issues, such as origin from refugee camp or otherwise, language, education levels, health literacy, drug and alcohol use, gambling, domestic abuse and previous medication uses.

In summary, there has been a major change in the health profile of refugees resettling in New Zealand between 1980 and 2014 and beyond, from a population with high rates of parasitic and bacterial infection and low rates of non-communicable diseases, to one where infection is much less, though not absent, and high rates of non-communicable diseases. This is not unique to New Zealand and will have an impact on the provision of healthcare for refugees, here and elsewhere.

The bottom line is this: health practitioners who are new to caring for resettling refugees might be worried that they might have to deal with unfamiliar and exotic tropical diseases; the truth is that most of their work will be with the familiar non-communicable diseases, in the context of an unfamiliar population group.

Competing interests:
Nil.
Acknowledgements:
The refugees themselves and the staff of the medical clinic, Mangere Refugee Resettlement Centre, for suggestions and support.
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Assessment of a clinical pathway for investigation of haematuria that reduces the need for cystoscopy

Peter J Davidson, Graham McGeoch, Brett Shand

ABSTRACT

AIM: To evaluate prospectively a clinical pathway for investigation of haematuria that involves an initial screening using a urinary biomarker of bladder cancer (Cxbladder Triage™ (CxbT)) in combination with either a renal ultrasound or a computed tomography imaging. Only test-positive patients are referred for specialist assessment and flexible cystoscopy.

METHODS: The clinical outcomes of 884 patients with haematuria who presented to their general practitioner were reviewed. Outcome measurements included the findings of laboratory tests, imaging, cystoscopies, specialist assessment and histology.

RESULTS: Forty-eight transitional cell carcinomas (TCC) and three small cell carcinomas were diagnosed in the study cohort. The clinical pathway missed a solitary, small, low-risk TCC. When combined, imaging and CxbT had a sensitivity of 98.1% and a negative predictive value of 99.9% to detect a bladder cancer. Follow-up for a median of 21 months showed no further new cases of bladder cancer had occurred in the patient cohort. Review of all new bladder cancers diagnosed in the 15 months following the study showed that none had been missed by haematuria assessment using the clinical pathway.

CONCLUSIONS: The combination of CxbT and imaging reliably identifies patients with haematuria who can be managed safely in primary care without the need for a secondary care referral and a flexible cystoscopy.

In an earlier issue of the *New Zealand Medical Journal*, we described the development of a clinical pathway for the investigation of patients with haematuria.[1] The pathway used imaging and a urinary biomarker assay of bladder cancer (Cxbladder Triage™ (CxbT)) to identify patients who required a referral for specialist assessment to exclude the possibility of a bladder malignancy (refer to Appendix). The imaging modality requested depended on the type of haematuria and the age of the patient: renal ultrasound for microhaematuria and patients <40 and >85 years of age with macrohaematuria, and intravenous computed tomography (IVU-CT) for all other cases of macrohaematuria. The pathway did not include urine cytology in the initial laboratory screening tests and used the high negative predictive potential of CxbT combined with appropriate imaging to identify patients who did not require a secondary care appointment and flexible cystoscopy. Patients were only referred for urological assessment and cystoscopy if their CxbT index was positive and/or their imaging showed a bladder or other urinary-tract abnormality. Urine cytology could be requested at this stage at the discretion of the urologist. Patients with persistent microhaematuria, a urine total

albumin:creatinine ratio >70, an eGFR <60 ml/min/1.73m^2 or newly diagnosed hypertension were referred to a nephrologist for evaluation. The pathway was a departure from international clinical guidelines that recommend cystoscopy as the gold standard for diagnosis of bladder cancer.[2,3] A previous retrospective analysis of a cohort of patients with haematuria showed that the clinical pathway would have detected all invasive urothelial carcinomas and that approximately one-third of patients could have safely avoided the need for an invasive flexible cystoscopy with negligible risk of a bladder cancer being missed.[1]

Since February 2018, patients with haematuria in the Canterbury region have been investigated under the guidelines of the new clinical pathway. To inform general practices of these changes, the pathway was made available on the Canterbury Community HealthPathways website.[4] A clinical review of the effectiveness and safety of the new pathway was carried out prospectively during the first year of its introduction. This paper reports the findings of this review.

Patients and methods

The Health and Disability Ethics Committee, Ministry of Health, New Zealand, advised that the clinical review did not require ethical approval, as it constituted monitoring and improvement of usual patient care carried out by the Canterbury District Health Board (CDHB).

Patients

The clinical records of 889 patients who had a CxbT test for investigation of haematuria between 1 February 2018 and 31 January 2019 were reviewed. Five patients were excluded from the analysis: one with a bleed from a catheter, and four because of inadequate information on their medical records, two of whom had declined their hospital appointment.

Within the CDHB region there is a population of 567,870 (2018/19 projection). A single group of urologists provide urological services to all patients within the CDHB region, in both the public and private sectors. Thus, the patients described in this paper represent a nearly complete community capture.

Data collection

Data was collected on the remaining 884 patients in a non-blinded manner and included: demographic characteristics, type of haematuria, presence of risk factors for bladder cancer (smoking, previous history of bladder cancer and radiation therapy of the pelvis) and the findings of laboratory tests, imaging, cystoscopies, specialist assessment and histology. A cystoscopy and histology were required for diagnosis of bladder cancer. Macrohaematuria was defined as blood clearly visible in a midstream urine sample, and microhaematuria was defined as >20x10^{6}L red blood cells in two of three samples collected seven days apart.

A follow-up review (median: 21 months; range: 16–27 months) was then carried out of all the patients who had not been diagnosed with bladder cancer to ensure that no malignancy had been missed. The patients' electronic records of inpatient admissions, outpatient clinics and histology results, and a search of the New Zealand Cancer Registry, were included in this review.

Finally, all the new diagnoses of bladder cancer in the CDHB region for a subsequent 15-month period from 1 February 2019 to 30 April 2020 were identified from surgical and pathology records. The patient records were reviewed to see whether any of these patients had previously been investigated by the new pathway for haematuria and had a bladder cancer missed.

Statistical analysis

The flow of patients through the three arms of the clinical pathway, grouped according to whether they had microhaematuria, macrohaematuria or were aged <40yr or >85, was examined graphically. The diagnostic accuracy of the various investigations in the pathway to detect bladder cancer was determined by calculation of accuracy, sensitivity, specificity and negative predictive value (NPV). The evaluation of CxbT used a segregation index cut-off value of <4.0 to indicate specialist assessment was required.[5]

Statistical power analysis showed that at least 600 patients would allow a precise estimate of the diagnostic accuracy of the indices, assuming a target sensitivity of 90% and a precision of sensitivity measurement

of 10%, and given the prevalence of bladder cancer observed in the review patient cohort of 5.8%.

Results

The clinical and demographic characteristics of the 884 patients are summarised in Table 1. All the patients lived in the funded area of the Canterbury DHB and were predominantly middle-aged or older, with 66% being male. Two-thirds of the patients presented with macrohaematuria. Approximately 43% of the patients were classified as having an increased risk of developing bladder cancer because of their smoking history (41%), a previous history of bladder cancer (0.001%) or having previously received radiation therapy of the pelvis (2%).

Table 1: Demographic and clinical characteristics of the 884 patients.

Parameter	
Male	584 (66%)
Female	300 (34%)
Age (years)	
Mean (±SD)	63.1 (16.2)
Median (range)	65 (14–97)
Type of haematuria	
Macrohaematuria	566 (64%)
Microhaematuria	318 (36%)
Smoking status	
Current smoker	71 (8%)
Previous smoker	293 (33%)
Never smoked	520 (59%)
Ethnicity	
NZ European	719 (81%)
Māori	23 (3%)
Pacific Islander	7 (1%)
Asian	43 (5%)
MELAA[a]	11 (1%)
Not stated	81 (9%)
Previous clinical history	
Bladder cancer	1 (0.001%)
Radiation therapy of pelvis[b]	21 (2%)

[a]Middle Eastern/Latin American/African.
[b]Prostate n=19, rectum n=2.

The flow of the patients through the three arms of the clinical pathway and the diagnoses for the cause of haematuria are shown in Figure 1. One hundred and seventeen patients were still referred to a specialist urologist despite their CxbT being normal and their imaging indicating no bladder cancer was present. Seventy patients were diagnosed with another urological condition, while in 47 cases the cause of haematuria could not be identified.

The clinical pathway detected all but one case of bladder cancer, with 48 patients (macrohaematuria: n=44; microhaematuria: n=4) diagnosed with a histologically confirmed (n=46), or clinically possible (n=2), transitional cell carcinoma (TCC) and three with a small cell carcinoma. The stage and grade of the 48 TCCs were low grade (pTa n=20 and CIS n=1), and high grade (pTa n=14, pT1 n=8 and pT2 n=3). Two further malignancies were designated cT2-3, as neither had a cystoscopy or histology (one was frail and 91 years old, and the other had widespread metastatic bowel cancer). The 51 cases of bladder cancer represented a prevalence rate of 5.77%.

Three hundred and forty-eight (39%) patients with haematuria and normal CxbT and radiology were managed in primary care alone. Two hundred and eighty-nine patients had a sample collected for urine cytology, with 64% of these requests made by a urologist at the time of the hospital clinic visit.

The ability of CxbT, imaging and the combination of CxbT and imaging to detect bladder cancer and the diagnostic accuracy of these investigations in the study cohort are summarised in Table 2. Five cancers were missed by CxbT. One of these was a superficial, high-grade lesion (pTaHG, 1cm in size). A second was considered from cytology to be high grade, but clinically it was thought to be most likely of bowel origin in a patient with extensive metastatic bowel cancer. No cystoscopy was performed, nor was a histology taken, in this patient. The other three cancers were low-grade pTa lesions. Although CxbT had relatively high

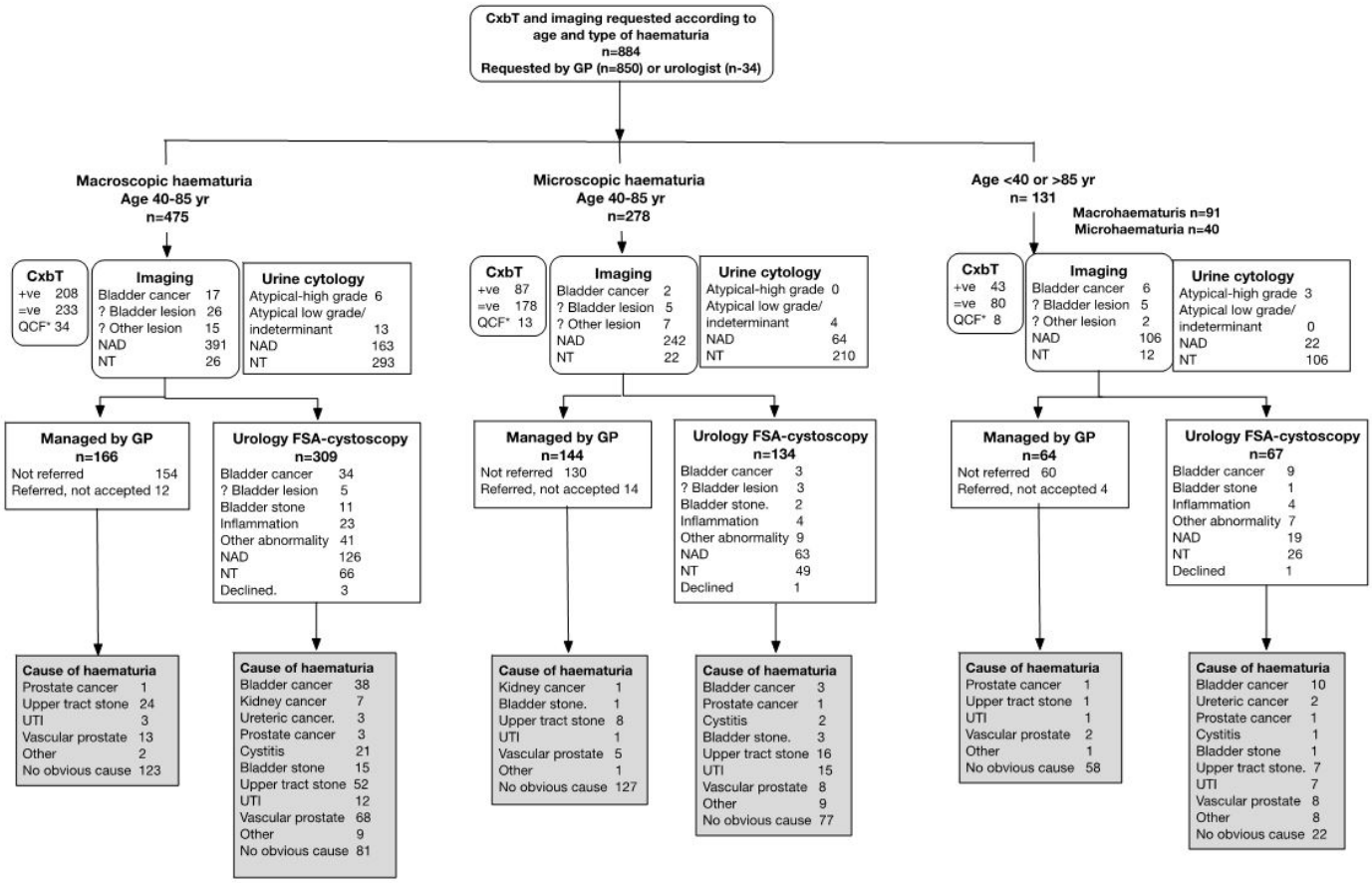
sensitivity to detect a bladder cancer and a high NPV of 98.9% to exclude the possibly of a lesion, the test had a low specificity with 39% of the tests returning a false-positive result. This level of diagnostic accuracy for CxbT is similar to that reported previously.[6–8] The mean of the CxbT segregation index was 3.97 (SD=0.92; range: 1.97–10.0), with 466 patients (53%) having a score less than the triage cut-off of 4.0. Approximately 10% of the patients (85 of 884) required a repeat CxbT assay because of quality control failures, mainly caused by interference of inflammatory products or a large number of white blood cells. Of these 85 patients, the repeat test provided a result in 28, and the second test did not meet quality standards in 15, while a repeat test was not requested in 42.

Imaging failed to detect 13 lesions (ultrasound: n=7; CT-IVU: n=5; ultrasound + CT-IVU: n=1), with nine of these lesions classified as low-grade lesions (pTa) and four as high-grade lesions (pT1: n=3; assessed by cytology: n=1). When combined, the pathway of CxbT and imaging had a sensitivity of 98.1% and an NPV of 99.9% and failed to detect a solitary, small, low-grade pTa bladder cancer.

Flexible cystoscopy detected bladder cancer in 48 patients, while the remaining three cancers were observed subsequently by rigid cystoscopy carried out at the time of transurethral resection of a bladder tumour (TURBT). One patient with widespread metastatic disease from bowel cancer did not have a cystoscopy.

Table 3 summarises the causes of haematuria and the percentage of each cause detected by the clinical pathway. Renal stones, vascular prostate and inflammatory conditions were the most common causes of haematuria. Inflammatory renal disease was the cause of microhaematuria in six cases, all of whom were referred to a nephrologist for management.[3] In approx-

Figure 1: Flow of the 884 patients through the three arms of the haematuria clinical pathway.



QCF: quality control failure; FSA: first specialist assessment; NAD: no abnormality detected; NT: not tested.

imately one-third of patients, the cause of haematuria was not determined.

Follow-up review of medical records of the 833 patients who had not been diagnosed with bladder cancer showed that one patient had been treated for a small papillary lesion on the bladder neck six months following a nephroureterectomy for a high-grade TCC of the kidney. No other patient had been admitted to hospital for management of a new bladder malignancy. A search of the New Zealand Cancer Registry confirmed this finding.

A review of all the subsequent bladder cancers diagnosed in the following 15 months identified 111 patients with a first diagnosis of bladder cancer, confirmed histologically. Seventy-one percent were identified through GP workup of haematuria, 23% incidentally through radiology, 2% incidentally through cystoscopy and 4% through secondary care investigation of haematuria. Of those coming through the GP workup of haematuria, 42 (53%) had a successful CxbT test and eight had a "quality control" failure of the test. Two

Table 2: Evaluation of the diagnostic accuracy of CxbT, imaging and cystoscopy to detect bladder cancer. The diagnostic parameters are expressed as percentages (95% confidence interval).

	Bladder cancer diagnosis (n=51)	**Diagnostic parameters**			
		Accuracy	**Sensitivity**	**Specificity**	**Negative predictive value**
Cxbladder triage		60.7% (57.3–64.1%)	89.4% (76.9–96.5%)	59.0% (55.4–62.4%)	98.9% (97.5–99.5%)
Bladder cancer indicated	41				
Bladder cancer not indicated	5				
Quality control failure	5				
Ultrasound		96.3% (94.0–97%)	65.2% (42.7–83.6%)	98.2% (96.3–99.3%)	97.9% (96.3–98.8%)
Bladder cancer detected	12				
Possible bladder cancer	3				
No bladder cancer detected	8				
Not tested	28				
CT-IVU		95.5% (93.4–97.1%)	81.6% (65.7–92.3%)	96.4% (94.4–97.9%)	98.8% (97.8–99.4%)
Bladder cancer detected	19				
Possible bladder cancer	12				
No bladder cancer detected	6				
Not tested	14				
Cxbladder Triage + imaging		98.4% (97.4–99.1%)	98.1% (89.6–99.9%)	98.4% (97.3–99.2%)	99.9% (99.2–99.9%)
Bladder cancer detected	47				
Possible bladder cancer	3				
No bladder cancer detected	1				

Table 3: Causes of haematuria in the study cohort.

	Male n=583		**Female n=301**	
Malignant lesions				
Bladder cancer	40	(6.9%)	11	(3.7%)
Kidney cancer TCC[a]	4	(0.7%)	-	-
Kidney cancer RCC[b]	1	(0.2%)	2	(0.7%)
Ureter cancer	3	(0.5%)	2	(0.7%)
Prostate cancer	5	(0.9%)	-	-
Inflammatory				
Urinary tract infection	15	(2.6%)	19	(6.3%)
Cystitis	19	(3.3%)	5	(1.7%)
Stones				
Upper tract	51	(8.7%)	24	(8.0%)
Bladder	18	(3.0%)	1	(0.3%)
Other causes				
Vascular prostate	81	(13.9%)	-	-
Anticoagulation	11	(1.9%)	1	(0.3%)
Renal disease	5	(0.8%)	-	
Catheter	3	(0.5%)	1	(0.3%)
Post-TURP	2	(0.3%)	-	
Exercise-induced	1	(0.2%)	1	(0.3%)
Urethral stricture	1	(0.2%)	-	
Urethral caruncle	-		1	(0.3%)
Primary amyloidosis	1	(0.2%)	-	
Endometriosis	-	-	1	(0.3%)
No cause identified	116	(19.9%)	64	(21.3%)
Not referred	179	(30.7%)	156	(51.9%)
Referred, not accepted	21	(3.6%)	8	(2.6%)
Referred, accepted, but patient declined	6	(1.0%)	4	(1.3%)

[a]Transitional cell carcinoma. [b]Renal cell carcinoma.

patients had a CxbT test that was <4 and a suspicious radiology. Both were found to have low-grade pTa malignancies. Only one patient had a bladder cancer missed in an earlier workup of haematuria. This patient had an ultrasound, but no CxbT, and a flexible cystoscopy that showed no abnormality. The cystoscopy was repeated three months later due to continued haematuria and the cancer was found.

Discussion

Successful treatment of invasive bladder cancer relies on early detection of the malignancy. Flexible cystoscopy supported by the findings of imaging and urine cytology have been the "gold standard" diagnostic procedures for investigation of patients with haematuria and a possible bladder cancer.[2,3] However, the invasive nature of cystoscopy and its relatively poor cost performance,[9] coupled with the low diagnostic accuracy of cytology for low-grade bladder cancers, emphasises the need for an improved clinical approach for investigation of haematuria.[10] To this end, over the last 10 years a large number of urinary biomarkers have been developed and assessed for the diagnosis and monitoring of bladder cancer.[11–14] The range and type of these biomarkers reflects the complex aetiology and development of bladder cancer, with assay profiles based on either the levels or presence of specific microRNAs,[15,16] proteins,[17] metabolites[18] or extracellular vesicals.[12] Despite extensive evaluation, none of these molecular biomarkers are included in clinical guidelines or recommended for use in daily clinical practice.[16,19–22]

The clinical pathway for investigation of haematuria evaluated in this paper was developed against this background and included the addition of CxbT in the initial laboratory investigations. This assay measures the level of five miRNAs to calculate a segregation index for stratification of patients.[6,7] miRNAs are promising candidates for the diagnosis of bladder cancer as they are involved in several processes associated with the development of these malignancies, including proliferation, invasion, migration and apoptosis.[23] Evaluation of the pathway during its development showed that CxbT improved the risk stratification of patients with haematuria and identified those in whom it was safe not to undertake cystoscopy.[1] The prospective review of the pathway and follow-up of the patients described in this paper confirmed that the clinical pathway was an effective clinical algorithm for investigation of haematuria and that it reliably identified patients with bladder cancer. Interestingly, the 5.8% prevalence of bladder cancer in the current review was lower than that observed in the patient cohort used for development of the clinical pathway (9.2%).[1] The reasons for this difference may be natural variation, an increased awareness of haematuria due to the communication around the change to the HealthPathway, or as a consequence of the relatively small size of the patient cohorts. We are currently carrying out reviews of the cost effectiveness, equity of access to haematuria assessment and compliance with the clinical pathway.

The risk of avoiding a cystoscopy is the possibility of missing a significant bladder cancer. Our results showed a false-negative CxbT result was obtained in five of the 52 patients diagnosed with bladder cancer, with one of these being a superficial (pTa) high-grade lesion, one likely to be a metastasis from a bowel cancer,not a transitional cell malignancy, and with the remaining three being low-grade pTa malignancies. Imaging detected the bladder cancer in four of these patients, while in the remaining patient a small, low-risk cancer (pTaLG) was detected three months later by cystoscopy following continued haematuria. These findings emphasise that an accurate risk stratification of patients with haematuria cannot be achieved using a urinary biomarker alone, and that the use of these tests in clinical pathways must be supported by appropriate imaging.

The adoption of the haematuria assessment pathway allowed 39% of patients to be fully cared for in primary practice, thus avoiding referral to secondary care. While this benefits the patient and the system, it is important to be certain that the clinical risk to the patient is not increased. Of the 884 haematuria patients undertaking the pathway (CxbT and radiology), only a single low-risk (low-grade pTa) cancer was missed. The NPV of 99.9% is consistent

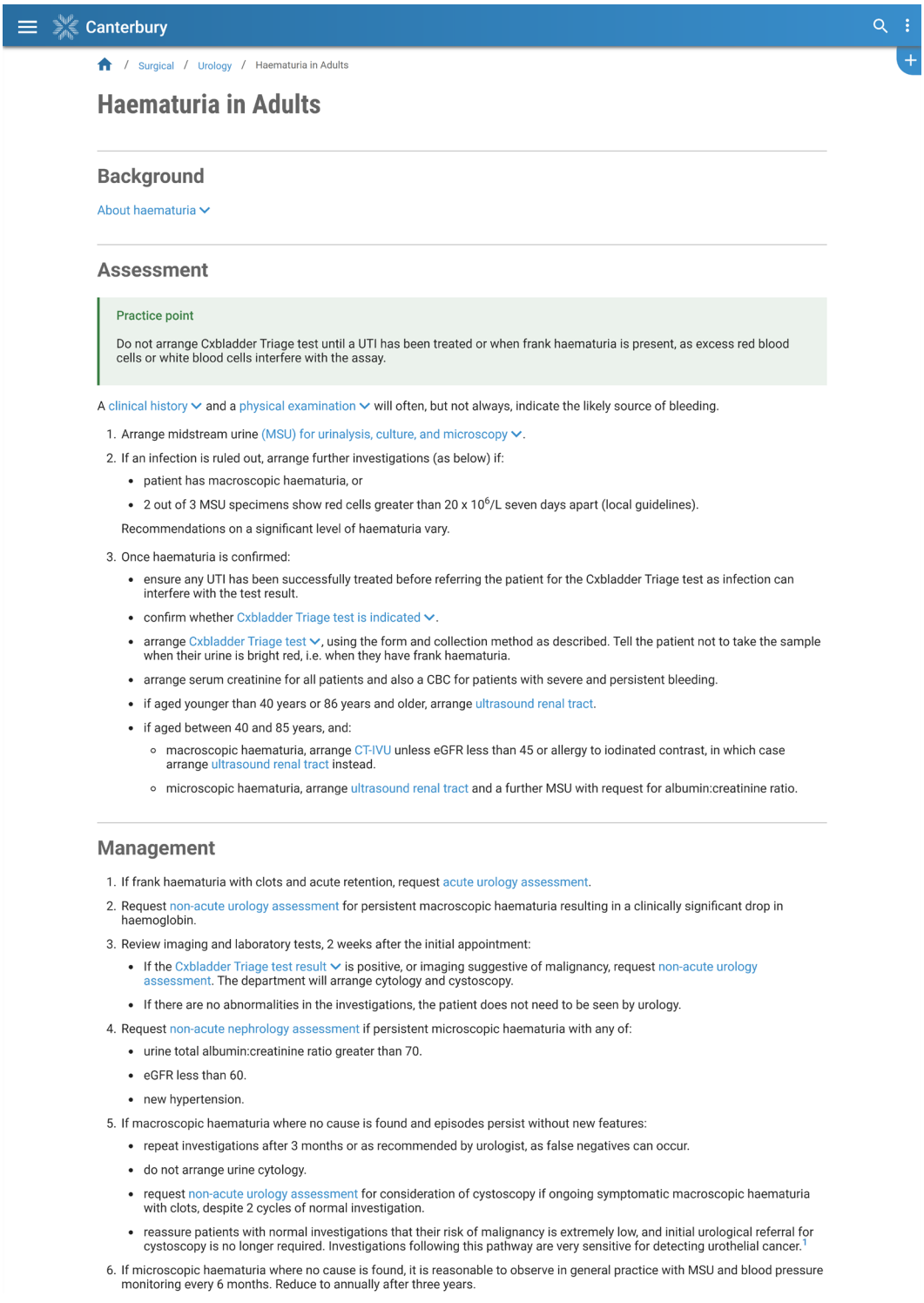
with previously published results.[1,5] The follow-up review of the clinical records of the 832 patients who did not have a bladder cancer detected by the new pathway identified a single similar low-risk cancer in a follow-up cystoscopy of a patient in whom the pathway had previously diagnosed an upper tract transitional cell malignancy. In addition, a review of all the newly diagnosed bladder cancers in the CDHB region over the following 15 months identified only one bladder cancer missed during a previous haematuria investigation. The haematuria investigation in this case had not followed the "pathway", and had not had a CxbT, but did have a cystoscopy that did not identify the cancer. Therefore, it is concluded that patients with haematuria and a negative "pathway" workup (CxbT and radiology) have a negligible clinical risk of missing a significant bladder cancer.

Finally, the argument could be made that there are other significant causes of haematuria. Of these, upper tract tumours and urinary tract stones are the most significant. These are readily identified on radiology as a part of the haematuria pathway. When evaluating the findings of the follow-up review of approximately 21 months, it is important to take into account that the development of non-invasive papillary carcinomas is relatively slow[24] and may vary according to tumour grade and stage.[24,25] It is therefore possible that a lesion may not have been identified within this time period.

In conclusion, we are not aware of any other study that has prospectively assessed the inclusion of a urinary biomarker to improve the risk stratification of patients with haematuria. The findings of our study add to the increasing evidence that biomarkers have a place in the assessment of haematuria, but that the results of these assays need to be supported by imaging of the bladder. Our study demonstrates that, when they are provided with CxbT results in combination with imaging, clinicians are able to reliably identify patients who can be assessed in primary care without the need for a secondary care referral and a flexible cystoscopy. We consider that in a well-integrated health system the management of these test-negative patients can be safely undertaken by general practitioners with support and oversight provided by a specialist urologist.

Appendix

Appendix Figure 1: Extract from Canterbury Community HealthPathways used by general practice for locally agreed guidance on over 800 conditions and situations. Each piece of underlined blue text represents a dropdown providing further clinical and process information.



Canterbury

/ Surgical / Urology / Haematuria in Adults

Haematuria in Adults

Background

About haematuria

Assessment

Practice point

Do not arrange Cxbladder Triage test until a UTI has been treated or when frank haematuria is present, as excess red blood cells or white blood cells interfere with the assay.

A clinical history and a physical examination will often, but not always, indicate the likely source of bleeding.

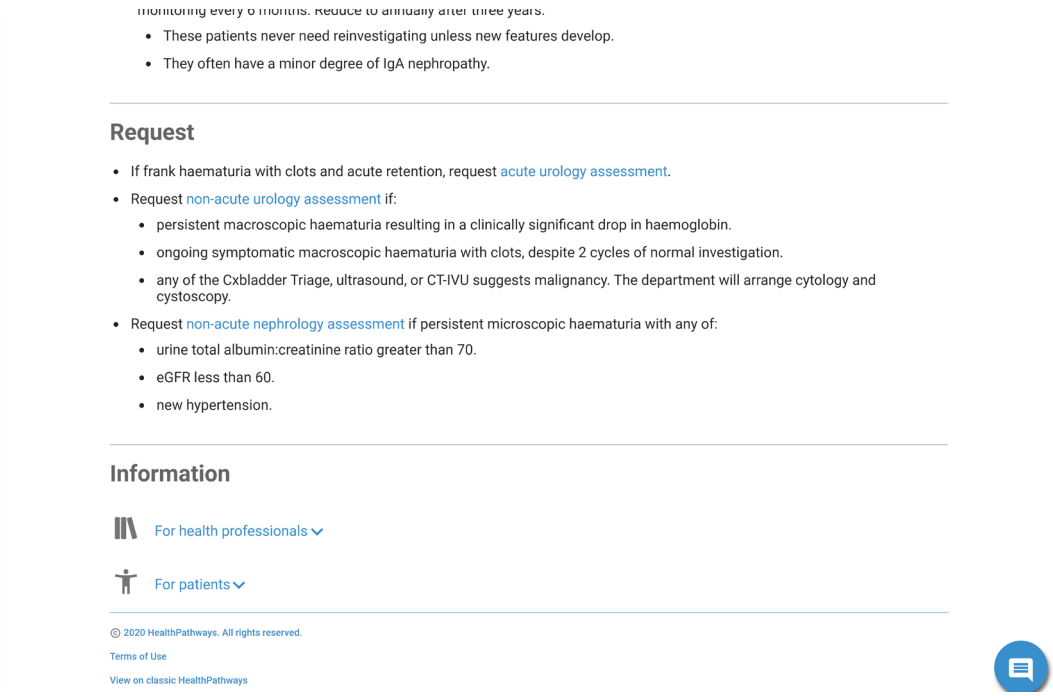
1. Arrange midstream urine (MSU) for urinalysis, culture, and microscopy.
2. If an infection is ruled out, arrange further investigations (as below) if:
   - patient has macroscopic haematuria, or
   - 2 out of 3 MSU specimens show red cells greater than 20 x 10^6/L seven days apart (local guidelines).

   Recommendations on a significant level of haematuria vary.
3. Once haematuria is confirmed:
   - ensure any UTI has been successfully treated before referring the patient for the Cxbladder Triage test as infection can interfere with the test result.
   - confirm whether Cxbladder Triage test is indicated.
   - arrange Cxbladder Triage test, using the form and collection method as described. Tell the patient not to take the sample when their urine is bright red, i.e. when they have frank haematuria.
   - arrange serum creatinine for all patients and also a CBC for patients with severe and persistent bleeding.
   - if aged younger than 40 years or 86 years and older, arrange ultrasound renal tract.
   - if aged between 40 and 85 years, and:
     - macroscopic haematuria, arrange CT-IVU unless eGFR less than 45 or allergy to iodinated contrast, in which case arrange ultrasound renal tract instead.
     - microscopic haematuria, arrange ultrasound renal tract and a further MSU with request for albumin:creatinine ratio.

Management

1. If frank haematuria with clots and acute retention, request acute urology assessment.
2. Request non-acute urology assessment for persistent macroscopic haematuria resulting in a clinically significant drop in haemoglobin.
3. Review imaging and laboratory tests, 2 weeks after the initial appointment:
   - If the Cxbladder Triage test result is positive, or imaging suggestive of malignancy, request non-acute urology assessment. The department will arrange cytology and cystoscopy.
   - If there are no abnormalities in the investigations, the patient does not need to be seen by urology.
4. Request non-acute nephrology assessment if persistent microscopic haematuria with any of:
   - urine total albumin:creatinine ratio greater than 70.
   - eGFR less than 60.
   - new hypertension.
5. If macroscopic haematuria where no cause is found and episodes persist without new features:
   - repeat investigations after 3 months or as recommended by urologist, as false negatives can occur.
   - do not arrange urine cytology.
   - request non-acute urology assessment for consideration of cystoscopy if ongoing symptomatic macroscopic haematuria with clots, despite 2 cycles of normal investigation.
   - reassure patients with normal investigations that their risk of malignancy is extremely low, and initial urological referral for cystoscopy is no longer required. Investigations following this pathway are very sensitive for detecting urothelial cancer.[1]
6. If microscopic haematuria where no cause is found, it is reasonable to observe in general practice with MSU and blood pressure monitoring every 6 months. Reduce to annually after three years.

Appendix Figure 1: Extract from Canterbury Community HealthPathways used by general practice for locally agreed guidance on over 800 conditions and situations. Each piece of underlined blue text represents a dropdown providing further clinical and process information (continued).



monitoring every 6 months. Reduce to annually after three years.

- These patients never need reinvestigating unless new features develop.
- They often have a minor degree of IgA nephropathy.

Request

- If frank haematuria with clots and acute retention, request acute urology assessment.
- Request non-acute urology assessment if:
  - persistent macroscopic haematuria resulting in a clinically significant drop in haemoglobin.
  - ongoing symptomatic macroscopic haematuria with clots, despite 2 cycles of normal investigation.
  - any of the Cxbladder Triage, ultrasound, or CT-IVU suggests malignancy. The department will arrange cytology and cystoscopy.
- Request non-acute nephrology assessment if persistent microscopic haematuria with any of:
  - urine total albumin:creatinine ratio greater than 70.
  - eGFR less than 60.
  - new hypertension.

Information

For health professionals

For patients

Terms of Use

View on classic HealthPathways

Competing interests:
Nil.
Acknowledgements:
Review of the clinical pathway for investigation of haematuria was conducted as part of the improvement of usual patient care by the Canterbury DHB who purchased the test kits and paid for analysis by Pacific Edge Ltd, who otherwise played no part in the study. The samples were collected using the usual methods of general practice testing and we would like to acknowledge the general practice teams and patients who diligently collected the samples. The authors acknowledge the assistance of Canterbury Southern Community Laboratories in the collection and administration of the CxbT samples and collation of the assay results. We are also grateful to Mrs Timi Boddington, Information Analyst, Planning and Funding, Canterbury DHB, and to Mrs Barbara Gordon and Mrs Liz Mitchell from the Canterbury Urology Research Trust for carrying out the follow-up reviews of the patients' medical records, and to Ma Yi, Biostatistician, Canterbury DHB for assistance with the statistical analyses.
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www.nzma.org.nz/journal-articles/assessment-of-a-clinical-pathway-for-investigation-of-haematuria-that-reduces-the-need-for-cystoscopy-open-access

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Drug-induced ocular inflammation

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ABSTRACT

AIM: Drug-induced ocular inflammation is rare and may be overlooked as a cause of uveitis. The main objective was to describe the causes of drug-induced ocular inflammation. Secondary objectives included uveitis complications and drug rechallenge reactions.

METHODS: A retrospective chart review at Auckland District Health Board's tertiary uveitis clinic (Auckland, New Zealand) was performed. Participants were identified using the uveitis database, which consists of 2,750 subjects. Fifty eyes of 35 subjects had drug-induced inflammation.

RESULTS: Drug-induced inflammation occurred in 1.3% of subjects with uveitis. Mean age was 66.8±15.6 years, and 25 subjects (71.4%) were female. Drugs responsible were bisphosphonates (24 subjects, 68.6%), brimonidine (one subject, 2.9%), etanercept (three subjects, 8.6%), immune checkpoint inhibitors (two subjects, 5.7%), BRAF inhibitors (three subjects, 8.6%), EGFR inhibitors (one subject, 2.9%) and allopurinol/perindopril (one subject, 2.9%). In subjects with bisphosphonate inflammation, anterior uveitis occurred in 22 (91.7%) and scleritis in two (8.3%). A positive rechallenge reaction occurred in two subjects with zoledronate and one with alendronate. Uveitis occurred in six subjects (17.1%) treated with cancer drugs including immune checkpoint inhibitors, BRAF inhibitors and EGFR protein kinase inhibitors. Subjects with cancer-drug-induced uveitis were managed with corticosteroids and five subjects were able to continue therapy; in one subject uveitis was uncontrollable and required drug cessation.

CONCLUSIONS: Ocular inflammation caused by bisphosphonates is usually mild and resolves on medication withdrawal. Uveitis seen in association with newer cancer medications can be more severe, but in most cases it can be managed without medication cessation.

Drug-induced ocular inflammation is relatively rare. The most common cause is bisphosphonates, but a wide number of drugs have been implicated, including, most recently, new forms of cancer drugs such as immune checkpoint inhibitors (ICPI), B-raf (BRAF) inhibitors and epidermal growth factor receptor (EGFR) tyrosine kinase inhibitors.

There are multiple mechanisms by which drugs may induce inflammation. Ocular inflammation induced by nitrogen-containing bisphosphonates is thought to be cytokine mediated[1,2], while inflammation with non-nitrogen containing bisphosphonates is idiosyncratic.[3] Cytokine mediated inflammation is also responsible for etanercept-induced uveitis.[4,5] The exact mechanism of brimonidine-induced uveitis is unknown. Possibilities for uveitis with cancer drugs include drug toxicity,[6] T cell-induced inflammation[6–9] and drug effects on subclinical uveal micrometastases.[6]

The majority of reports of drug-induced ocular inflammation are isolated case reports or small case series. The primary objective of this study was to describe the causes of drug-induced ocular inflammation. Secondary objectives included the determination of visual outcomes, complications and the outcomes of drug rechallenge.

Methods

This study received ethics approval from the Auckland District Health Board Review Committee (ethics NTX/12/EXP/085) and adhered to the tenets of the Declaration of Helsinki. The uveitis database was used to

identify subjects presenting with uveitis at Auckland District Health Board (Auckland, New Zealand) between 1 January 2008 and 1 January 2020. Subjects were excluded if they developed intraocular inflammation following intravitreal drug injection (sterile endophthalmitis).

A retrospective chart review was performed. Relevant case details were transcribed onto a standardised proforma, including demographics, inciting medication and medication indication, treatment, as well as drug discontinuation (dechallenge) and rechallenge data. Uveitic complications of band keratopathy, peripheral anterior synechiae, posterior synechiae, ocular hypertension, glaucoma, hypotony, papillitis, choroidal neovascular membrane, cystoid macula oedema (CMO) and epiretinal membrane were recorded. Ocular hypertension was defined as an intraocular pressure of ≥24mmHg. Severe vision loss (SVL) was defined, according to the Standardisation of Uveitis Nomenclature criteria, as a permanent reduction in best-corrected visual acuity (BCVA) of ≤6/60 and moderate vision loss (MVL) as a BCVA of ≤6/15.[10]

Results

The uveitis database at Auckland District Health Board (Auckland, New Zealand) consisted of 2,750 subjects. Drug-induced ocular inflammation was observed in 50 eyes of 35 subjects, representing 1.3% of subjects seen with uveitis during the study period. Subject demographics and drugs causing ocular inflammation are reported in Table 1. Mean age was 66.8±15.6 years and 25 subjects (71.4%) were female. Twenty-seven (77.1%) subjects were ≥60 years old at presentation.

The most frequent drug to cause a reaction was bisphosphonates (24 subjects, 68.6%). No subjects experienced SVL. MVL was observed in five (10%) eyes due to uncorrected refractive error (n=2, 40%), cataract (n=2, 40%) and pre-existing glaucoma (n=1, 20%).

Table 1: Subject demographics.

	N=35
Age	Mean 66.8 years ± 15.6
Female	25 (71.4%)
Ethnicity	
Caucasian	28 (80%)
Asian	5 (14.3%)
Pacific Islander	1 (2.9%)
Not stated	1 (2.9%)
Drug	
Zoledronate	22 (62.9%)
Alendronate	2 (5.7%)
Brimonidine	1 (2.9%)
Etanercept	3 (8.6%)
Erlotinib	1 (2.9%)
Vemurafenib	2 (5.7%)
Dabrafenib	1 (2.9%)
Nivolumab	1 (2.9%)
Pembrolizumab	1 (2.9%)
Allopurinol/perindopril	1 (2.9%)

Table 2: Episodes of ocular inflammation due to intravenous zoledronate and oral alendronate.

Subject	Age (years)	Gender	Laterality	Presenting visual acuity	Inflammation type	Time from drug to onset (days)	Time to resolution (days)	Positive rechallenge	Cx	Final visual acuity
Unilateral										
1	68.1	F	L	6/9	Anterior	3	20	N	OHT	6/7.5
2	65.6	F	L	6/7.5	Anterior	1	39	N	N	6/7.5
3	74.9	M	R	6/6	Anterior	6	6	N	N	6/9
4	80.2	F	L	6/18	Anterior	2	47	N	PS	6/9
5	80.1	F	L	6/9	Anterior	4	62	N	N	6/7.5
6	84.6	F	L	6/15	Anterior	5	24	N	PS	6/7.5
7	68.9	F	L	6/6	Anterior	2	63	N	N	6/6
8	77.0	F	R	6/12	Anterior	3	25	N	PS	6/9
9	81.3	F	R	6/7.5	Scleritis	5	28	N	N	6/6
10	81.0	F	R	6/9	Anterior	5	29	N	N	6/7.5
11	67.7	F	R	6/6	Anterior	2	33	N	N	6/7.5
12	71.4	F	L	6/9	Anterior	12	37	N	N	6/9
13	57.6	F	L	6/6	Anterior	4	72	Y	N	6/6
14	83.5	F	R	6/9	Anterior	20	21	Y	N	6/9
15	74.4	F	R	6/48	Anterior	7	43	N	N	6/7.5
16	76.0	F	L	NR	Scleritis	2	42	N	Cataract	6/9
17	71.8	F	L	6/12	Anterior	7	14	N	PS	6/15
18	68.3	F	L	6/7.5	Anterior	6	19	N	PS	6/9
19	63.0	F	R	6/6	Anterior	60	30	Y	N	6/9
Simultaneous bilateral										
20	60.8	F	R	6/7.5	Anterior	6	11	N	N	6/7.5
			L	6/7.5	Anterior	6	11	N	N	6/7.5
21	68.8	F	R	6/9	Anterior	7	52	N	N	6/5
			L	6/6	Anterior	7	33	N	N	6/5
22	79.4	M	R	6/60	Anterior	3	34	N	PS, cataract	6/24
			L	6/30	Anterior	3	34	N	PS	6/9
23	50.6	M	R	6/7.5	Anterior	7	22	N	N	6/6
			L	6/12	Anterior	7	22	N	N	6/6
24	75.1	F	R	6/15	Anterior	10	32	N	CMO	6/10
			L	6/10	Anterior	10	14	N		6/7.5

F=female, M=male; L=left, R=right, NR=not recorded, anterior=anterior uveitis, Cx=complication, OHT=ocular hypertension, N=no complications, PS=posterior synechiae.

Bisphosphonates

Bisphosphonate-induced inflammation occurred with zoledronate (22 subjects, 26 eyes) and alendronate (two subjects, three eyes).

Ocular inflammation following intravenous zoledronate developed 24 hours to 20 days (median: five days) after drug infusion. Eighteen (81.8%) subjects had unilateral involvement and four (18.2%) subjects had bilateral involvement. Nineteen (86.4%) subjects were female. Table 2 summarises episodes of ocular inflammation in subjects due to zoledronate . Scleritis occurred in two (9.1%) subjects: one with unilateral anterior non-necrotising scleritis, and one with unilateral anterior and posterior non-necrotising scleritis. All remaining subjects developed anterior uveitis.

Two subjects, both females, had uveitis related to oral alendronate, aged 63 and 75, shown as subject 19 and subject 24 on Table 2, respectively. Both had anterior uveitis resolving with topical corticosteroids.

Two (9.1%) patients were rechallenged with intravenous zoledronate . Both had a positive rechallenge reaction. Both subjects had complete resolution of anterior uveitis after their first episode with recurrence on re-exposure; no further episodes of uveitis occurred once the drug was ceased. In the remaining 20 (90.9%) subjects zoledronate was discontinued after their initial episode with no recurrence.

One subject with alendronate-induced uveitis discontinued the drug after their first episode with no further episodes, while the other subject continued alendronate. The subject that continued alendronate experienced a recurrent anterior uveitis 17.4 months later with no further episodes once the drug was discontinued; uveitis screen did not reveal other causes for uveitis.

All subjects with anterior uveitis were treated with topical prednisolone acetate 1% and none required systemic treatment. Inflammation resolved within 6–72 days (median: 31 days). The subject with unilateral anterior non-necrotising scleritis was treated with oral prednisone and inflammation resolved in 28 days. The subject with anterior and posterior scleritis was treated with topical corticosteroids and oral non-steroidal anti-inflammatory medications and scleritis resolved after 42 days.

All subjects recovered fully with treatment with no recurrence during the follow-up period once the drug was discontinued. Uveitic complications of posterior synechiae were observed in seven (24.1%) eyes and a secondary cataract developed in two (6.9%) eyes. One (3.4%) eye developed CMO, which resolved with topical treatment. Two eyes (6.9%) had MVL: one from cataract and one from uncorrected refractive error.

Topical brimonidine 0.2%

One subject had recurrent bilateral anterior uveitis due to topical brimonidine. This was an 82-year-old Caucasian female treated with topical brimonidine for primary open angle glaucoma. She developed bilateral anterior uveitis 57 days after commencing brimonidine, which resolved with topical prednisolone acetate 1%. Brimonidine was not discontinued after her first episode of uveitis.

She experienced recurrent bilateral anterior uveitis 7.8 months after her first episode. This second episode was managed with topical corticosteroids and resolved in 38 days. Following this second episode, brimonidine was discontinued and she had no further episodes in 5.1 years follow-up. There were no uveitic complications and uveitis screen was negative for other causes.

Tumour necrosis factor (TNF) inhibitor—subcutaneous etanercept

Etanercept-induced inflammation was observed in three subjects shown in Table 3. None of the subjects had ocular inflammation prior to commencing etanercept.

A dechallenge reaction was seen in one subject. One subject had recurrence when the drug was continued, and one had no recurrence following drug rechallenge.

A 30-year-old Asian male developed a right-sided anterior uveitis after commencing etanercept, which resolved with topical corticosteroids. Etanercept was not discontinued and a further episode of right eye anterior and intermediate uveitis occurred 2.0 years after his first episode. This second episode required topical and systemic corticosteroids, was resistant to treatment until etanercept was stopped and

Table 3: Etanercept-induced ocular inflammation.

Subject	Drug indication	Age/ Gende	Laterality	Presenting visual acuity	Ocular inflam-mation type	Time from drug to inflam-mation (days)	Treatment	Time of reso-lution (days)	Drug rechal-lenge	Cx	Final visual acuity
1	RA	66/M	R	6/7.5	Anterior uveitis	90	Topical PF	101	No	OHT	6/9
			L	6/7.5	Anterior uveitis	90	Topical PF	101	No	OHT	6/7.5
2	AS	30/M	R	6/15	Anterior uveitis	108	Topical PF	42	Yes	nil	6/6
3	AS	14/F	L	6/12	Anterior uveitis & pos-terior scleritis	390	Topical PF, periocular steroid injection, oral prednisone	45	Yes	nil	6/6

F=female, M=male, RA=rheumatoid arthritis, AS=ankylosing spondylitis, R=right, L=left, PF=prednisolone acetate 1%, Cx=complication, OHT=ocular hypertension.

took 108 days to resolve. No further episodes of uveitis occurred following drug cessation.

Drug rechallenge was observed in a 14-year-old Asian male with ankylosing spondylitis. His initial episode of anterior uveitis and posterior scleritis required topical and systemic corticosteroids and periocular steroid together with cessation of etanercept to settle. He had a drug rechallenge due to worsening joint disease 118 days after his ocular inflammation had resolved with no further recurrence.

Immune check point inhibitors (ICPI)—intravenous nivolumab and intravenous pembrolizumab

Two subjects in the uveitis database developed ICPI-related ocular inflammation.

A 50-year-old Caucasian male was receiving intravenous nivolumab infusions for metastatic renal cell carcinoma. He developed bilateral anterior and intermediate uveitis 160 days after his initial infusion with presenting visual acuities of 6/7.5 in both eyes. Uveitis was treated with topical corticosteroids resolving in 148 days. He developed left eye CMO, which resolved with topical steroid. His oncology team discontinued his nivolumab due to treatment failure and cancer progression. He had no further episodes of inflammation after stopping nivolumab during 4.9 months follow-up.

Pembrolizumab-induced bilateral uveitis was observed in a 71-year-old Caucasian man receiving infusions for mesothelioma. Bilateral anterior and intermediate uveitis developed 33 days after his initial infusion and was treated with topical and systemic corticosteroids, resolving after 17 days. His pembrolizumab was deferred, but due to tumour progression, he had a subsequent rechallenge. Initially his eyes remained quiet for 127 days, but then he developed recurrent bilateral anterior uveitis two days after his pembrolizumab dose was doubled. This second episode of uveitis was treated with topical corticosteroids and he developed secondary uveitic cataracts. He was maintained on topical corticosteroids along with pembrolizumab infusions and had no further recurrences in one-year follow-up until death from metastatic cancer.

B-raf (BRAF) inhibitors—oral vemurafenib and oral dabrafenib

Two subjects in the series had vemurafenib-induced uveitis, and another had dabrafenib-induced uveitis, summarised in Table 4.

All three subjects were receiving BRAF inhibitors for metastatic melanoma and had bilateral simultaneous uveitis. Inflammation was treated with local and systemic corticosteroids. Two subjects were able to

continue the drug but in the subject with dabrafenib-induced inflammation, uveitis was unresponsive to systemic corticosteroid therapy and required drug cessation.

All subjects developed uveitic complications. Subject 2 on Table 4 required bilateral trabeculectomies and a right glaucoma drainage device for their uveitic glaucoma.

The subject with dabrafenib-induced uveitis developed drug-induced skin toxicity with a rash and nodular tattoo reaction related to red tattoo ink. This subject had severe anterior and intermediate uveitis at initial presentation with vision reduced in count fingers in the left eye. Her dabrafenib infusions were temporarily suspended and uveitis treated with topical and systemic corticosteroids. She had a dabrafenib rechallenge with subsequent recurrent uveitis that was unable to be controlled with corticosteroid therapy and required drug cessation. There was no evidence of melanoma recurrence during follow-up once dabrafenib was discontinued.

Epidermal growth factor receptor (EGFR) tyrosine kinase inhibitor—oral erlotinib

Erlotinib-related bilateral anterior uveitis occurred in a 76-year-old Caucasian man with lung adenocarcinoma. He developed simultaneous bilateral anterior uveitis 3.8 months after his initial dose and was managed with topical corticosteroid, resolving in 71 days. He was maintained on long-term topical steroid with no recurrence of inflammation following drug rechallenge. He developed uveitic cataracts and bilateral posterior synechiae. He was followed for a total duration of 3.1 years prior to death from metastatic disease with final visual acuities of 6/9 right eye and 6/15 left eye. MVL in the left eye was due to uncorrected refractive error.

Allopurinol/perindopril

A 54-year-old Asian female developed drug rash with eosinophilia and systemic symptoms (DRESS) syndrome due to either

Table 4: BRAF inhibitor induced ocular inflammation.

Subject	Drug	Age/ gender	Laterality	Presenting visual acuity	Ocular inflammation type	Time from infusion to inflammation (days)	Treatment	Time to resolution (days)	Drug discontinued	Cx	Final visual acuity
1	VM	70.2/F	R	6/9	Anterior	1,299	Topical PF	27	No	Cataract, CMO, ERM	6/9
			L	6/18	Anterior	1,326	Topical PF	31	No	CMO, ERM	6/9
2	VM	38.7/M	R	6/24	Intermediate	968	Topical PF, prednisone, orbital floor steroid injection	Ongoing	No	Cataract, PS, glaucoma, hypotony, papillitis, CNVM, CMO, ERM	6/9
			L	6/12	Intermediate	2,141	Topical PF, prednisone	Ongoing	No	Cataract, glaucoma	6/6
3	DB	54.2/F	R	6/6	Anterior & intermediate	1,377	Topical PF, prednisone	517	Yes	OHT, CMO	6/6
			L	Count fingers	Anterior & intermediate	1,377	Topical PF, prednisone	517	Yes	PS, OHT	6/6

F=female, M=male, R=right, L=left,CMO=cystoid macular oedema, ERM=epiretinal membrane, PS=posterior synechiae, CNVM=choroidal neovascular membrane, OHT=ocular hypertension, PF=prednisolone acetate 1%, VM=vemurafenib, DB=Dabrafenib, Cx=complication.

allopurinol or perindopril. She developed bilateral anterior and posterior scleritis 64 days after her initial allopurinol dose and 99 days after her initial perindopril dose. Her intraocular pressures were raised on presentation at 32mmHg right and 37mmHg left. Both drugs were discontinued.

Her scleritis was difficult to manage, requiring high-dose prednisone. Second-line immunosuppression with typical disease-modifying anti-rheumatic drugs (DMARDs) were initially contraindicated due to hepatitis secondary to DRESS. She was later started on methotrexate and active scleritis resolved after nine months.

She developed bilateral posterior subcapsular cataracts and bilateral uveitic glaucoma requiring glaucoma drainage devices. At her final follow-up, visual acuities were 6/45 right eye and 6/7.5 left eye. MVL occurred in her right eye due to cataract.

Discussion

Although presumed rare, there are few reports on the incidence of drug-induced ocular inflammation. It has been reported at less than 0.5%[11] and at our tertiary uveitis clinic comprised 1.3% of all uveitis cases. Twenty-seven subjects (77.1%) were ≥60 years, so it is an important cause of ocular inflammation in this age group.

Naranjo et al[12] proposed criteria to establish the causality of adverse events by drugs. Data contributing to causality include dechallenge, rechallenge and dose-related effects.

Bisphosphonates

Uveitis occurs in 0.29%[13] to 1.1%[14–16] and scleritis in 0.63%[13] of individuals taking bisphosphonates. Population-based studies have shown a low incidence of inflammatory eye reactions (IER) with bisphosphonates and rates of severe IER are reported to be very low.[17] In our series, only two subjects required systemic treatment and one had cystoid macular oedema, which resolved with treatment. In most, inflammation rapidly resolved with drug cessation and the use of topical corticosteroids.[2] A cycloplegic agent may be required to prevent/break posterior synechiae; seven (24.1%) eyes in this series had posterior synechiae.

Within the current study, all three subjects on bisphosphonates undergoing a drug rechallenge experienced recurrent inflammation. Most studies in the literature support recurrence of uveitis following drug rechallenge. Within small case series, positive rechallenge reactions has been documented for conjunctivitis,[18] scleritis,[19] episcleritis[18] and anterior uveitis[3,18] and again show that discontinuing bisphosphonate was required for ocular inflammation to resolve. Furthermore, uveitis recurrence was demonstrated when switching from one bisphosphonate to a different bisphosphonate agent.[20]

Conversely, Patel et al[14] did not find recurrent inflammation with repeated zoledronate infusions in three subjects with rechallenge. Additionally, Banal et al[21] found no recurrence of a unilateral anterior uveitis when zoledronate was switched to pamidronate in a single case report.

Immunologic or toxic reactions caused by the release of inflammatory cytokines are thought to be the mechanism of bisphosphonate-induced uveitis.[1,2] Uveitis can occur with non-nitrogen, halogen-containing bisphosphonates[3] and is likely an idiosyncratic reaction with these bisphosphonates,[3] therefore changing a subject onto one of these bisphosphonates may be prudent after an episode of inflammation.

Ocular hypotensive medication—brimonidine

Brimonidine is a selective alpha 2-adrenergic receptor agonist that is used for the treatment of glaucoma and ocular hypertension.

There have been a small number of case reports describing granulomatous anterior uveitis,[22–26] which tends to develop 6–9 months after initiation of medication.[2] The condition may be asynchronous, and second eye involvement can develop up to a year after the first eye.[26]

In this series, anterior uveitis recurred 7.8 months after the initial episode when brimonidine was not discontinued, but there were no further episodes following drug cessation. Other reports of dechallenge[22,26] and rechallenge[22] data make the association definite.

Tumour necrosis factor (TNF) inhibitors—etanercept

TNF is a pro-inflammatory cytokine and is the target of many immunomodulatory medications including infliximab, adalimumab and etanercept. Etanercept is a soluble TNF receptor that binds both TNF-alpha and TNF-beta and is most likely in this class to be associated with drug-induced uveitis.[2]

Ocular inflammation—which can be anterior or posterior uveitis, or scleritis—typically develops three months to two years after initiation of treatment and largely resolved after discontinuing the medication with some requiring systemic corticosteroid therapy to further settle down inflammation.[2,5,27–30]

Lim et al[27] reviewed all cases of uveitis occurring in patients treated with etanercept, infliximab and adalimumab in their national database over an eight-year period. They excluded subjects with underlying disease likely to be associated with uveitis and included those cases they felt showed causality between the drug and uveitis. The majority (43 out of 59, 72.8%) of cases were due to etanercept, 23.7% (n=14) due to infliximab and 3.4% (n=2) due to adalimumab. Etanercept was significantly more likely associated with uveitis than either infliximab (OR 5.375) or adalimumab (OR 8.60). There were also dechallenge/rechallenge data for a limited number of subjects within the etanercept group, which strengthened the association of the drug with uveitis causation.[27,28]

In our series, following cessation of etanercept in two subjects no further episodes of ocular inflammation occurred, suggesting inflammation was due to etanercept rather than the subjects' underlying autoimmune disease. In subjects developing ocular inflammation while on etanercept, alternative therapeutic options should be discussed with the subject's rheumatologist.

Cancer therapies—ICPI, BRAF inhibitors, EGFR protein kinase inhibitor

Uveitis has been documented with newer cancer immunomodulatory agents including ICPI, BRAF inhibitors and EGFR tyrosine kinase inhibitors. Six (17.1%) subjects in this study had uveitis related to cancer therapies.

ICPIs are used in the treatment of solid tumours like melanoma. Tumour cells evade host defences by activating inhibitory receptors on tumour-specific T cells; this can downregulate T-cell function allowing cancer cells to survive. ICPIs prevent activation of inhibitory receptors on tumour-specific T cells, thus enabling the T cells to become activated and kill the tumour cells.[31] Nivolumab and pembrolizumab inhibit programmed cell death protein 1 receptor, which blocks inhibitory T-cell checkpoints. ICPI-induced uveitis have been reported in all morphologies—anterior, intermediate and posterior—with anterior being most common.[31] A Vogt–Koyanagi–Harada-like syndrome has also been described including a sunset-glow fundus appearance and extraocular manifestations of hearing loss, meningismus, vitiligo and poliosis.[9,31,32]

Dysregulation of MAPK signalling and BRAF gene mutations are found in melanomas.[8] Inhibition of BRAF inhibits melanoma cell proliferation and is used in the treatment of metastatic cancer. These agents include vemurafenib and dabrafenib. Uveitis is most commonly reported with vemurafenib and fewer cases with dabrafenib.[7,33,34] Scleritis can also occur.[35] In a review of 568 subjects receiving vemurafenib, 4% developed drug-induced uveitis and were treated with ocular and systemic corticosteroid without discontinuing the drug.[6] Anterior uveitis is most common followed by intermediate uveitis.[6]

EGFR activating mutations occur in about 20% of non-small cell lung cancers and are associated with poor prognosis.[36] Erlotinib is a tyrosine kinase inhibitor and is used as a chemotherapy for non-small cell lung cancer and pancreatic cancer.[37] Anterior uveitis has been reported within six weeks of therapy[36,38] and can be treated with local steroid without stopping therapy.[39] Recurrence has been reported with lowered dosage suggesting uveitis is idiosyncratic rather than dose dependent toxicity.[36]

All these cancer therapies are potentially lifesaving. It is important to weigh the risks and benefits of these agents. If it is potentially lifesaving, it should not be discontinued; the drug reaction should be

treated locally instead.[36,39,40] There have been few cases of severe ocular inflammation requiring drug cessation.[41,42] Fortunately, the majority of drug-induced uveitis improve with topical, regional or systemic corticosteroid therapy without needing to discontinue therapy. The risk of biologic and non-biologic DMARDs in the treatment of uveitis in these patients is unknown. Those that continued therapy experienced relapses of uveitis unless maintained on corticosteroid.[31]

In this series nivolumab was discontinued without recurrence. Pembrolizumab-induced uveitis recurred following rechallenge and continued local steroid therapy prevented further recurrences while continuing the drug. Vemurafenib-induced intermediate uveitis was also treated with continued local steroid therapy to prevent recurrent uveitis. In all cases complications of chronic uveitis including cataract, CMO, glaucoma and posterior synechiae occurred. One subject developed significant uveitic glaucoma requiring glaucoma surgery. Severe anterior and intermediate uveitis related to dabrafenib occurred in one subject reducing vision to count fingers in one eye at presentation; the drug was temporarily suspended then rechallenged with recurrent uncontrollable uveitis that required drug cessation. Withdrawal, discontinuation and rechallenge data exists for verurafenib[40] and erlotinib[36], strengthening the association between these drugs and uveitis.

Allopurinol/perindopril

Both allopurinol[43] and perindopril[33] can induce DRESS syndrome. However, ocular inflammation from allopurinol- and perindopril-induced DRESS syndrome has not been described previously. Furthermore, this is the first case of scleritis as an ocular manifestation of DRESS syndrome.

DRESS syndrome is a delayed type IVb hypersensitivity reaction with a mortality of up to 10%.[45] It is a severe, idiosyncratic multisystem reaction to a drug and commonly occurs within eight weeks after starting the offending drug. Treatment involves early recognition, prompt cessation of all suspected drugs and supportive local and systemic treatment including corticosteroids.[46]

Cicatrising conjunctivitis is the most common ocular manifestation of DRESS syndrome; intraocular inflammation is rare. Cases of uveitis (anterior, intermediate, panuveitis,)[46,47] and two cases of uveal effusion syndrome[48,49] have been reported in the literature. This is the first case of scleritis as a symptom of DRESS syndrome.

Conclusion

Drug-induced ocular inflammation is an uncommon but important cause of uveitis. Management begins with consideration of a drug-related event and requires clinician awareness. Anterior uveitis is the most common clinical picture, visual acuity tends to be minimally affected and, if the drug is ceased, uveitis does not recur. Severe cases, while rare, can cause future management concerns; our series demonstrates that recurrent uveitis can occur with repeat administration of the medication. An approach with pre-treatment of topical steroid before an infusion may have merit, but it requires study to see if this reduces risk of recurrence.

Immunomodulatory cancer drugs require special consideration. Inflammation can range from minimal to severe, requiring local and sometimes systemic corticosteroid treatment. The risk of persistent ocular inflammation needs to be balanced with potential cancer progression if the drug is discontinued. Chronic mild inflammation can be managed with long-term topical therapy to prevent recurrence while maintaining a lifesaving drug. In cases of severe vision threatening inflammation, the drug may, however, need to be discontinued. In all such cases, careful communication and joint care with the treating oncologist is recommended.

Competing interests:
Nil.

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Unplanned admissions to the Wellington Hospital intensive care unit before, during and after New Zealand's COVID-19 lockdown

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ABSTRACT

AIM: To evaluate rates of unplanned ICU admissions before, during and after New Zealand's COVID-19 Alert Level 4/3 lockdown, and to describe the characteristics and outcomes of patients admitted to Wellington ICU during lockdown in comparison to historical controls.

METHOD: We conducted a retrospective cohort study using the Wellington Hospital ICU database and included patients with an unplanned ICU admission during the first 35 weeks of the year from 2015 to 2020 inclusive. The primary variable of interest was the rate of unplanned ICU admission in 2020 compared with historical controls. We also described the characteristics and outcomes of patients with unplanned admissions to ICU during the 2020 COVID-19 lockdown compared to historical controls.

RESULTS: During the five weeks of Alert Level Four, and the subsequent two weeks of Alert Level Three, the number of unplanned ICU admissions per day fell to 1.65±1.52 compared to a historical average of 2.56±1.52 ICU unplanned ICU admissions per day (P<0.0001). The observed reduction in ICU admission rates appeared to occur for most categories of ICU admission diagnosis but was not evident for patients with neurologic disorders. The characteristics and outcomes of patients who had unplanned admissions to Wellington ICU during the COVID-19 lockdown were broadly similar to historical controls. The rate of unplanned ICU admissions in 2020 before and after the lockdown period were similar to historical controls.

CONCLUSION: In this study, we observed a reduction in unplanned admissions to Wellington Hospital ICU associated with New Zealand's initial COVID-19 lockdown.

Coronavirus disease 2019 (COVID-19) has placed unprecedented demand on healthcare services around the world. In some countries, surges in infection rates have overwhelmed the capacity of hospitals. Reported rates of intensive care unit (ICU) admission among patients with COVID-19 disease have varied widely from 3% to 100%.[1] Although the true rate of ICU admission among patients with COVID-19 is not certain, it is clear that many patients who are admitted to the ICU require prolonged periods of invasive mechanical ventilation. Because such specialised care can only safely be provided by trained ICU staff in an ICU environment, ICU capacity is an important issue to consider in relation to the readiness of hospital systems to deal with surges in infection rates. New Zealand has among the lowest level of ICU beds per capita in the OECD at four per 100,000 population.[2] This compares to Australia at nine, France at 16 and Germany at 34.[2] During business as usual, the degree of capacity constraint is such that in 2018, 17% of all New Zealand elective surgical operations that required planned post-operative admission to an ICU had to be postponed because of the lack of an available ICU bed.[3] The comparable rate for Australian ICUs over the same time

period was 1.7%.[3] Accordingly, during the COVID-19 epidemic, ICU capacity is a potential point of particular vulnerability in the New Zealand healthcare system. While plans to mitigate the critical lack of ICU capacity by purchasing ventilators and other respiratory equipment, using non-ICU areas and non-ICU staff to care for ICU patients, have been developed, the most important component of New Zealand's COVID-19 response to date has been the public health response. New Zealand's five-week restrictive Alert Level 4 lockdown and subsequent two-week Alert Level 3 lockdown phase resulted in prolonged elimination of COVID-19 from New Zealand. The association between these interventions and the unplanned (emergency) admissions to the ICU have not been reported. This information is important because the degree to which lockdowns can effect unplanned ICU admissions is a relevant consideration in determining the risk of ICU capacity being overwhelmed in subsequent COVID-19 surges where lockdowns are imposed. Accordingly, we undertook a retrospective study to evaluate rates of unplanned ICU admissions before, during, and after New Zealand's COVID-19 Alert Level 4/3 lockdown. We also sought to describe the characteristics and outcomes of patients admitted to Wellington ICU during lockdown in comparison to historical controls.

Method

Study design, setting and oversight

We conducted a retrospective cohort study using data from the Wellington Hospital ICU database, which contains information on all admissions to the ICU. Wellington ICU is a 24-bed facility providing tertiary services to a population of 1.1 million New Zealanders from 10 hospitals across seven other District Health Boards in the lower North Island and upper South Island.

The study was approved by the New Zealand Health and Disability Ethics Committee (Ref 20/NTB/219). As the study involved retrospective review of deidentified data, requirements for informed consent were waived.

Study population

Patients were eligible for inclusion if they had an unplanned admission to Wellington ICU during the first 35 weeks of the year in any year from 2015 to 2020 inclusive. Unplanned ICU admissions were defined as all admissions except for those that were planned to occur following elective surgery.

For the purposes of comparing the characteristics and outcomes of patients admitted during COVID-19 lockdown we focused on the period from 25 March until 12 May inclusive, which corresponded to the five weeks of New Zealand's Alert Level Four and the subsequent two weeks of Alert Level Three.[4] Patients admitted in 2020 were defined as the COVID-19 lockdown cohort. Those patients admitted from 2015 to 2019 were defined as the historical controls.

Exposures and variables of interest

The primary exposure of interest was the 2020 COVID-19 lockdown. The primary variable of interest was the rate of unplanned ICU admission. However, we also sought to describe the demographics, illness severity, reasons for ICU admission, ICU admission duration, ICU mortality and hospital outcomes of patients with unplanned admissions to ICU during the 2020 COVID-19 lockdown compared to historical controls.

Recorded data

Age, gender and ethnicity were recorded. Ethnicity was categorised using the New Zealand Ministry of Health's ethnic group priority order with each person assigned to a single ethnic group.[5] We recorded the source of ICU admission divided into the following categories: (i) operating theatre following emergency surgery; (ii) emergency department; (iii) hospital ward; (iv) transfer from another hospital (except for from another ICU); and (v) transfer from another ICU. We recorded the illness severity using the Acute Physiology and Chronic Health Evaluation II (APACHE-II) score. The APACHE-II score is calculated based on the presence of comorbidities and the most deranged physiological variables from the first 24 hours in the ICU. The APACHE-II score can range from 0 to 71, with a higher score indicating more severe disease and a higher risk of death. ICU admission diagnoses were aggregated by body system using APACHE-II diagnostic categories. We recorded the ICU length of stay, the ICU mortality, and the discharge destination from Wellington Hospital, where the ICU is situated.

Statistical analyses

The principal comparison was of the unplanned daily ICU admission rates in the pre-lockdown, lockdown and post-lockdown periods with admission rates in 2020 compared to historical controls based on the average admission rates obtained from equivalent weeks of the year from 2015 to 2019 inclusive.

We compared the demographics, ICU admission characteristics, illness severity, ICU admission durations, ICU mortality and hospital outcomes of patients admitted during the lockdown compared with historical controls. To provide further information, we reported the ICU admission diagnoses by body system for 2020 and for each of the preceding five years.

Comparisons between groups were performed using chi-square tests for proportions, Student's t tests for normally distributed data and Wilcoxon rank-sum tests otherwise with results reported as an n with percentages, means±SDs, or median (interquartile range), respectively.

All analyses were performed using Microsoft Excel 2010. A two-sided p value of less than 0.05 was used to indicate statistical significance.

Results

The number of ICU admissions per month during the first 35 weeks of 2020 compared to the historical average based on ICU admission rates in the equivalent weeks from the prior five years are shown in Figure 1. In the 13 weeks of 2020 prior to lockdown there were an average of 2.41±1.40 unplanned ICU admissions per day compared to the historical average of 2.61±1.40 unplanned ICU admissions per day (P=0.23). During the five weeks of Alert Level Four, and the subsequent two weeks of Alert Level Three, the number of unplanned ICU admissions per day fell to 1.65±1.52 compared to a historical average of 2.56±1.52 ICU unplanned ICU admissions per day (P<0.0001). Since the end of Alert Level 3 in Wellington there have been 2.60±1.52 unplanned ICU admissions per day compared to a historical average of 2.79±1.51 unplanned ICU admissions per day (P=0.29).

The characteristics and outcomes of patients with an unplanned admission to Wellington ICU during New Zealand's COVID-19 lockdown and of the patients admitted in the equivalent weeks of the year from the prior five years were similar and are shown in Table 1. Additional data on the breakdown of the COVID-19 and historical control admissions by ethnicity are shown in Table 2.

A breakdown of ICU admission diagnoses categorised by body system during the 2020 lockdown dates and during the preceding five years is shown in Figure 2. The number of admissions in the cardiovascular, gastrointestinal, sepsis, trauma and metabolic categories was lower than any of the preceding five years. The greatest number of admissions was in the neurologic category where admission rates were just above the median of the prior 5 years (Table 3).

Discussion

In this single-centre retrospective cohort study conducted at Wellington Hospital ICU we observed a highly statistically significant reduction in unplanned ICU admissions associated with New Zealand's COVID-19 lockdown. The number of unplanned ICU admissions decreased by just over a third compared to historical controls, with the reduction in admissions appearing to begin in the first week of Alert Level 4. The observed reduction in ICU admission rates appeared to occur for most categories of ICU admission diagnosis because, except for patients with neurologic disorders, observed unplanned ICU admission rates were low by historical standards. Unplanned ICU admission rates quickly returned to historical levels in the post-lockdown period.

One potential concern with the lockdown is that patients with potentially life-threatening diseases may not have presented to hospital. Our data do not preclude this possibility; however, we observed that the characteristics and outcomes of patients who had unplanned admissions to Wellington ICU during the COVID-19 lockdown where broadly similar to historical controls. In particular, the breakdown of patients with unplanned

Table 1: Characteristics and outcomes of unplanned admissions to Wellington ICU during New Zealand's COVID-19 Alert Level 3 and Alert Level 4 lockdown compared with historical controls.*

Characteristic	COVID-19 lockdown (n=81)	Historical controls (n=628)	P value
Age – yr	58.3±16.8	57.8±17.9	0.80
Female sex – no. (%)	35 (43.2%)	268 (42.6%)	1.0
Ethnic group – no. (%)			0.31†
European	56 (69.1%)	419 (66.7%)	N/A
Māori	11 (13.6%)	102 (16.2%)	N/A
Pacific Peoples	6 (7.4%)	68 (10.8%)	N/A
Asian	7 (8.6%)	29 (4.6%)	N/A
Middle Eastern / Latin American / African	3 (3.7%)	7 (1.1%)	N/A
Other	0 (0.0%)	1 (0.2%)	N/A
Residual categories‡	0 (0.0%)	2 0.3%)	N/A
Source of admission to ICU – no. (%)			0.38†
OT following emergency surgery	24 (29.6%)	172 (27.4%)	N/A
Emergency department	18 (22.2%)	161 (25.6%)	N/A
Hospital ward	19 (23.5%)	168 (26.8%)	N/A
Transfer from another hospital (except from another ICU)	13 (16.0%)	59 (9.4%)	N/A
Transfer from another ICU	7 (8.6%)	68 (10.8%)	N/A
APACHE-II score ¶	47.2±20.7	50.3±24.1	0.21
APACHE-II diagnostic category – no. (%)			0.23†
Cardiovascular	19 (23.5%)	164 (26.1%)	N/A
Gastrointestinal	9 (11.1%)	81 (12.9%)	N/A
Neurologic	23 (28.4%)	102 (16.2%)	N/A
Respiratory	12 (14.8%)	75 (11.9%)	N/A
Sepsis	5 (6.2%)	56 (8.9%)	N/A
Trauma	7 (8.6%)	62 (9.9%)	N/A
Metabolic	1 (1.2%)	32 (5.1%)	N/A
Genitourinary	0 (0.0%)	29 (4.6%)	N/A
Musculoskeletal	3 (3.7%)	8 (1.3%)	N/A
Haematological	1 (1.2%)	8 (1.3%)	N/A
Gynaecological	1 (1.2%)	3 (0.5%)	N/A
Other	0 (0%)	8 (1.3%)	N/A
ICU length of stay – hours, median [IQR]	44 [22–86]	53 [22–90]	0.58
ICU mortality – no. (%)	10 (12.3%)	92 (14.6%)	0.74
Hospital outcome – no. (%)			0.28†
Discharged home	34 (42.0%)	292 (46.5%)	N/A
Discharged to another hospital (except for another ICU)	31 (38.3%)	188 (29.9%)	N/A
Discharged to another ICU	2 (2.5%)	18 (2.9%)	N/A
Died	13 (16.0%)	127 (20.2%)	N/A
Discharged to long-term care facility	0 (0.0%)	2 (0.3%)	N/A
Unknown	1 (1.2%)	1 (0.2%)	N/A

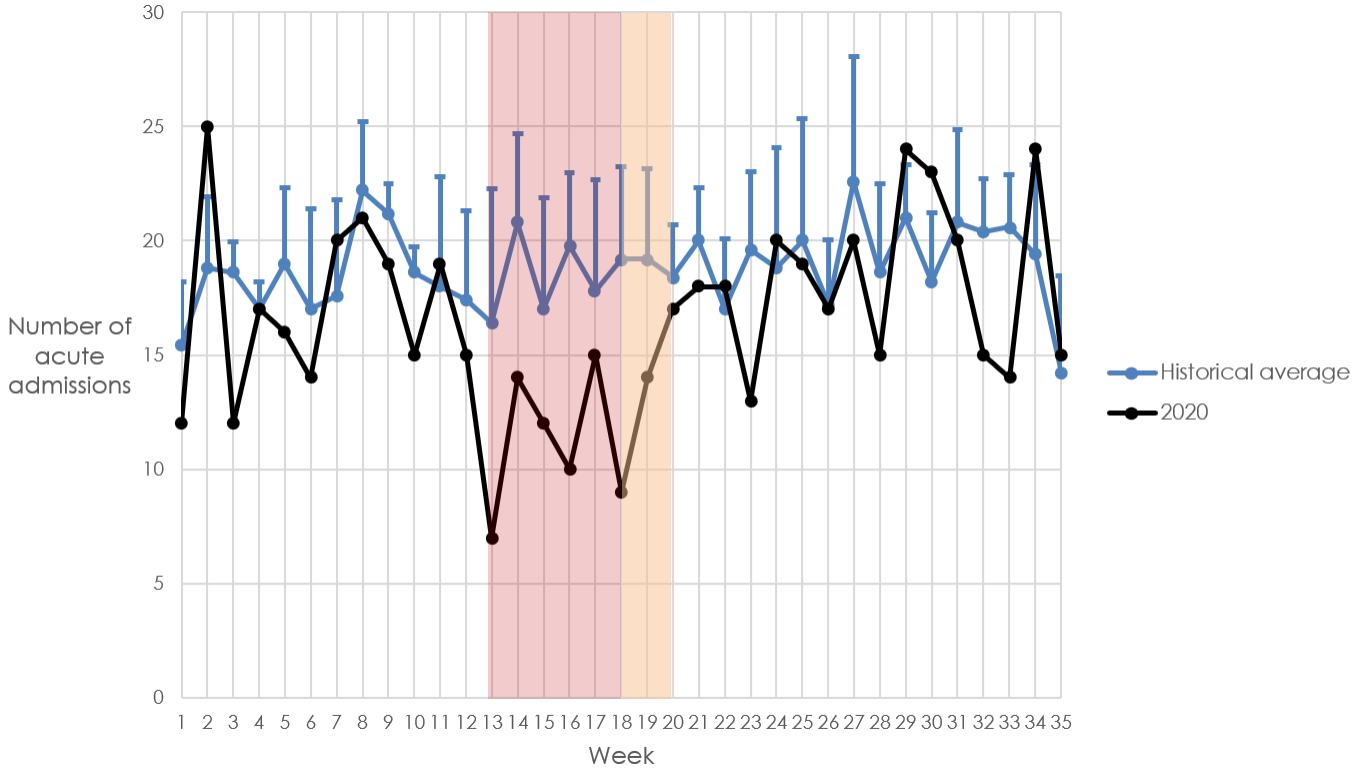
*Unplanned ICU admissions were defined as all ICU admissions except for those that were booked to occur after elective surgery. Data for historical controls were obtained from the equivalent dates to the 2020 COVID-19 lockdown but from the 2015 to 2019 inclusive.
†P value calculated using X^2 disregarding cells with a frequency less than five.
‡Residual categories includes "don't know"; "refused to answer"; "response unidentifiable"; "not stated".
¶Scores on the APACHE II range from 0 to 71, with higher scores indicating more severe disease and a higher risk of death.
Abbreviations: APACHE: Acute Physiology and Chronic Health Evaluation; ICU: Intensive Care Unit; OT: operating theatre.

Table 2: Detailed breakdown of unplanned ICU admissions by ethnic group.*

Ethnic group - n (%)	COVID-19 lockdown (n=81)	Historical controls (n=628)
European not further defined	2 (2.5%)	8 (1.3%)
New Zealand European	50 (61.7%)	363 (57.8%)
Other European	4 (4.9%)	48 (7.6%)
NZ Māori	11 (13.6%)	102 (16.2%)
Pacific people not further defined	0 (0%)	2 (0.3%)
Samoan	3 (3.7%)	36 (5.7%)
Cook Island Māori	0 (0%)	7 (1.1%)
Tongan	0 (0%)	4 (0.6%)
Niuean	0 (0%)	0 (0%)
Tokelauan	1 (1.2%)	12 (1.9%)
Fijian	1 (1.2%)	6 (1.0%)
Other Pacific People	1 (1.2%)	1 (0.2%)
Asian not further defined	2 (2.5%)	2 (0.3%)
South East Asian	1 (1.2%)	4 (0.6%)
Chinese	1 (1.2%)	8 (1.3%)
Indian	3 (3.7%)	11 (1.8%)
Other Asian	0 (0%)	4 (0.6%)
Middle Eastern	0 (0%)	2 (0.3%)
Latin American	0 (0%)	0 (0%)
African	3 (3.7%)	5 (0.8%)
Other ethnicity	0 (0%)	1 (0.2%)
Don’t know	0 (0%)	0 (0%)
Refused to answer	0 (0%)	0 (0%)
Response unidentifiable	0 (0%)	1 (0.2%)
Not stated	0 (0%)	1 (0.2%)

*For people who identified as belonged to more than one ethnic group, the following ethnic group priority order was used to allocate each person to a single category: NZ Māori, Tokelauan, Fijian, Niuean, Tongan, Cook Island Maori, Samoan, Pacific people not further defined, South East Asian, Indian, Chinese, Other Asian, Asian not further defined, Latin American/Hispanic, African, Middle Eastern, Other ethnicity, Other European, European not further defined, NZ European, don’t know, refuse to answer, response unidentifiable, not stated.

Figure 1: Unplanned admissions to Wellington ICU by week before, during and after COVID-19 Alert Levels 3 and 4.*

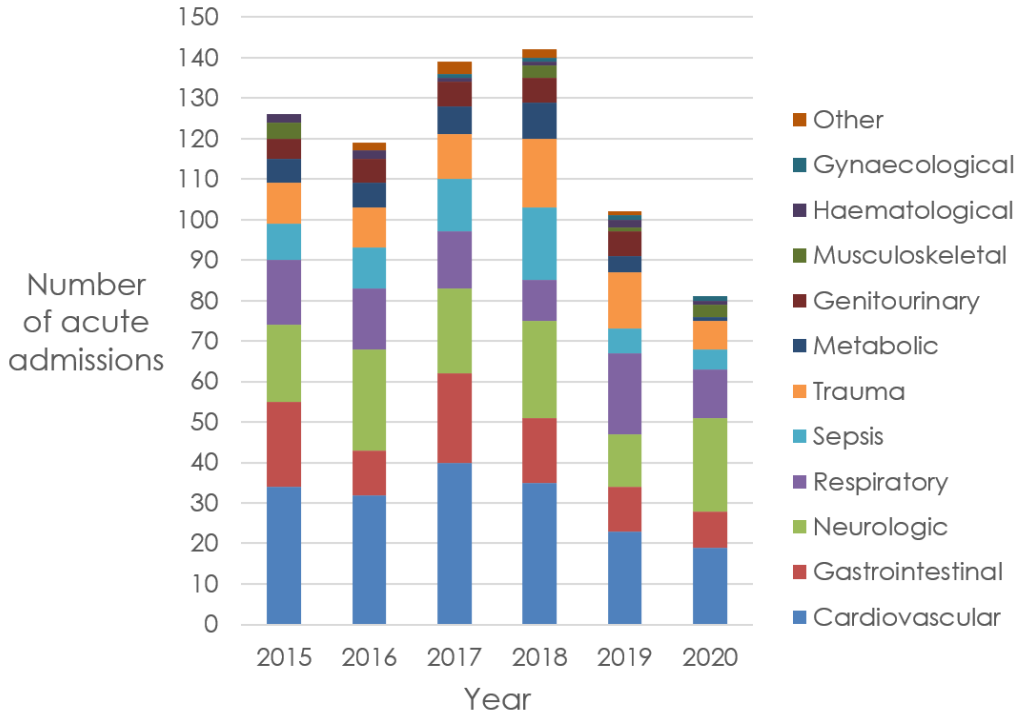


*Red shading corresponds to the dates of Alert Level 4 (from 25 March until 26 April); orange shading corresponds to the dates of Alert Level 3 (from 27 April until 13 May). Historical averages were calculated using ICU admission data for equivalent weeks of the year 2015 to 2019 inclusive with error bars representing the standard deviation; only positive error bars are shown.

Table 3: Unplanned ICU admissions by body system.

Admission category	COVID-19 lockdown	Historical controls		
	Number of admissions	Median [IQR]	Minimum	Maximum
Cardiovascular	19	34 [32–35]	23	40
Gastrointestinal	9	16 [11–21]	11	22
Neurologic	23	21 [19–24]	13	25
Respiratory	12	15 [14–16]	10	20
Sepsis	5	10 [9–13]	6	18
Trauma	7	11 [10–14]	10	17
Metabolic	1	6 [6–7]	4	9
Genitourinary	0	6 [6–6]	5	6
Musculoskeletal	3	1 [0–3]	0	4
Haematological	1	2 [1–2]	1	2
Gynaecological	1	1 [0–1]	0	1
Other	0	2 [1–2]	0	3

Figure 2: Unplanned admissions to Wellington ICU from 25 March until 13 May by year categorised by body system.*



*In 2020 these dates correspond to Alert Level 4 (from 25 March until 26 April) and Alert Level 3 (from 27 April until 13 May).
Abbreviations: ICU: intensive care unit.

admissions by ethnic group does not support the hypothesis that access to ICU during COVID-19 differed by ethnic group.

Our findings are consistent with prior studies evaluating the association between COVID-19 lockdowns and hospital presentations. These include a New Zealand study which reported a 43% reduction in injury-related presentations to level one trauma centre during lockdown.[6] International studies have shown a consistent and significant reduction in acute heart failure presentations in Italy,[7] paediatric emergency department presentations in Italy,[8] tertiary-care ophthalmology presentations in India,[9] and oral and maxillofacial trauma presentations to a central London hospital.[10] To our knowledge this is the first study to evaluate the association between a COVID-19-related lockdown and unplanned ICU admission rates. Only one patient with COVID-19 was admitted to Wellington ICU during the COVID-19 lockdown. As a consequence, the data presented here largely reflect the association between lockdown and ICU admissions that are unrelated to COVID-19. The observation that unplanned ICU admission rates fell concurrently with the start of Alert Level 4 and that the number of unplanned ICU admissions per day was just over a third lower than historical levels has potential implications to New Zealand's planning for future surges in infections. If these findings are confirmed in other New Zealand ICUs this would suggest that the available ICU capacity freed up by a lockdown, will substantially exceed the amount of ICU capacity that would be freed up by simply cancelling elective operations that require patients to receive post-operative ICU care.

While our study provides comprehensive data on a highly statistically significant association between New Zealand's COVID-19 lockdown and a reduction in unplanned admissions to Wellington Hospital ICU, it has several limitations. Firstly, our sample size is small and true differences between the characteristics of the COVID-19 cohort and historical controls may not have been evident in our analyses due to a lack of statistical power to detect such differences.

Secondly, our retrospective design does not allow us to attribute a causal link between the period of lockdown and observed unplanned admission rates. Accordingly, we cannot be certain that similar reductions an unplanned ICU admission rates would be observed in future lockdowns. Thirdly, it is unclear whether or not our findings are generalisable to hospitals outside of New Zealand or, indeed, whether they even apply to other New Zealand hospitals. Finally, our observation that rates of unplanned ICU admissions in all categories except for those in patients with neurologic disorders were low by historical standards is based on a small number of events and may have occurred due to the play of chance. We cannot preclude the possibility that the drop in unplanned ICU admissions associated with lockdown is attributable to reductions in admissions in a more limited number of diagnostic categories.

Our findings should prompt further research evaluating the association between the COVID-19 lockdown and unplanned ICU admission rates in other New Zealand hospitals and comparative studies that evaluate whether the association between lockdowns and unplanned ICU admissions differed in other countries that took a less restrictive approach to lockdown.

Conclusions

In this study, we observed a reduction in unplanned admissions to Wellington Hospital ICU associated with New Zealand's initial COVID-19 lockdown. There were no significant differences in the characteristics of patients who had an unplanned admission to Wellington ICU during the COVID-19 lockdown compared with historical controls.

Competing interests:
Nil.

Acknowledgements:
This research was conducted during the tenure of a Health Research Council of New Zealand Clinical Practitioner Research Fellowship held by Paul Young. The Medical Research Institute of New Zealand is supported by Independent Research Organisation funding from the Health Research Council of New Zealand.

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Consensus statement on the treatment of transplant-eligible patients with newly diagnosed multiple myeloma in New Zealand

Nicole Chien, Ken Romeril, Bart Baker, Hugh Goodman, Henry Chan, on behalf of the Myeloma Interest Group

ABSTRACT

Multiple myeloma is the second most common blood cancer in New Zealand with higher incidence in Māori and Pacific Island populations. It remains an incurable disease but the rapidly changing treatment landscape has led to improved outcome. In response to recent changes in funding of anti-myeloma therapy in New Zealand, the New Zealand Myeloma Interest Group has reviewed the latest literature and updated the treatment pathway of transplant-eligible patients with newly diagnosed multiple myeloma.

In New Zealand, around 400 new cases of multiple myeloma (MM) are reported each year. This equates to an age standardised incidence rate of 5.19 cases per 100,000 population, which is similar to other western countries and is increasing with time. The incidence is higher in Māori and Pacific Islanders.[1] The MM treatment landscape has rapidly evolved over the last two decades, with increasing number of novel agents and immunotherapies available. These agents are effective and usually well tolerated. They have led to a significant improvement in outcome in MM patients.[1,2] PHARMAC, the pharmaceutical management agency in New Zealand, has recently made changes to funding for anti-myeloma therapy, which included unrestricted access to bortezomib and lenalidomide maintenance therapy. The New Zealand Myeloma Interest Group has taken this opportunity to review and update the national treatment pathway accordingly. These recommendations aim to unify upfront therapy for transplant-eligible MM patients in New Zealand and form the basis of ensuring equity and consistency of MM care in New Zealand. This goal is in line with national Cancer Action Plan, as published by the New Zealand Cancer Control Agency.[3] However, these recommendations are for guidance only, and final patient treatment decisions should be made at clinicians' discretion, taking into consideration all patient factors.

Method

The New Zealand Myeloma Interest Group is comprised of representative haematologists from District Health Boards around the country with a special interest and expertise in MM. We reviewed the currently available evidence, including randomised controlled trials, retrospective data and conference abstracts, and interpreted these in the context of treatment options available in New Zealand to form a recommendation that is best suited for our population.

Induction chemotherapy

The funded front-line option for induction chemotherapy remains bortezomib-based treatment for transplant-eligible patients. The preferred regimen is to combine bortezomib with an alkylating agent such as

ISSN 1175-8716

cyclophosphamide and dexamethasone. In younger patients or those with suboptimal response, defined as less than a very good partial response by International Myeloma Working Group (IMWG) criteria, changing to bortezomib–thalidomide–dexamethasone (VTD) regimen (Table 1) prior to autologous stem cell transplant (ASCT) can be considered. VTD has been shown to improve responses in the upfront setting compared to bortezomib–cyclophosphamide–dexamethasone combination; however, whether this translates to survival outcome is unknown.[4] The decision will need to be balanced against the increased risk of neurological toxicity with the VTD regimen, as reported in the IFM2013-04 study,[4] although this trial used twice-weekly bortezomib instead of the weekly regimen used in New Zealand. The optimal number of induction cycles has not been clearly defined by current evidence but, based on international practice, a minimum of four cycles is recommended.[5,6]

The group recognises that the more effective regimen of lenalidomide–bortezomib–dexamethasone is currently recommended in many countries as upfront induction chemotherapy, based on its improved response and outcome.[7] However, this regimen is not currently available as induction, as lenalidomide is not funded for front-line induction treatment in New Zealand.

High-dose therapy and autologous stem cell transplant

High-dose therapy with autologous stem cell transplant remains an integral part of front-line therapy in newly diagnosed MM, even in the era of novel agents. ASCT has been shown to significantly improve the depth of response and progression-free survival (PFS) but not overall survival (OS).[8,9] This may be partly due to the short follow-up in trials and the availability of effective salvage agents. Based on the improved PFS, it is recommended that eligible patients should be considered for front-line ASCT rather than delaying to relapse. This recommendation is further supported by the result of IFM2009 trial, which showed 21% patients were unable to receive ASCT at relapse due to disease refractoriness.[8]

Until recently, the role of tandem ASCT has been unclear, and published data have shown conflicting results. However, recently, two large randomised controlled trials, the EMN02 trial and updated result

Table 1: Recommended regimens and dosing.

Regimen	Dosing
CyBorD induction	Bortezomib 1.5mg/m^2 SC Cyclophosphamide 300mg/m^2 PO Dexamethasone 40mg PO All given on days 1, 8, 15 and 22 of 28-day cycle
VTD induction	Bortezomib 1.5mg/m^2 SC, days 1, 8, 15 and 22 Thalidomide 50–100mg daily PO Dexamethasone 40mg PO, days 1, 8, 15 and 22 28-day cycle
Modified RVD consolidation	Bortezomib 1.5mg/m^2 SC, days 1, 8, 15 and 22 Lenalidomide 10mg daily PO, days 1–21 Dexamethasone 20–40mg PO, days 1, 8, 15 and 22 28-day cycle

from STaMINA trial (on as-treated analysis), have shown improvements in PFS for patients treated with tandem ASCT over single ASCT in patients with high-risk cytogenetic abnormalities.[9,10] However, in the EMN02 trial this difference did not reach statistical significance. The definitions of high-risk disease were different between these two trials and the number of patients with high-risk cytogenetic was small. The subgroup analysis showed the PFS improvement to be significant in those with 17p deletion (del17p) in the EMN02 study, while the benefit in other high-risk groups have yet to be published.[9] There does not appear to be an OS difference between tandem or single ASCT.[9,10] Based on these results, the group is recommending tandem transplant for patients with del17p by fluorescence in situ hybridisation (FISH). Tandem ASCT is currently not uniformly recommended for other high-risk patients based on clinical or genetic factors, due to a lack of strong evidence supporting this approach and potentially increased toxicities. However, this should be reviewed on an individual patient basis.

Most international guidelines are moving away from using chronological age to determine transplant eligibility. Instead, assessment should be based on biological age, performance status and coexisting comorbidities. Multiple retrospective studies have shown the feasibility of ASCT in elderly patients to achieve equivalent survival outcomes compared to younger patients.[11,12] Although toxicity during ASCT appears to be increased in the older transplant patients, including length of hospital stay and infection, transplant related mortality is reported to be between 1% and 1.5%, which is comparable to the younger population.[13,14] The definition of elderly differed between trials but generally used cut off between 65 to 70 years of age. It is worth noting that these evidences are mainly based on large retrospective analyses, and therefore an inherent bias cannot be excluded. Consideration should be given to reduce the conditioning melphalan dose to 140mg/m^2 in older or frailer patients, but this should also be balanced against treatment efficacy, as the reduced dose may compromise outcomes in patients with suboptimal response prior to ASCT.[11,15] Assessment using tools like the haematopoietic stem cell comorbidities index has been shown to correlate with survival outcome and may aid in patient selection and decisions on conditioning intensity.[16]

Post-transplant consolidation therapy

In New Zealand, bortezomib-based consolidation has been given to patients, as maintenance therapy was not available and bortezomib was funded for up to nine cycles in the front-line setting. Recently, lenalidomide maintenance has become available, prompting a review of the need for consolidation therapy.

When conventional chemotherapy was used as induction and maintenance therapy was not given, consolidation with proteasome inhibitor (PI)- or IMiD-based regimens have been shown to deepen responses and improve PFS outcomes, although no consistent OS benefit has been demonstrated.[17–19] However, in the era of novel agent-based induction treatment and post-ASCT maintenance, the role of consolidation is less clear. In the STaMINA trial, there was no advantage of RVD consolidation compared to patients who received single ASCT followed immediately by lenalidomide maintenance.[20] The EMN02 trial showed consolidation therapy improves PFS in the upfront setting, but the follow-up is too short at this stage to determine if this benefit is maintained in the ASCT cohort.[9]

As the benefit of consolidation therapy in the post-ASCT setting is unclear at this stage, its routine use is not supported by the group. However, it remains a valid option for patients who have a high-risk disease or suboptimal response. Traditionally, up to four cycles of consolidation were given post ASCT in New Zealand. In more recent international trials, if consolidation therapy is included, two cycles are typically used. Based on these factors, we propose that if consolidation is to be used, it can be given for two to four cycles. One proposed consolidation regimen is the modified RVD regimen (Table 1). Although this modified regimen has not been tested in prospective studies, it has the same bortezomib and lenalidomide dosing schedule as other commonly used anti-MM regimens in New Zealand.

The dose of 10mg of lenalidomide was proposed, as this would still fall within the latest PHARMAC Special Authority funding criteria for lenalidomide maintenance. The group will aim to collect data on the use of this consolidation regimen and its impact on patient outcome.

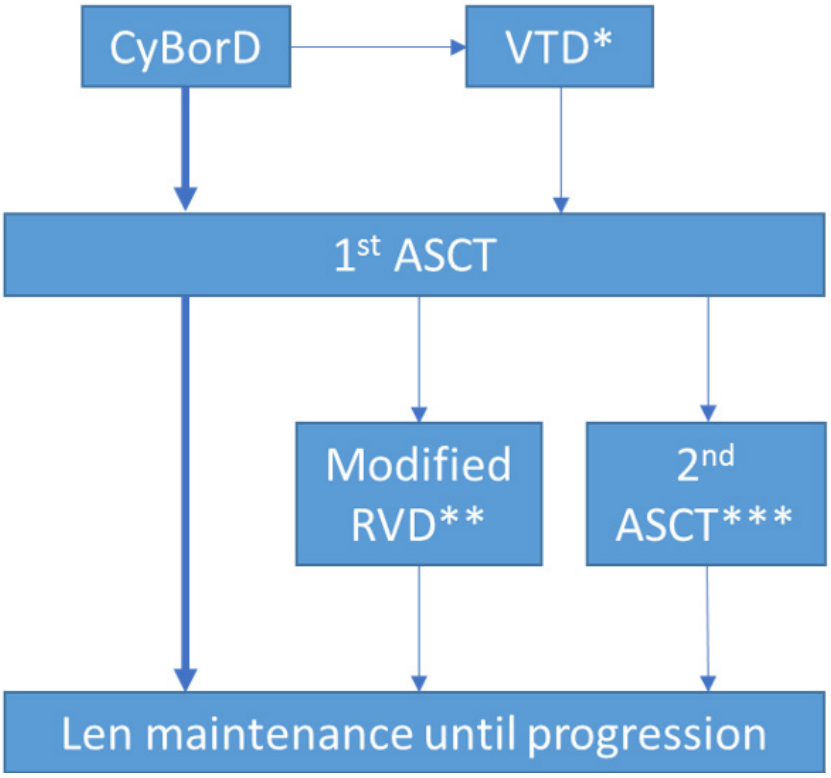
Maintenance therapy

Lenalidomide maintenance has become the standard of care as part of front-line therapy, based on results of multiple trials showing that it deepens responses, which translates to a PFS benefit, although OS benefit is less consistently shown.[21–25] The benefit is particularly seen in patients who have not achieved a complete response prior to maintenance; however, patients who are minimal residual disease (MRD) negative also benefited.[24,26]

Not all trials included baseline cytogenetic results, and therefore the evidence for patients with high-risk cytogenetic abnormalities has been less robust. In a meta-analysis and the Myeloma XI trial, there appears to be PFS benefit for those with high-risk cytogenetic compared to observation.[24,25] Based on these results, lenalidomide maintenance should be recommended for all patients post ASCT unless there is a contraindication.

Lenalidomide maintenance therapy can be started up to six months post ASCT, as per the current funding criteria, although in the studies it was generally started around 100 days after the ASCT. Lenalidomide should be continued until disease progression or if patients experience intolerant side effects. Recent data suggest that a shortened length of maintenance compromises outcome.[10] There is a small increase in secondary malignancies, but the benefit outweighs this risk.[21,24,25]

Figure 1: Treatment pathway for transplant-eligible, newly diagnosed multiple myeloma patients.



*May consider VTD induction for younger patients (<65) or those with a suboptimal response to CyBorD.
** Modified RVD maybe considered for patients who have a suboptimal response to ASCT (ie, less than VGPR) or have high-risk clinical features.
*** Tandem/double ASCT maybe considered for patients with high-risk FISH cytogenics

PI-based maintenance strategies have been investigated in clinical trials. In HOVON-65/GMMG-HD4, bortezomib-based maintenance improved outcome particularly for patients with high-risk cytogenetic.[27] However, the standard arm used conventional chemotherapy for induction versus bortezomib-based induction, making it difficult to determine whether the improved outcome is solely due to bortezomib maintenance. There is no randomised controlled trial comparing a PI-based with an IMiD-based maintenance strategy. Retrospective single-centre data suggest they may be equally efficacious, especially in high-risk cytogenetic patients.[28,29] Based on the currently available data, bortezomib maintenance therapy is not recommended routinely but can be considered for patients who cannot tolerate lenalidomide maintenance and have high-risk diseases. Ixazomib maintenance has been tested as post-transplant maintenance treatment in a prospective study. Although it has shown an improved progression-free survival compared with placebo, the degree of clinical benefit appears to be small.[30] Currently, this is not funded in New Zealand.

Conclusion

The treatment landscape of MM changes rapidly as evidence evolves. The increasing number of novel agents available continues to improve outcomes, although the cost is making public funding difficult in many countries. The New Zealand Myeloma Interest Group has formed the above consensus recommendation (Figure 1) based on best available evidence and modified to suit the New Zealand setting.

Competing interests:
Dr Romeril reports grants from Celgene, outside the submitted work.
Dr Chan reports grants, personal fees and non-financial support from Janssen, non-financial support from Celgene, personal fees from Abbvie, non-financial support from Amgen, outside the submitted work.

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Why does Pharmac neglect inflammatory bowel disease?

Andrew McCombie, Malcolm Arnold, Marian O'Connor, Richard Stein, James Fulforth, Belinda Brown, Richard Gearry

Crohn's disease (CD) and ulcerative colitis (UC), collectively known as inflammatory bowel disease (IBD), are chronic, incurable, inflammatory diseases. Symptoms are severe and include bloody diarrhoea, abdominal pain, fatigue and inflammation in the anal area; extraintestinal comorbidities can also occur, including arthritis, liver disease, iritis and skin lesions. CD and UC follow a relapsing and remitting course and in times of flare can lead to hospitalisation, often coupled with abdominal and perianal surgery, followed by varying periods of recovery. New Zealand has the third highest prevalence of IBD in the world,[1] and the incidence is still increasing.[2,3] A burden-of-disease report published in 2017 reported that IBD costs New Zealand an estimated $245,000,000 in healthcare costs and lost productivity.[1]

What IBD treatments are presently available in New Zealand?

Treatments for IBD have improved over recent years, moving from corticosteroids to immunomodulators (such as azathioprine, mercaptopurine and methotrexate) to biological therapies. Biological therapies, such as the anti-tumour necrosis factor (anti-TNF) drugs infliximab and adalimumab, have made a significant difference to the lives of patients with IBD.[4,5] For many this has reduced steroid use, hospitalisation and surgery. However, not everyone responds to anti-TNF drugs, and others lose response after a period of time due to anti-drug antibodies and refractory disease.[6]

Patients who lose response to anti-TNF drugs are left with few medical options. Enduring ongoing symptoms leads to a reduced quality of life, a reduced ability to attend education and work and an increased healthcare utilisation. Many patients will require a bowel resection and some will require a permanent stoma, often at a young age.

Faced with few other options, New Zealand gastroenterologists often trial double dosing of either infliximab or adalimumab when patients lose response to standard doses. This can be effective for some but incurs a doubling of cost and an increased risk of adverse effects. Furthermore, many patients may not respond completely.[7]

What other options are available?

Internationally there are numerous other drugs available (Table 1) for the treatment of IBD. Many of these drugs are funded by countries with a lower OECD ranking than New Zealand. The two most established drugs are ustekinumab (approved in New Zealand by Medsafe in early 2018) and vedolizumab (currently awaiting Medsafe registration). Importantly, these drugs have a different mechanism of action to the anti-TNF drugs, meaning that patients who do not respond to an anti-TNF drug will be more likely to respond to either ustekinumab or vedolizumab, rather than another anti-TNF drug. Ustekinumab blocks the interleukin (IL)-23/12 receptor, leading to a reduced inflammatory response. Vedolizumab provides gut-specific immunosuppression by blocking α4β7 integrin, leading to a reduction in leucocyte trafficking to areas of inflamed gut. Both

drugs have been shown to be safe, efficacious and cost effective, including in patients who have lost response to anti-TNF drugs. They are available and funded in most western countries.

Despite compelling Phase 3 trial efficacy and safety data,[8–11] multiple supportive cost utility analyses[12–14] and real-world data from many countries,[11, 14–16] New Zealanders with IBD do not have access to these drugs. Furthermore, despite positive recommendations from the Pharmacology and Therapeutics Advisory Committee's Gastrointestinal Sub-committee (which exists to provide objective evidence to Pharmac)[17,18] and intensive lobbying from the New Zealand Society of Gastroenterology, Crohn's and Colitis New Zealand and the New Zealand IBD Nurses Group, Pharmac refuses to fund these drugs.

How does this compare to other diseases?

Pharmac has been celebrated as a successful organisation that has reduced the cost of buying pharmaceuticals for New Zealanders. However, there is also a dark side to the current Pharmac decision-making model for drug funding. There are now major inequities in access to drugs for different diseases. Over time, the lack of investment in new drugs has left New Zealand patients with some diseases worse off than others. For example, IBD is often grouped with a number of rheumatological diseases (eg, rheumatoid arthritis and ankylosing spondylitis) and psoriasis as immune-mediated inflam-

Table 1: Comparison of access to new drugs for IBD between New Zealand and other countries, including IBD incidence and prevalence.

Drug	New Zealand	Australia	United Kingdom	Canada	Spain	Israel
Infliximab	2007	2007	2002 (CD) and 2008 (UC)	2001	2000	2000
Adalimumab	2009	2008	2003	2004	2003	2008
Golimumab	Not funded	2017	2010	2013	2014	2012
Certolizumab	Not funded	Not funded	Not funded	Not funded	2014	2014
Vedolizumab	Not funded	2015	2015	2014	2015	2015
Ustekinumab	Not funded	2017	2017	2016	2017	2017
Tofacitinib	Not funded	Positive PBAC[1] recommendation likely 2020	2018	2018	2018	2018
Estimated IBD prevalence	0.5% (~)	0.3% (~)	0.5% (310,000)	0.7% (300,000)	Unknown	0.4% (35,000)
IBD incidence (cases/100,000)	39	37	26	52	35	30
OECD[2] ranking of gross domestic product per capita	20	10	16	15	24	22

[1]PBAC = Pharmaceutical Benefits Advisory Committee.
[2]OECD= Organisation for Economic Co-operation and Development.

matory diseases (IMIDs). As shown in Table 2, ongoing investment in treatments for rheumatological diseases and psoriasis has continued over time, whereas no new drug has been funded for IBD since 2009. This is despite the availability of new drugs and the documented multifactorial impact of IBD on patients and the healthcare system. Furthermore, in recent years the cost of infliximab and adalimumab have fallen substantially, with no reinvestment of the resultant savings into these diseases.

Unlike other IMIDs, IBD is a frequent cause of hospital admission, surgery and unplanned care, including emergency department visits. Furthermore, patients are, on average, younger than those with other IMIDs yet have at least as much disability, work impairment, educational disruption and psychological distress.[19] Recently, the paediatric IBD population was shown to be at an increased risk of suicide,[20–22] which aligns with similar reports for the adult population.[23]

What are the consequences of not funding new therapy?

As Pharmac ignores these mainstream treatments, it is patients and their families who are faced with less-desirable alternatives, including invasive surgery that often leads to permanent stoma, repeat hospitalisations, prolonged steroid use with associated adverse effects and, perhaps worst of all, a need to live with devastating and embarrassing symptoms that keep them away from work, study and social and interpersonal relationships. Despite patients with IBD having fewer educational opportunities and increased difficulty maintaining their employment and sometimes their relationships,[1] Pharmac continues to ignore these indirect costs.

Recently, a meeting was held between Dr Malcolm Arnold (President, NZSG), Professor Richard Gearry (gastroenterologist) and Pharmac staff via Zoom at 3pm on Monday 31 August 2020. It is telling that when questioned about the frequency of double dosing of infliximab for patients with IBD and how this would affect cost–utility analyses for new drugs, Pharmac staff admitted that they do not have these data and do not know how often double dosing occurs, nor whether it is effective. They did admit that double infliximab dosing would cost twice as much as standard dosing. It is disturbing that Pharmac continues to deny New Zealand patients effective treatments despite not having collected the crucial data on which to base these decisions.

Conclusion

In our opinion, at the very least, new medical therapies should be funded by Pharmac for patients who fail to respond to, or lose response to, anti-TNF therapy. Gastroenterologists, IBD nurses and patients in New Zealand have grown increasingly frus-

Table 2: Comparison of funded drugs for immune mediated inflammatory diseases in New Zealand.

Drug	Rheumatology (RhA, AS, JA)[1]	Dermatology (psoriasis)	Gastroenterology (IBD)
Infliximab	Registered by Medsafe in 2000. Individual DHB funding with variable use across specialties since mid-late 2000s		
Adalimumab	RA 2006; AS/PsA 2009; JA 2013	2009	2009
Etanercept	<2003	Not effective	Not effective
Rituximab	2013	Not effective	Not effective
Tocilizumab	JA 2013; RA 2014	Not effective	Not effective
Secukinumab	Not effective	2018	Not effective (may worsen)

[1]Rha=Rheumatoid Arthritis; AS=Ankylosing spondylitis; JA=Juvenile arthritis.

trated with the treatment of IBD being well behind the rest of the western world and the inequity with which IBD is treated compared with other diseases in New Zealand. A petition "That the House of Representatives urge the Government to provide funding for the drug ustekinumab to be made available to those New Zealanders with severe Crohn's disease and ulcerative colitis, for whom all other funded medical treatments have failed" (https://www.wecantwait.nz/) has so far garnered more than 30,000 signatures in less than two months. This was presented to parliament on 2 December 2020. It is time for patients with IBD, and the medical practitioners who endeavour to provide them with expert care, to be able to access treatments that are routinely available in other countries and for Pharmac to be held to account for the decisions they make and the way in which they make them.

Competing interests:
Nil.

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Training clinicians to lead clinical IT projects

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ABSTRACT

Across New Zealand, a huge programme of work is being initiated to improve the health information systems of our sector. The goals of this plan are to address major risks and issues such as cybersecurity and our inability to securely share health data across organisations for clinical care. To fulfil the promise of planned health IT initiatives, we must involve clinicians of all disciplines to help lead, design and implement projects. However, there is currently little pragmatic training available for clinicians to learn how to do so. In 2019, Waitematā District Health Board and the National Institute for Health Innovation developed and delivered a 'hands-on' Clinical Digital Academy training programme for multidisciplinary clinicians. This paper describes the programme, the initial cohort's evaluation feedback and recommendations for the future.

Digital health has evolved rapidly over the last two decades, creating enormous potential to transform the healthcare sector. The Ministry of Health is developing a national Digital Health Strategic Framework[1] and is currently working on enabling digital health systems across the country. The Ministry of Health has also measured the country against the Global Digital Health Index,[2] showing that one of the areas of weakness within the index is training of the workforce. Across the Northern Region, we have an extremely large portfolio of planned clinical IT projects, underpinned by a regional Information Systems Strategic Plan (ISSP) that sets the direction for information communications technology platforms and services that support new models of care and better health outcomes for the people in our region.[3]

At Waitematā District Health Board (DHB), our experience is that clinical leadership is required to be involved in the design and implementation of clinical IT systems. IT systems need to enable and improve the clinical workflow and hospital processes that they support. They must be designed to make clinicians' jobs easier, rather than adding more steps that clinicians either do not perceive to be of benefit or cannot make work as part of clinical care.

To guide this design and development, clinicians who understand the processes and workflows need to be involved. Shepherding in these changes and the move to digital tools also need to be led by active clinicians. These people can work with frontline staff, understand their concerns and show clinicians how to get the best out of their IT systems. Many clinicians are interested in being a part of this but may not have the confidence, skills or opportunities to do so.

Internationally, it has been recognised that undergraduate and postgraduate health-professional training in health informatics has been limited,[4,5] and that a consistent approach and a clear framework for clinical informatics/IT leadership roles is going to be required for the future.[6–8]

We found there was a lack of practical options for training multidisciplinary clinicians in the skills that may be required to lead clinical IT projects. Existing (at that time) university-based postgraduate degrees in health informatics or IT professional courses did not include the hands-on systems used in DHBs or practical learnings from those actively leading clinical IT projects in our health sector. Certification systems (such as Certified Health Informatician Australasia (CHIA)) or professional

ISSN 1175-8716

bodies (such as the Australasian College of Health Informatics (ACHI), now the Australasian Institute of Digital Health (HISA)) were not always appropriate for all clinicians or considered feasible within the DHB context. Clinicians other than doctors can also find it difficult to get time and funding for external education programmes. As a result, we decided to develop the Clinical Digital Academy (CDA) for clinicians in our DHB.

Our intention is to develop a clinical IT/informatics workforce that can lead clinical IT change within the health sector. In doing so, we recognised that clinical IT/informatics leaders are:

- from all clinical disciplines within the health sector
- able to lead clinical change enabled by health IT/technology and bring clinical services and teams along on the journey
- the bridge between clinical expertise and workflows, health-sector experience and IT
- trained in basic informatics, IT and digital health
- recognised in the DHB as advocates for improving clinical workflows, patient outcomes and patient/whānau experience.

Waitematā DHB Clinical Digital Academy (CDA)

A block course was co-designed and developed between the DHB's Institute for Innovation and Improvement (i3) and the National Institute for Health Innovation (NIHI), which is part of UniServices at the University of Auckland.

We started with a review of existing clinical informatics competency domains from several international bodies[4,9–11] and combined them with our own learnings and expertise on leading clinical IT change within the organisation and beyond. A first draft of content topics was reviewed by the participants, who provided input into the design of the course and the learning objectives. The final agreed learning objectives were that participants would learn to:

- converse across clinical, operational and IT domains, particularly in the systems used at our DHB
- assess and use the DHB's health data to inform clinical practice and improvement projects
- consider ethical, equity, privacy and security concerns around the use of IT, technology and health data
- develop new IT/technology developments and projects using appropriate design methods and processes that are aligned with the DHB's digital health service vision
- manage clinical change enabled by IT/technology
- evaluate the impact of IT/technology projects.

The week-long block course consisted of six modules that covered: vision and context; health information systems; data visualisation and analytics; design and evaluation; leading clinical IT change; ethics; and future considerations. Table 1 provides a summary of the course content. The course was facilitated by four key DHB and NIHI experts, and sessions were taught by clinical and topic experts both locally and internationally, including clinical IT leaders, IT professionals, DHB decision makers, data analysts, academics, senior physicians, primary care clinicians and experts in specific fields such as ethics. At the conclusion of the week, participants we expected to submit a proposal for a clinical IT project within their service by incorporating the learning from the week. This was assessed and feedback was given by the CDA facilitators.

Evaluation of the first CDA

The CDA was run in September 2019. The initial cohort of CDA participants were selected from DHB clinicians who had previously indicated their interest in IT and informatics, or who applied to attend through their line managers and clinical heads. The 15 participants included senior and junior medical officers, allied health professionals and nurses from community, hospital and primary care settings. Prior to completing the course, the CDA participants

Table 1: Topics covered during the CDA.

Module	Topics covered
1. Vision and context	Overview of the national, regional and DHB digital health vision for the future, including recent and planned projects, successes and failures in the past, introduction to the people, roles and responsibilities
2. Health information systems	DHB information systems ecosystem and data flows from collection to storage to extraction for use, including interoperability and quality issues and primary care information systems
3. Data visualisation and analytics	Practical sessions on building forms and data analytics using DHB tools
4. Design and evaluation	Engagement with end users, co-design methods, digital development pathway, formative research methods, evaluation and approval pathway for clinical apps, research methods and evaluation and monitoring for digital tools
5. Leading clinical IT change	DHB project processes and tools, business-case process, costings and benefits measurement, risk assessment and mitigation and leading clinical IT change projects, including communication and training, adoption of technology and sustainability
6. The future and other considerations	Equity, ethics, data sovereignty, privacy, cybersecurity, AI, big data, social media, telehealth/virtual consults and automation/robotic processing

were asked about their confidence in using health IT and leading IT-enabled clinical change, and their understanding of health information systems.

Immediately following completion of the CDA, participants completed an anonymous online evaluation of the programme via REDCap (n=15). The purpose of this evaluation was to:

- gain feedback on participant experiences
- assess the perceived impacts of the programme and changes in understanding and confidence related to health systems and clinical IT
- obtain suggestions for how the CDA could be improved
- seek interest in further training and fellowship positions.

Quantitative data were analysed and summarised using descriptive quantitative analyses, including means, standard deviations and proportions. Qualitative comments were analysed using a simple, general-inductive thematic approach to identify common themes and meanings from the data.

Participants said the strengths of the course included: the content (breadth of topics, emerging topics, practical toolkits, focus on clinician-led projects); the calibre and multidisciplinary nature of presenters ("wealth of knowledge and experience", "speakers were dynamic and relevant", "the interaction between speakers"); the mix of talks and practical sessions; the diversity within the class; and the culture (informal, conducive to discussions, energetic, flexible, integrated, interested, open to feedback and

ideas). All participants stated they would recommend the CDA to their colleagues. Thirteen (87%) participants said that running the course full time over one week was a good way to run the course and stated that this structure was the best for getting time off from clinical duties, that it was good for building momentum and knowledge and that it allowed time to get to know other participants.

During the CDA, we used an online discussion forum as a place to continue conversations, ask questions, share documents and ask students to rate the content of each day. Although the format of this forum was identified in the evaluation as not ideal, participants appreciated having such a shared space.

The questions assessing confidence in using health IT and leading IT-enabled clinical change and their understanding of health information systems asked before the CDA were repeated in the evaluation. Mean ratings can be seen in Table 2. Participants' self-rating of their level of confidence in using health IT and leading IT-enabled clinical change increased significantly after the course. Students' self-rated level of understanding of regional ISSP and DHB health information systems also significantly increased after the course; however, it was still not particularly high. For example, the mean level of understanding of the DHB health information systems rose from a mean of 2.55 (indicating knowledge of the existence of the system) to a mean of 3.47 (indicating familiarity with, and an ability to answer questions about, the systems).

All participants (n=15; 100%) reported that the course had inspired them to do more training or take up other educational opportunities in the area. All participants (n=15; 100%) also said that, if it were available, they would want more training in the area. The areas they identified that they were interested in additional training included: data analytics; SQL database; form creation/building; creation of test plans; smartphone app development; clinical IT generally; and business case/proposal writing.

A total of eight (53%) of the CDA participants reported they were potentially interested in completing formal postgraduate (tertiary) courses in this area. The remaining seven (47%) said they were not, for reasons such as lack of time, no perceivable benefit and it being too much of a commitment. Less than half (n=7; 47%)

Table 2: Change in rated levels of understanding and confidence.

	Pre course (n=11)		**Post course (n=15)**		**p**
	Mean	**SD**	**Mean**	**SD**	
Participants' ratings of their level of understanding (1=no understanding, 2=knowledge of the existence of the system, 3=familiar and can answer questions, 4=daily interaction, 5=expert)					
Of the regional ISSP	1.64	1.03	2.64	0.84	0.013
Of DHB health information systems	2.55	1.04	3.47	0.74	0.014
Of the DHB data/business intelligence tool	2.64	1.12	3.13	0.83	0.206
Participants' ratings of their confidence (1=no confidence, 5=extremely confident)					
In the use of health IT in their job	3.09	0.94	4.07	0.59	0.004
In leading IT-enabled clinical change in their service	2.91	1.14	4.00	0.65	0.005
In leading IT-enabled clinical change in a different service	2.09	0.83	3.20	0.56	<0.00

reported that they are interested in applying for accreditation in the area.

In regards to ongoing networking, participants identified the following as important aspects: regular scheduled networking events/meet-ups (n=8); opportunities for collaboration, sharing ideas, helping others and getting assistance and feedback (n=9); and updates from participants (n=2).

Conclusion and next steps

Waitematā DHB's CDA can be seen as a successful first foray into the practically focused training of clinicians in health IT within the health sector in New Zealand. Clinicians were hungry for further training and appreciated the practical, hands-on focus with our clinical IT leaders. Participants also indicated that they were inspired by the CDA to take up further challenges.

It was always planned that the block course would be followed by a number of 12-month Clinical Digital Academy Fellowships—part-time roles to lead clinical IT projects with the support and mentorship of the i3 and the DHB's Health Information Group. Two graduates of the programme have taken up these fellowship positions. Furthermore, three graduates have been supported to take up other digital roles within i3 or the health service. There are three graduates that report actively leading digital initiatives in their services, and others report promoting the use of digital systems within their clinical roles.

Although developed for the context of Waitematā DHB, the CDA could be used as a model for other DHBs and health-sector settings. As described, our course is a mixture of digital health education and local practical experiences. The balance of university and local organisational expert teachers would need to be adapted for different contexts.

However, much more than the CDA is required. Digital health needs to be included in all clinical professional training from undergraduate level onwards.[4–7] It is our view that it also needs to be included in all ongoing education programmes within our health services to lift the overall level of digital literacy and confidence of all staff. This is recognised in the Global Digital Health Index, where two of the 19 indicators are about digital health being integrated in health and health-related professional pre-service training and in-service training.[2] New Zealand (scored by the New Zealand Ministry of Health in May 2018) rated itself as Phase 3 for workforce indicators overall (out of 5), stating that less than 25% of health and health-related professionals have digital health in pre-service training curricula, and a digital health curriculum is "proposed and under review" as part of in-service training for health professionals in the workforce.

It is planned that the CDA will be run at Waitematā DHB at least annually to continue to grow the number of clinicians with digital expertise within the DHB. In light of the huge gains that have been made as part of the response to the COVID-19 pandemic, we envisage that this type of training will be even more relevant to our health workforce going forward.

Competing interests:
Dr Dobson reports grants from Waitematā District Health Board during the conduct of the CDA. Robyn Whittaker and Rosie Dobson work for the National Institute for Health Innovation, Auckland UniServices Ltd, which may in the future receive further funding to deliver the CDA.

Acknowledgements:
We wish to acknowledge all of those who participated in teaching and provided support throughout the CDA (Dale Bramley, Karen Bartholomew, Kevin Blair, Stuart Bloomfield, Andrew Cave, David Grayson, Peter Groom, Will Hewitt, Jono Hoogerbrug, Judith McCool, Elna Meller, Karen Nelson, David Ryan, Vanessa Selak, Chris Southen, Rochelle Style, Jonathan Wallace, Eric Topol and Ted Adams) and our initial cohort of participants in the CDA.

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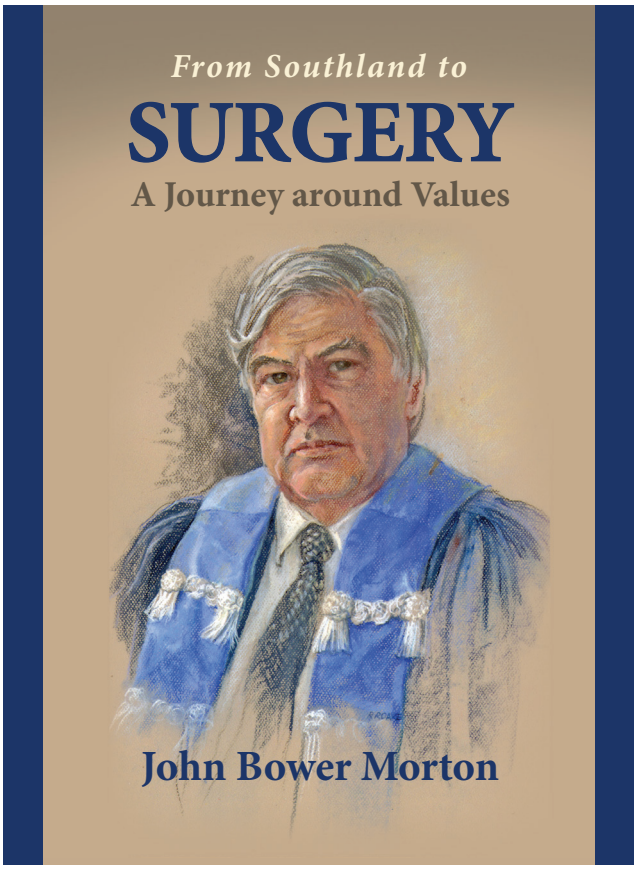
ISSN 1175-8716

From Southland to Surgery: A Journey around Values

Richard Acland



John Bower Morton. Published by the Cotter Medical History Trust, 2020. ISBN 9780473543402. Contains 154 pages. Price NZ$30.00. Available at www.cottermuseum.co.nz or PO Box 2301 Christchurch 8140.

Professor John Morton has not only written an intriguing catalogue of the Christchurch surgical scene in the latter part of the 20th century, but has also provided a well-considered philosophy for medical care.

In his preface, he highlights the challenges of writing an autobiography. ‘The style I have adopted attempts to break from the freeze-dried mode of scientific writing in which humanistic excursions are not relevant, and confession is a sign of weakness and self-indulgence.’

The book is both a memoir of his early rural Southland life, and his life in medicine.

He was an academic surgeon who promoted wisdom: ‘I believe that it is more important to train budding surgeons to think, rather than teaching techniques.’

Not only was he at the forefront of the Renal Transplant Service in Christchurch,

but also the development of the subspecialty of peripheral vascular surgery.

He provides some fascinating anecdotes about special patients as well as his relationship with key surgeons; but, disappointingly, no operating theatre anecdotes, nor any reference to anesthetic colleagues.

The book does detail some of the impressive surgical developments that occurred during this time, not least the introduction of laparoscopic surgery.

He witnessed the evolution of surgical practice in Christchurch from a robust system dominated by Christ's College educated visiting practitioners to a more academically focused department of full-time surgeons.

John's surgical career was cut short by a stroke, and as a result he redirected his energies into nonsurgical matters. He highlights his professional relationships with key personnel where many impressive goals were achieved, not least the reconfiguration of the RMO out-of-hours roster. He had a keen interest in the evolution of medical ethics, a subject he taught with passion at the clinical school.

Canterbury has reaped the rewards of having this impressive man devote his career away from his Southland heritage.

I congratulate Professor Morton on writing this book, an excellent reference for those with an interest in the wider aspects of medical care.

Competing interests:
Nil.

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www.nzma.org.nz/journal-articles/from-southland-to-surgery-a-journey-around-values

The Dunedin Hospital Appeal for Radium

December 1920

The honorary medical staff of the Dunedin Hospital are making a public appeal for funds in order to provide an adequate equipment in the radium and X-ray department.

The response to the appeal has been gratifying; the X-ray department will be brought thoroughly up to date, and a considerable sum of money, which, with the Government subsidy, now amounts to about £3000, will be available for the purchase of a further supply of radium. When that purchase is completed the Dunedin Hospital will have about £5000 worth for the treatment of patients.

A much larger supply, however, is hoped for. The results of radium treatment at the Dunedin Hospital have been decidedly encouraging, and with increasing experience successes are multiplying and disappointments diminishing. The staff aim at establishing a radium institute available for use by patients from all parts of the Dominion. Those who can afford it will be charged a moderate fee for services rendered; those in poor circumstances will receive treatment gratuitously.

Dr. Robert Jack, Professor of Physics at the Otago University and Consulting Physicist to the Dunedin Hospital, is at present on a visit to Great Britain, and has been authorised to make the purchase of radium, and also to obtain all necessary information regarding the installation of an outfit for collecting and storing radium emanation, so that a larger number of patients will be able to be treated simultaneously, and medical practitioners at a distance can have emanation tubes forwarded to them for the purpose of treating cases who do not wish to come to Dunedin.

The larger the stock of radium, the more successful will be the Dunedin Hospital in dealing with the ever-increasing number of cases which can be benefited by radium treatment. The Medical School also will undoubtedly reap the obvious advantage of having a busy radium clinic closely connected with it.

A number of practitioners, in the Otago district particularly, have indicated their sympathy with the movement by subscribing to the fund amounts varying from one hundred pounds to one guinea, and it is thought that many wellwishers in other parts of the Dominion, especially those who have been connected with the Medical School, would like to give something to the fund.

Donations will be thankfully received by Dr. L. E. Barnett, of Dunedin, Chairman and Treasurer of the Radium and X-Ray Committee.

The money collected now amounts to about £1700, and the Government gives a subsidy of 24s. for every pound.

URL:
www.nzma.org.nz/journal-articles/the-dunedin-hospital-appeal-for-radium

Proceedings of the 251st Otago Medical School Research Society PhD Student Speaker Awards

Type 2 diabetes is associated with increased activation of brain regions that regulate sympathetic drive to the heart

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Aim

Type 2 diabetes mellitus (DM) might cause serious heart complications. The heart is partly controlled by the brain via the parasympathetic and sympathetic nervous systems, but although increased sympathetic drive to the heart is observed in DM, the brain regions responsible are unknown. Beta-blockers and other current therapies for heart complications target the heart instead of the sympathetic drive from the brain, and they are less effective in DM than non-DM individuals. We therefore aimed to determine whether DM is associated with altered neuronal activation patterns in the main brain regions regulating sympathetic drive to the heart, namely, the rostral ventrolateral medulla (RVLM), the hypothalamic paraventricular nucleus (PVN) and the nucleus tractus solitarius (NTS). We hypothesised that there would be higher activation of neurons in each of these regions in DM.

Method

In the brains of 20-week-old male DM and non-DM Zucker Diabetic Fatty rats, double-label immunohistochemistry was performed for ΔFosB (a marker of chronic neuronal activation) and tyrosine hydroxylase (TH, a marker of sympathetic neurons) in the RVLM and NTS, and for ΔFosB and either oxytocin, vasopressin or corticotrophin-releasing hormone in the PVN. Data were analysed using unpaired t-tests and all results are expressed as mean ± SEM.

Result

More activated TH-positive neurons were observed in the RVLM of DM (9±1, N=10) compared to non-DM rats (3±0, N=8; P<0.001), and more activated corticotrophin-releasing hormone-positive neurons were observed in the PVN of DM rats (DM: 74±3, n=8 vs non-DM: 59±5, N=7; P<0.05). Moreover, there was increased labelling of ΔFosB in the NTS of DM (25 ± 4, N = 10) compared to non-DM rats (15±2, N=8; P<0.05).

In conclusion, this is the first study to show that DM is associated with higher activation of neurons in brain regions regulating cardiac sympathetic drive. Understanding the alterations in central neural circuits that are activated in DM may eventually lead to more effective pharmacological therapies for diabetic heart disease.

Improved gene transfer for the treatment of neurological disease using modified viral vector AAV-PHP.eB

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Aim

Methods that effectively deliver therapeutics to the central nervous system (CNS) are crucial for the treatment of neurological diseases. The use of adeno-associated viral (AAV) vectors for gene therapy is appealing, as some vectors can cross the blood-brain barrier, allowing them to be administered via minimally invasive methods that are feasible for translation to humans. A novel AAV vector evolved from AAV9 in-vivo, AAV-PHP.eB, has been reported to produce more effective CNS transduction than AAV9 in some strains of mice, but not in others. The present study compared the efficacy of two AAV vectors, AAV-PHP.eB and AAV9, in targeting mouse CNS and peripheral tissues after administration via various routes, and in two genetically diverse mouse strains.

Method

C57BL/6 mice were administered a combination of AAV-PHP.eB and AAV9 encoding different coloured fluorescent reporter proteins, either by intravenous injection (N=9), intranasal injection (N=6), or intrahippocampal injection (N=5). B6C3 mice (N=4) received the same vectors via intravenous injection. Four weeks after vector administration, tissue sections were examined for reporter protein expression and cell-type transduction.

Result

In C57BL/6 mice, AAV-PHP.eB led to higher brain transduction than AAV9 ($P<0.05$, t-test), but lower liver transduction. However, both vectors produced only minimal brain transduction in B6C3 mice. The two vectors also showed equal transduction efficiency after intrahippocampal and intranasal injection. AAV-PHP.eB transduced more neuronal than glial cells ($P<0.05$, t-test).

Modification of AAV vectors to improve CNS transduction may be a viable method for overcoming the challenges of invasive administration. However, there appear to be critical blood brain barrier differences, even between mouse strains, that determine the transport of vectors from the bloodstream to the CNS. These findings highlight the need for vectors modified to suit specific features of the human blood-brain barrier for treatment of human disease.

A crossover comparison of four cardiopulmonary exercise testing modalities in severe lower-limb osteoarthritis patients

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Aim

Cardiopulmonary exercise testing (CPET) is the gold standard for assessment of cardiorespiratory fitness (VO_{2peak}). Preoperatively, it is used to risk stratify and guide perioperative patient care. Traditionally performed on a cycle, preoperative CPET is difficult for the approximately 10% of New Zealand adults with lower-limb osteoarthritis (OA). The arm ergometer is an alternative modality, utilising the upper body only. However, in healthy individuals, VO_{2peak} can be ~30% lower, compared to cycling. The purpose of this study was to compare CPET variables and subjective responses on four different exercise modalities, in patients with OA scheduled for hip or knee arthroplasty (THA/TKA).

Method

In this crossover (within-participants) study, fourteen participants (10 female; age=68±7y; body mass index-=31.4±4.3kg.m-2) scheduled for THA (N=5) or TKA (N=9) completed CPET on a cycle, treadmill (TM), cross trainer (XT) and arm ergometer (AE). VO_{2peak}, peak heart rate (HRpeak), and pain scores (rated 0–10) were measured, then analysed using a repeated measures analysis of variance.

Result

VO_{2peak} was greater on the TM, XT and cycle (21.7±4.7, 21.2±4.3 and 19.6±4.4 ml.min-1. kg-1, respectively) compared to AE (15.7±3.8 ml.min-1. kg-1; $P=0.001$). HRpeak was higher on the XT than AE (150±17 vs 137±15 beats.min-1; $P=0.001$), but not different to cycle or TM modalities (145 and 141 beats.min-1 respectively, $P>0.48$). Peak exercise pain scores were lower on AE (1.7±2.1), compared with TM, XT and cycle (4.5±3, 4.5±2.6 and 4.3±2.9; $P=0.01$ vs. AE).

Pain scores were higher during CPET using the lower limbs (TM, XT and cycle), compared to AE, in patients scheduled for THA/TKA. Despite this pain, VO_{2peak} was higher on these lower-limb modalities, compared to AE.

An old drug for new tricks; metformin as a chemotherapeutic agent for lung cancer.

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Aim

Crizotinib is an effective first-line therapy for the treatment of EML4-ALK+ lung cancer. However, resistance usually develops after one year. Epidemiological studies have shown that the diabetes drug metformin was associated with a reduced incidence of cancer. Previous in vitro work also found that metformin acts synergistically with low concentrations of crizotinib to reduce cell viability in H3122 ALK+ lung cancer cells. This study aimed to examine if the in vitro synergism translated in vivo in a xenograft lung cancer model. The toxicity of the drug combination was also examined.

Method

Tumor-bearing Nu/J mice received daily administration of vehicle (olive oil), metformin (100 mg/kg), crizotinib (25 mg/kg) or the combination, orally for 14 days (6-7/group). Tumor volume was measured daily. For toxicity testing, Balb/c mice received the same treatment regimen. Full necropsies were performed following the completion of both studies.

Result

Metformin, crizotinib and the combination significantly decreased tumour volume compared to vehicle (612, 424 and 552 vs 943 mm3, respectively). It was also hypothesized that metformin would increase crizotinib concentrations via inhibition of CYP3A4, but no treatments resulted in a CYP3A4 activity change compared to vehicle. This supports the combination efficacy finding, whereby combining the drugs did not enhance tumor suppression as metformin does not increase crizotinib plasma concentrations. All treatments produced no toxicity, as

shown by ALT and creatinine plasma levels under the normal threshold.

All drugs were efficacious in reducing the tumour growth rate; however, the combination had no additional therapeutic benefit compared to crizotinib alone. Nevertheless, metformin alone had a significant decrease in tumor volume compared to vehicle, proving efficacy in vivo and should be considered as a potential chemotherapeutic agent. This finding provides justification to further examine the value of metformin in cancer therapy.

Proactive provision of long-acting reversible contraception to New Zealand adolescents.

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Aim

New Zealand adolescents are at risk of unintended pregnancy by not routinely using contraceptives, or using methods with higher failure rates. Adolescents face barriers accessing most forms of contraception, including long-acting reversible contraceptive (LARC) methods. Addressing the barriers could improve uptake of effective methods of contraception, reducing the risk of unintended adolescent pregnancy. On these grounds, we investigated the concept of proactive LARC provision, with tiered contraceptive counselling. Before assessing costs and feasibility of a proactive programme, we must determine the acceptability of such a programme. To gauge acceptability, we consulted with New Zealand adolescents (recipients) and New Zealand general practitioners (GPs) (providers). Our research questions were: (1) Would proactive provision of LARCs be acceptable to adolescents? (2) Would proactive provision of LARCs to adolescents be acceptable to GPs?

Method

We consulted female adolescents in four focus groups (FGs). We discussed topics of sexual health, contraception, and specifically discussed proactive LARC provision. We performed nine GP semi-structured interviews—these began with discussion of adolescent sexual health and contraception and then we discussed proactive LARC provision. We used a general inductive thematic analysis approach to analyse transcripts.

Result

The FG and GP participants were generally positive about the concept. Emergent FG themes were reproductive health fear, sex and body shame, adolescents' requirements for sexual health provision, barriers to contraception and sexual health knowledge. Emergent GP themes were contraceptive decision making, the GP role, sexual activity, social context, gauging adolescent understanding, and youth.

Our FGs and interviews indicate that the concept of proactive LARC provision is acceptable to both adolescents and to GPs. Proactive contraception provision to increase adolescent uptake of effective contraceptive methods is therefore a concept worth pursuing. Such an initiative would improve adolescents' contraceptive knowledge, and could decrease unintended teenage pregnancy by empowering adolescents to control their fertility in a way that suits them.

Rheumatoid arthritis patients' perspectives on tapering biologic therapy: a qualitative study.

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Aim

Implementation of 'treat-to-target' strategies aimed at achieving and maintaining tight disease control, and the development of biologic therapy targeting specific inflammatory mediators has made remission possible for many people with rheumatoid arthritis (RA). Based on the success of preliminary clinical trials, tapering of biologics has been increasingly advocated for the long-term management of RA patients on biologics in sustained remission. However, insights into the possibility of tapering biologics from the perspective of RA patients is lacking. This study sought to better understand RA patients' perceptions of tapering biologics.

Method

Participants diagnosed with RA and currently taking biologics participated in six focus groups (N=43) or individual interviews (N=2). Interviews and focus group sessions were audio-recorded and transcribed verbatim. Qualitative analysis of the transcripts was carried out using general inductive thematic analysis.

Result

Five themes emerged: fear of the uncertainty of outcome, trade-offs between quality of life and the risk of adverse effects, relief from medication burden, healthcare system support and preference for involvement in decision-making. Participants acknowledged tapering their biologics would provide some relief and freedom in their daily life but were fearful of disease relapse. They were willing to accept the risk of adverse effects associated with long-term biologic treatment in exchange for a better quality of life. When considering tapering, participants wanted assurance of access to treatment and consultation if a flare occurs. Furthermore, participants would prefer to be engaged in shared decision-making with their rheumatologist when making the decision to taper biologics.

Concerns of uncontrolled disease and prompt access to treatment when disease flares

are among the key issues that need to be addressed. Decision aids to support shared decision-making approach may facilitate a greater patients' understanding of the trade-offs between risks and benefits involved in tapering their biologic, leading to greater acceptance and adherence to treatment.

The effects of leptin mutations and diet-induced obesity on glucose homeostasis in the zebrafish.

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Aim

Leptin is classically thought to be an adipostatic signal communicating information from the adipose tissue to the brain, thereby regulating energy intake and expenditure. Recently, it has been suggested that in the zebrafish (Danio rerio), contrary to humans and other mammals, leptin does not regulate adipostasis but glucose homeostasis. From an evolutionary perspective, this suggests that leptin originated as a glucoregulatory hormone. The aim of this study was to elucidate the effects of leptin mutations and diet-induced weight gain on glucose homeostasis in the zebrafish

Method

We utilized the clustered regularly interspaced short palindromic repeats (CRISPR) system to generate knockout mutant zebrafish for both leptin-a and leptin-b, and for the leptin receptor. Six-month old male mutant fish and wild type control fish (N=11 per group) were exposed to either a six-week long overfeeding regime or normal feeding conditions. Body weights and standard length were measured weekly. Glucose tolerance tests were performed to assess changes in glucose homeostasis at the end of the feeding paradigm.

Result

Under normal feeding conditions, no effect of genotype was found on bodyweight (285±10.14mg vs 289±11.06mg) or standard length (28.79±0.97mm vs 28.94±1.06mm). Glucose tolerance on the other hand was significantly reduced in leptin receptor and leptin-a knockout zebrafish, determined by a two-way ANOVA ($P<0.05$). The overfeeding paradigm revealed an effect of leptin on bodyweight and somatic growth, as leptin receptor and leptin-a knockout zebrafish displayed aggravated bodyweight gain and increased standard length compared to leptin-b and wild type fish (two-way ANOVA, $P<0.05$).

These results show that in zebrafish, under normal feeding conditions, leptin regulates glucose homeostasis but not body weight. Only in times of nutrient excess, leptin appears to regulate body weight, somatic growth and glucose homeostasis.

URL:
www.nzma.org.nz/journal-articles/proceedings-of-the-251st-otago-medical-school-research-society-phd-student-speaker-awards

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