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Exploring the response to the COVID-19 pandemic at the rural hospital–base hospital interface: experiences of New Zealand rural hospital doctors

Garry Nixon, Katharina Blattner, Stephen Withington, Rory Miller, Tim Stokes

In many overseas countries, those living in rural areas have experienced poorer health outcomes as a consequence of the COVID-19 pandemic than their compatriots living in cities. This study interviewed 17 senior doctors in different New Zealand rural hospitals about their experience planning for the pandemic in its early stages. In particular this study considered their interactions with the local DHB and base hospital. There was considerable variability in how well the rural doctors felt supported by their DHB. It was common to feel both forgotten by the DHB and at the same time overwhelmed by masses of often contradictory information that was not always relevant to their situation. Established clinical leadership and a stable workforce aided pandemic preparations, as did pre-existing high quality relationships with the local DHB. The rural doctors were concerned about the ability of their local facilities to handle large numbers of seriously unwell and highly infectious patients, but were even more concerned about the ability of the system to transport those needing advanced care to the base hospital. Having the needs of rural health considered at a national level, rather than DHB by DHB, could have improved the response. Many were very relieved that the system had not been tested the way it has been in other countries.

Food, nutrition and cancer: perspectives and experiences of New Zealand cancer survivors

Rana Peniamina, Cheryl Davies, Losa Moata'ane, Louise Signal, Huia Tavite, Lisa Te Morenga, Rachael McLean

We interviewed cancer survivors from three New Zealand ethnic groups (Māori, Pacific Peoples, NZ European) about their experiences of food and nutrition during and after cancer treatment. Most reported they had received little or no nutrition advice or support as part of their cancer care. For some, that meant they did not realise nutrition could be important for cancer outcomes. Many said they wanted their cancer care team to provide them with advice and information about what to eat to help them with their recovery during treatment and prevent cancer coming back in the future. In addition, support (eg, access to a dietitian, financial/practical support) is needed to help cancer patients eat well to support their recovery and ongoing health beyond treatment, and to reduce inequities in cancer outcomes.

Breast cancer costs in New Zealand's public health system

Chunhuan Lao, Mohana Mondal, Marion Kuper-Hommel, Ian Campbell, Michael P Cameron, Ross Lawrenson

The costs of treating breast cancer in New Zealand's public health system are substantial and have been increasing. Most of the cost was in the first year post diagnosis, and surgery and immunotherapy cost accounted for the biggest proportion. The greatest costs were for the treatment of younger women and those with more advanced disease

Use and results of systemic treatments for de novo and recurrent metastatic breast cancer: a population-based cohort study

Chunhuan Lao, Marion Kuper-Hommel, Ian Campbell, Mark Elwood, Ross Lawrenson

Although Māori patients had good access to systemic treatment for metastatic breast cancer, Pacific women with metastatic breast cancer were less likely to receive chemotherapy and trastuzumab (herceptin) than non-Pacific women. Endocrine therapy, chemotherapy and trastuzumab all improved survival in patients with the specific biomarkers that are used to target therapy.

Barriers to physical activity in prostate cancer survivors

Asmita Patel, Grant M Schofield, Justin WL Keogh

Physical activity is beneficial for patients throughout the prostate cancer continuum, from diagnosis through to survivorship. The majority of prostate cancer survivors are not engaging in sufficient physical activity to achieve health-related gain. This qualitative study designed to identify barriers to physical activity in 16 prostate cancer survivors found only two of the six barriers for physical activity directly related to having had prostate cancer. With an increase in prostate cancer survivorship, practitioners who treat prostate cancer patients or see prostate cancer survivors on a regular basis for the monitoring of prostate specific antigen (PSA) levels and for other conditions are ideally positioned to provide advice or referral for physical activity or physical activity programmes.

He Pikinga Waiora Kimi Ora lifestyle programme: case study of a successful community-based Indigenous diabetes intervention

Bridgette Masters-Awatere, Shemana Cassim, Jade Tamatea, Nina Scott, Chae Simpson, Cherie Paekau

This paper describes a co-designed programme that involved collaboration between Māori healthcare providers, community members, research advisors and wider community agencies. Together they developed and implemented the Kimi Ora lifestyle programme that was tailored to work with Māori communities in a responsive and flexible manner. Kimi Ora resulted in successful biomedical outcomes, high level of engagement and 100% participant retention.

Addressing equity: a 10-year review of strabismus surgery in 0–19-year-olds in the New Zealand public health system

Cheefong Chong, Alexandra Lawrence, Dan Allbon

Disproportionately fewer strabismus surgeries were performed in Māori. Disproportionately fewer strabismus surgeries were performed in Pacific Peoples. Minority ethnic groups are less likely to receive secondary operations following a primary procedure when compared to European ethnic group. There appears to be inter-regional variation in the incidence of surgeries performed, which could reflect inter-regional disparities in access surgical services. The findings could also suggest earlier access to surgical services for Europeans when compared to all minority ethnic groups.

A distance-based approach to rurality and remoteness in health: concept, methodology and correlates of a patient-centred health services spatial accessibility index

Emmanuel Jo, Chris Lane, Keri McArthur, Fei Xu

How many health practitioners will be required to meet the needs of patients in rural and remote areas in New Zealand in future years? That was a question that the analytics team in the Health Workforce Directorate of the Ministry of Health was trying to answer, but there wasn't a reliable way to identify which rural and remote patients should be targeted. To identify such rural and remote patients, the team calculated a "distance score" based on how far they live from primary care facilities and from hospitals with extensive specialist and emergency services. The 20% of patients with the highest distance scores live mainly in smaller towns and rural and remote areas and have a relatively high proportion of older people, Māori and people living in high socioeconomic deprivation. Being able to identify these patients means the Ministry of Health has a better understanding of which health services are currently serving these patients and where resources need to be put to improve services to them.

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New Zealand's staffed ICU bed capacity and COVID-19 surge capacity

Paul J Young, Alex Psirides, Stephen Streat

Coronavirus disease 2019 (COVID-19) has placed unprecedented demand on healthcare around the world. In 2020, COVID-19 case numbers in many countries required intensive care units (ICUs) to adapt to treat critically ill patients when demand for beds exceeded staffed capacity.[1,2] New Zealand has one of the lowest levels of ICU beds per capita in the OECD at 4 per 100,000 population.[3] This compares to Australia at 9, France at 16, and Germany at 34.[3] In 2018, in New Zealand, 17% of elective surgical operations for which post-operative admission to an ICU was planned were postponed due to the lack of an available ICU bed, compared with 1.7% in Australia.[4] As surges of COVID-19 ICU admissions that exceed capacity are associated with high mortality rates,[1,2] New Zealand's comparatively low ICU capacity is a potential point of vulnerability in our COVID-19 response.

New Zealand's elimination strategy resulted in comparatively small numbers of COVID-19 patients being admitted to ICUs in 2020[5] but has not contained a delta outbreak which began in August 2021. This outbreak is leading to rising case numbers despite severe restrictions and an active vaccination programme. Some Australian jurisdictions experienced similar issues. Australian ICU capacity and capability to accommodate surges in COVID-19 case numbers was recently evaluated and reported,[6] but comparable measures for New Zealand have not been reported. Accordingly, we surveyed senior ICU staff from New Zealand's public hospitals to assess the number of current staffed ICU beds and capacity to staff "surge" ICU capacity (a potentially rapid increase in critical care resources to match exceptional demand). We used the same survey used to evaluate Australian ICU capacity in March 2020[7] and August 2021.[6] In brief, we asked about ICU bed numbers, staffing, surge capacity, and availability of equipment. "Staffed" ICU capacity indicated equipped ICU beds fully staffed with specialised ICU nurses (with a nurse-to-patient ratio of 1:1), whereas "additional physical ICU beds" indicated equipped bed spaces that were not staffed.

We obtained responses relating to all New Zealand public hospitals. Respondents indicated there were 176 staffed ICU beds in 25 ICUs in 24 public hospitals of which 15 were dedicated paediatric ICU beds. An additional 104 physical beds within ICUs that were not staffed were identified. A total of 49 non-negative-pressure and 68 negative-pressure *single* rooms in ICUs were identified nationally with the remaining ICU beds in shared spaces. Areas with high air exchange or negative pressure that could be used to care for critically ill COVID-19 patients exclusively were identified in 64% of hospitals. The total number of ICU beds in such areas nationally was 132. Outside of ICUs, 289 beds that might be used to care for critically ill patients within "surge areas" were identified. Accordingly, a total of 565 beds that, if staffed, could be used to care for critically ill patients were identified nationwide. Respondents indicated a total of 535 ventilators available in their respective hospitals (excluding anaesthetic machines).

Stated numbers of staff available for such surge capacity for a period of one month varied considerably by ICU. A total of 130.6 (range, 0 to 20), 99 (range, 0 to 20), and 356 (range, 0 to 115) full time equivalent (FTE) specialists, junior doctors, and nurses respectively were identified as being able to contribute to surge capacity. Of the 356 FTE nurses, 100 were identified as being able to provide high-dependency care only.

Our data suggest that, when this survey was completed between 15 October and 1 November 2021, New Zealand's staffed ICU bed capacity was approximately 3.5 staffed ICU beds per 100,000 population.[8] In comparison, the most recent Australian survey identified staffed ICU bed numbers varied by state, from 6 to 10.8 per 100,000 population[6]. In Australia, the most recent ICU survey identified 1882.7 FTE ICU nurses (~73/million population[9]) available to staff surge capacity.[6] We identified 356 FTE of nurses (~70/million population[8]) available to staff surge capacity. Based on a pre-pandemic staffing ratio of 5.3 FTE of nurses to staff one ICU bed 24 hours a day, 365 days a year, this would be sufficient to open 67 surge beds. When this surge capacity is added to baseline staffed ICU capacity, the reported maximum total number of ICU beds in New Zealand that could be staffed for a surge before nurse-to-patient ratios would need to be reduced is 243.

These responses from senior clinicians in all New Zealand public hospitals reflect the current real-world capacity and surge capability readily available to them, and allow direct comparison with Australian data obtained using the same methodology.[6] It is possible that respondents were not aware of all non-ICU nursing staff who might potentially contribute to the surge workforce. However, because we used the highest number when a range of potential staff numbers was provided by a respondent, our numbers may overestimate available staffing. We did not account for ventilators that were held in national stores rather than in hospitals and did not consider capacity available in private hospitals.

Despite these issues, our data suggest that New Zealand's public hospital ICU capacity is substantially lower than Australia's on a per capita basis and that our surge capacity is likely to be limited by available nursing staff.

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REFERENCES

1. Bravata DM, Perkins AJ, Myers LJ, et al. Association of Intensive Care Unit Patient Load and Demand With Mortality Rates in US Department of Veterans Affairs Hospitals During the COVID-19 Pandemic. JAMA Netw Open. 2021; 4:e2034266.
2. Kadri SS, Sun J, Lawandi A, et al. Association Between Caseload Surge and COVID-19 Survival in 558 U.S. Hospitals, March to August 2020. Ann Intern Med. 2021; 174:1240-51.
3. OECD [Internet]. Intensive care beds capacity [cited 2021 Nov 10]. Available from: http://www.oecd.org/coronavirus/en/data-insights/intensive-care-beds-capacity
4. ANZICS [Internet]. Activity Report [cited 2020 Nov 10]. Available from: https://www.anzics.com.au/wp-content/uploads/2019/05/ANZICS_CTG_Activity_Report_201718.pdf
5. Oliu-Barton M, Pradelski BSR, Aghion P, et al. SARS-CoV-2 elimination, not mitigation, creates best outcomes for health, the economy, and civil liberties. Lancet. 2021;397:2234-6.
6. Litton E, Huckson S, Chavan S, et al. Increasing ICU capacity to accommodate higher demand during the COVID-19 pandemic. Med J Aust. 2021.
7. Litton E, Bucci T, Chavan S, et al. Surge capacity of intensive care units in case of acute increase in demand caused by COVID-19 in Australia. Med J Aust. 2020; 212:463-7.
8. Stats NZ [Internet]. Population [cited 2021 Nov 10]. Available from: https://www.stats.govt.nz/topics/population
9. Australian Bureau of Statistics [Internet]. National, state and territory population [cited 2021 Nov 10]. Available from: https://www.abs.gov.au/statistics/people/population/national-state-and-territory-population/latest-release

Exploring the response to the COVID-19 pandemic at the rural hospital–base hospital interface: experiences of New Zealand rural hospital doctors

Garry Nixon, Katharina Blattner, Stephen Withington, Rory Miller, Tim Stokes

ABSTRACT

AIM: The COVID-19 pandemic stress-tested health systems globally and accentuated pre-existing health inequities. There is little understanding of the impact that the 2020 pandemic preparations had on New Zealand's rural hospitals. This study explores rural hospital doctors' experiences of the COVID-19 pandemic, with an emphasis on the rural hospital–base hospital interface.

METHODS: Seventeen semi-structured interviews were conducted with rural hospital doctors across New Zealand. A thematic analysis using a framework-guided rapid analysis method was undertaken.

RESULTS: The regular communication channels and processes linking rural hospitals to their urban base hospitals were disrupted as the pandemic began. Established local leadership facilitated a rural hospital's ability to make an effective local response. District health board (DHB) support for their rural hospitals varied widely and largely reflected the status of the pre-pandemic relationship. DHB understanding of rural hospital facilities and processes was considered to be poor. Ongoing uncertainty around managing and transferring acutely unwell patients with COVID-19 remained. Equity concerns centred on access to advanced care.

CONCLUSION: The experience of the COVID-19 pandemic has highlighted the resilience of rural hospitals as well as the challenges they face in operating at the margins of the healthcare system.

The COVID-19 pandemic has stress-tested health systems around the world and in doing so has accentuated pre-existing health inequities.[1] This includes disparities in health outcomes and access to health services for rural populations. In the United States, for example, COVID-19 case fatality rates are higher in rural areas, and rural hospitals have struggled to deliver the advanced respiratory support needed by many COVID-19 patients.[2,3]

Although New Zealand has to date been spared the worst health and socioeconomic impacts, there was no certainty that this would be the case in the pandemic's early stages. New Zealand's rural hospitals, along with the health system as a whole, needed to plan for the scenarios that were at the time unfolding in Europe and North America. The Ministry of Health (MoH) reports COVID-19 case data at a district health board (DHB) level, which does not permit accurate urban–rural comparisons. Rural clinicians' impressions that rural hospitals (especially those in tourist areas) were dealing with a disproportionate number of the very

early COVID-19 cases requiring hospital admission is supported by the available data and news releases.[4,5] The first COVID-19-related death in New Zealand occurred in a rural hospital.[6] In some regions, the level 4 lockdown saw an exodus from the cities to rural areas, compounding the pressure on rural health services.[7] Iwi in Northland and the East Coast set up road blocks to keep COVID-19 out of their areas.[8] These factors combined to heighten the anxiety and sense of urgency felt by those working in the rural health sector.

Even before factoring in access to advanced respiratory care, rural New Zealand is a high-risk population with respect to the COVID-19 pandemic. New Zealand's rural towns have on average the lowest socioeconomic status, highest proportion of Māori, oldest age structure and highest levels of dependency of any of New Zealand's geographic categories.[9,10] There is evidence of poorer health outcomes for residents of rural towns, an effect that is accentuated for Māori.[11] Māori retain a strong historical memory of the disproportionate burden their rurally based communities bore during previous pandemics, and in 2020 the projected COVID-19 infection fatality rate for Māori was 50% higher than for non-Māori.[12,13]

New Zealand's rural hospitals are estimated to serve at least 10% of New Zealand's total population.[14]

Rural hospitals deliver a range of inpatient, outpatient and community services. These services are often integrated and do not align neatly with the concepts of "primary" and "secondary" care that are used to organise urban services.[15–18] International definitions of rural hospitals are varied and highly country dependent.[19]

In 2008 the Medical Council of New Zealand (MCNZ) recognised the scope of rural hospital medicine (RHM) and the Royal New Zealand College of General Practitioners' (RNZCGP) Division of RHM (DRHMNZ) was established along with a vocational RHM training programme. Although there is no formally recognised MoH definition of rural hospitals in New Zealand, the defining features of rural hospitals accepted by the MCNZ and DRHMNZ are their geographic distance from specialist services, their acute in-patient bed capacity and their predominantly generalist workforce.[20] Rural hospitals work closely with their relevant clinical referral facilities or base hospitals. The current DRHMNZ list of 24 rural hospitals, used for purposes of its training programme, is shown in Figure 1.[20,21] New Zealand's rural hospitals have neither the specialist anaesthetists/intensivists nor the facilities necessary to manage ventilated patients beyond brief periods in an emergency situation prior to transfer to a base hospital. Rural hospitals continue to face chronic medical staffing shortages and remain heavily reliant on locums.[22] The extent to which New Zealand rural hospitals improve access to healthcare, improve health outcomes and improve health equity for rural communities, particularly for Māori and Pacific peoples, is currently unknown.

By applying pressure to a poorly understood part of the health system, the pandemic has provided an opportunity to further our understanding of rural healthcare delivery in New Zealand. The aim of this study was to explore rural hospital doctors' experiences of the COVID-19 pandemic, with particular emphasis on the rural hospital–base hospital interface.

Methods

Participants

Rural hospital doctors working clinically at the frontline during the pandemic were invited by email to participate in the study. Recruitment of participants was facilitated by the Rural Hospital Clinical Leaders Forum. Sampling was purposive with the aim of recruiting one representative from each rural hospital across the country: 21 of the 24 rural hospitals recognised by the RNZCGP DRHMNZ were invited to participate (logistical factors prevented an approach to all 24 rural hospitals). Those rural hospitals that had not provided a response were then directly contacted by email with a further invitation for one of their medical staff to participate. Access was facilitated through four of the authors (GN, KB, SW and RM) being known to participants both as peers and through regional and national rural hospital medicine networks.

Data collection

Semi-structured individual interviews were conducted via videoconference (Zoom) by a member of the research team (GN, TS or SW) between August and October 2020.[23] The interview schedule explored each participant's view of the base hospital–rural hospital interface during the pandemic, and included questions regarding inter-hospital transfers as well as processes for ensuring equity of access to services. Each interview lasted between 30–40 minutes and was recorded and transcribed using Zoom's inbuilt automatic transcription service. The researchers took notes during the interviews to record participants' responses in detail. At the completion of each interview, the interviewer listened to the recording to check the accuracy of the participant's responses in the transcription, and to ensure the documented responses were a comprehensive account of the interview.

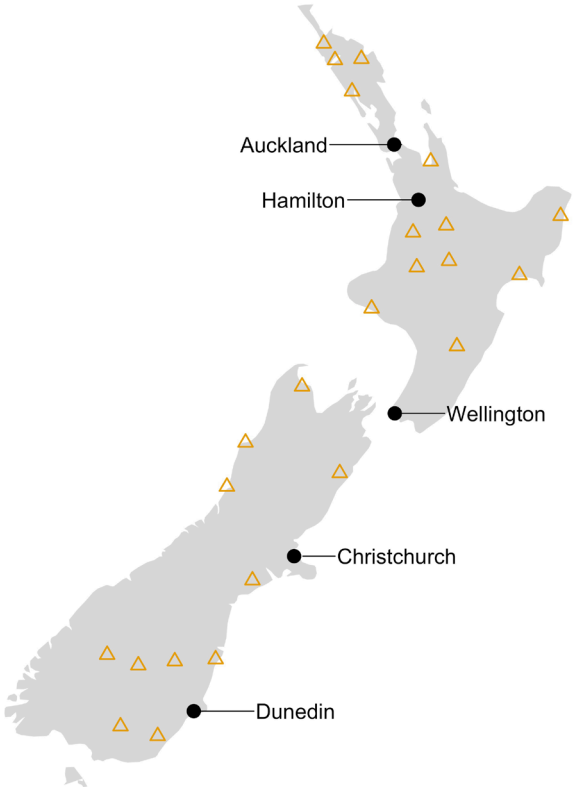
Analysis

A thematic analysis was conducted using a framework-guided rapid analysis method.[24] KB, GN and TS developed a structured template by which the data were classified according to the study topic guide questions. The interview data (including corrected transcripts and the interviewer's summary) were converted to a standard summary format. All interview summaries and templates were individually reviewed by each team member. The research team then met (via videoconference and once in person) to review summary responses and templates and to refine emerging themes with reference to the original recorded responses. Similar themes were grouped together and relationships between themes explored.

Researcher positionality

The research subject and setting was part of the real-life experience of all members of the research team except TS. Although "insider status" can be a research strength, it is important that the research remains rigorous.[25] In this study, rigour was promoted by (1) acknowledging the insider status of the researchers in participant information and consent forms and (2) a whole-team approach to analysis, which included the participation of TS, who is not a rural hospital doctor.

Figure 1: New Zealand's rural hospitals.[20,21]



Ethics

Ethics approval was obtained from the University of Otago Human Ethics Committee D20/150.

Results

Seventeen interviews were conducted with rural hospital doctors representing 17 rural hospitals (four failed to respond). Ten participants were based in North Island rural hospitals and seven in South Island rural hospitals. The majority of participants were vocationally registered in RHM and two were senior RHM registrars. Participant characteristics are shown in Table 1. Participants were designated a number (P1–P17) and were referred to throughout the study by this coding (eg, P5).

Participants' accounts covered five themes: initial reaction to COVID-19 pandemic, local leadership, the rural hospital–DHB relationship, understanding the rural hospital context and access to advanced care.

Initial reaction to the COVID-19 pandemic

Participants' accounts as the pandemic began portrayed a sense of being alone, waiting and worrying. The usual communication channels and everyday processes linking rural hospitals to their relevant base hospitals had been disrupted. The role rural hospitals would take in the pandemic was uncertain. With DHBs assumed to be preoccupied with preparations within their base hospitals, participants reported being left to themselves, without clear directives:

> *"[F]or those first two and a half weeks we essentially were rudderless. Yeah it was quite a big moment… Holy shit we are on our own." – P2*

At the same time, rural hospitals were receiving an enormous barrage of information, which was difficult to get on top of, let alone make sense of:

> *"[We were] feeling very battered around by rapidly changing information coming from a number of different places that was frequently changing and often mutually contradictory." – P4*

Rural hospital teams rapidly realised that they would have to take responsibility for their own pandemic planning:

> *"So we felt we were left to ourselves… we had to blunder our way through that." – P3*

Local leadership

Going into the pandemic, hospitals either had, or did not have, established local leadership. Established local leadership facilitated a rural hospital's ability to make an effective local response. Small, flexible and well-connected teams could respond and adapt quickly. Participants described how their hospital teams divided up responsibilities and actively looked after each other:

> *"[We] know each other well enough to know 'this person is going to be really good at this, that person is going to be really good at that'. We identified support: 'second- in- command' and support people that were particularly there to safety- net those clinical leads or site managers who were going to be bombarded." – P5*

Established local leadership also meant that hospitals had the mandate and thus the confidence to adapt policies and other advice coming from outside to ensure these were locally relevant. The local leadership thus acted as an information filter.

In rural hospitals where established local leadership was absent, an effective and timely local response was initially more challenging. However, participants described how their existing small, well-connected teams helped individuals step up into a clinical leadership role and also enabled the local leadership team to be confident in making their own decisions for their community:

> *"From a motivation point of view, we've always had a number of individuals that stand out as the local 'Clinical Directors' even though that's not a recognised official role." – P16*

> *"We came together as a senior medical officer group and started to make our own decisions that were relevant for our community and our hospital. That was when we started to gain strength and confidence in our response." – P5*

Table 1: Characteristics of participating doctors.

Characteristic	Number of participating doctors
Age (years)	
30–40	7
41–50	7
51–60	3
Ethnicity	
European / Pākehā	13
Māori	1
Other	3
Duration of rural hospital practice (years)	
0–5	7
5–15	7
>15	3
Vocational qualification	
FRNZCGP[a] and FDRHMNZ[b]	8
FDRHMNZ[b]	5
FRNZCGP[a]	1
Registrar in training	2
Nil	1
Clinical leadership role	7

[a] Fellow of Royal New Zealand College of General Practitioners.

[b] Fellow Division of Rural Hospital Medicine New Zealand.

The rural hospital–DHB relationship

District health boards' support for their rural hospitals varied widely and largely reflected the status of the pre-existing relationship prior to the pandemic. Where there were established relationships (at both managerial and clinician level), the communication channels were better developed and the engagement was more effective:

> *"Relationships that existed prior… it makes things much easier, our Clinical Director had very well established links with… [DHB CEO]… that I think was essential in trying to get that visibility." – P7*

Rural hospitals that had previously faced major events had established clear processes with their DHB and drew on that experience to manage their response.

Participants who perceived a highly functional and supportive relationship with their DHB emphasised the importance of autonomy and of adapting policy and procedures to the local context:

> *"The DHB can tell you what their advice is, but in rural hospitals you have to make your own or devise, your own plan and setup. The DHB can't tell you exactly what to do, but they would give recommendations and I generally found that they were supportive, but were giving us freedom." – P9*

However, many participants reported feeling unsupported by their DHBs, describing a continued pattern of poor communication:

> *"[It] just again highlighted this big mess of confusion and mixed messages and incoherence from the centre to the periphery." – P13*

This resulted in an inability to establish clear processes, including those for patient transfer for advanced care. Some participants even went so far as to see their hospital being completely forgotten about by the DHB. Others saw the opportunity to reconsider what their future relationship with the DHB should look like:

> *"I think there has been a tendency to… have an umbilical cord, if you like. 'You know what we need, when we need it', and perhaps not so much to have the confidence to break that and to go out on our own. And I think what happened during this pandemic, was it really forced us to do that." – P5*

Understanding the rural hospital context

Participants thought DHBs had a poor understanding of rural hospital facilities and processes. In particular, facilities and processes were not set up in such a way that base hospital plans and protocols, especially those around escalating respiratory support, could simply be rolled-out with no adaptation to the local rural hospital context.

Participants from many rural hospitals also discussed the lack of "surge capacity" (defined as elective activities that can be temporarily halted in order to increase capacity for acute care), which was not well understood at base hospital level.

Local hospitals frequently responded with practical adaptations and innovation, often taking a "number 8 wire" approach:

> *"We managed in the end to work out something, a system whereby we could convert the positive pressure rooms into [negative] pressure rooms with some kiwi ingenuity and extractor fans and taping up things, but they all took a while to work out and to get it signed off by the right people." – P7*

The lack of understanding regarding the rural hospital context was also present in participant narratives that highlighted the absence of "fit-for-rural-hospital-purpose" guidance. The RNZCGP was providing guidance from early on for primary care and medical specialist colleges for secondary care. At the base hospital level, multiple hospital specialty guidelines (often conflicting) were gradually forthcoming, but there was no input from a rural hospital perspective:

> *"[If] they [specialities] want us to follow their best advice procedures, they need to be involving us in the discussion that helps apply to our setting, rather than just tell it. We're not going to be a mini paediatric ward. We're not going to be a mini respiratory ward following their processes and protocols." – P4*

Participants reflected that, to address this issue in future, rural hospitals needed to work together to raise their profile as a clinical specialty of equal standing to general practice and other specialist care.

Access to advanced care for COVID-19 patients

All participants raised concern regarding ongoing uncertainty around managing and transferring acutely unwell patients with COVID-19. There was often no explicit guidance and no mutually agreed arrangements around access to advanced care for rural hospital patients. Participants were not confident they could get patients to the right place in a timely way if the worst-case scenario had eventuated. Two particular issues were highlighted to be of concern: ambulance services and transfer issues.

Ambulance services, a key stakeholder for the escalation of care for rural patients, were subject to centralised, national processes and policies, which were frequently not aligned to local or even regional protocols. The inability to adapt these to the rural context was concerning:

> *"[St John] was initially just saying that they weren't going to transport anyone where there was a respiratory problem… anyone who's needing any kind of respiratory support… I know it was raised at a national level, because it was St John's policy. I think one of the things that was very difficult was that this was unilaterally declared by St John to the DHB and to us all, so there was no balancing of risks, it didn't seem to us." – P4*

Transfer issues were seen as particularly problematic when participants viewed their rural hospital–DHB relationship to be poor. Here the DHB would give unilateral advice to the rural hospital, which the hospital had no choice but to follow. Such advice covered a number of situations, including admitting patients with suspected COVID-19 to the rural hospital and helicopter retrieval of acutely unwell patients with suspected COVID-19:

> *"[The] advice from [DHB base hospital] was that we were to admit, nobody that had suspected COVID… [instead] they were to be put in the ambulance and transferred two hours up the road to [name of base hospital]. There was no thought about what that meant in terms of transfer resources and how that would look for a nurse and two hours in the back of an ambulance in PPE." – P16*

> *"[We] were told we couldn't have a helicopter retrieval—the ambulance would not transfer anyone who was query COVID…" – P16*

Overall, participants thought that rural patients did not have equitable access to specialist and advanced care prior to the pandemic and that the pandemic would simply exacerbate this existing inequity. Some participants seemed resigned to the continuation of this business-as-usual situation:

> *"[We] definitively dodged a bullet… but… that's what we do all the time…" – P8*

Others were more optimistic, recognising the good intent from DHBs, while also acknowledging further progress is needed to better work together in future across the sector:

> *"We were extremely worried about it [equitable access for advanced care] and I think [name of DHB] were not insensitive to those issues. And I think that's one of the things that drove them being quite proactive about including us because they saw our communities in the rural hospitals being vulnerable to be fair, I think there was a real commitment at the DHB level to try and fight against that. I don't know if they necessarily understood the complexities of that as well as we did and whether they actually put in place effective measures." – P4*

Discussion

This study has found that the experience of planning for the pandemic highlighted the challenges rural hospitals face in operating at the margins of the healthcare system. In the early pandemic phase, participants felt "forgotten" and at the same time overwhelmed by large amounts of contradictory information. This initial phase was followed

by a realisation that a local response was needed, something that small, well-connected teams were able to rapidly deliver. Pragmatic innovation and flexibility were features of the local responses. Local leaders proved to be important facilitators, proactively managing external relationships and acting as a filter that adapted centrally generated policy and guidelines to the local context. A notable finding was the large variation in participants' experiences of the rural hospital–base hospital interface, something that was largely determined by the quality of the pre-existing relationship with the relevant DHB. All participants raised concerns regarding ongoing uncertainty around the management and transfer of acutely unwell patients with COVID-19.

Although rural hospitals provide a spectrum of primary and secondary services, they are all small components of much larger urban-centric DHB structures and national professional bodies. Rural hospitals are not a homogenous group and there is no national strategy or policy that considers their role. It is not surprising that national and regional bodies failed to provide rural hospitals with clear direction during the pandemic. This left their senior RHM staff to synthesise copious volumes of only partially relevant primary and secondary care guidelines and policies. This experience adds weight to the statement in the Health and Disability System Review interim report that there is a "clear need for a better understanding of the form, structure and function of rural hospitals and their contribution to health service delivery, and have a strategy for their development."[26]

Those rural hospitals with established clinical leadership roles entered the pandemic with a clear advantage over those where leadership was non-existent or distant. Clinical leadership and clinical governance have been slow to evolve in New Zealand's rural hospital sector,[27] although there is evidence of progress.[22] The pandemic may have accelerated this process by highlighting the need for leadership at a time of crisis and by encouraging younger or informal leaders to step up into formal leadership roles. Prior to 2008 and the establishment by MCNZ of the RHM scope, medical staff in rural hospitals were poorly connected to their peers in other hospitals. The RHM professional structure has not yet matured to the point it can offer the level of clinical direction that came from other Colleges during the pandemic, but it created a network that facilitated information sharing and helped overcome some of the isolation experienced during the pandemic.

There was a universal sense among the participants of this study that the DHBs had a poor understanding of rural hospitals' facilities and capabilities, but this was not what determined the quality of the relationship. More important was that the base hospital listened to their rural colleagues respected them as experts in the rural context and provided both the support and the autonomy to develop local solutions. The principle of subsidiarity is considered in the charter of at least one New Zealand rural health service and may usefully underpin all highly functional DHB–rural health service relationships.[28]

Equity concerns centred on access to advanced care. Transferring large numbers of highly infectious patients requiring ventilatory support would have presented a major challenge needing careful planning and agreed protocols. When considering rural hospital to base hospital transfers, consideration needs to be given to both the mode of transfer and the appropriate clinical thresholds for transfer. It is concerning that most participants felt that this issue (acute inter-hospital transfer) remained unresolved, and they were only able to express relief that this part of the system remained untested. Planning in the key area of inter-hospital transfer seems to have been complicated by the different perspectives of the three essential players: the ambulance service (centralised nationally), the base hospital referral service (DHB with a regional perspective) and the rural hospital (with a local perspective).

Limitations

The study's perspective is that of individual medical staff and does not include the views of other rural hospital staff or the wider rural community. Nor does the study consider the perspectives of those working in base hospitals and DHB offices on the "other side" of the interface explored here. The early phase of the pandemic was an exceptional time characterised by uncertainty and anxiety. Care needs to be taken

in extrapolating the findings in this study to more "normal" times.

Implications and future research

Rural hospitals matter to New Zealand rural communities, which is best demonstrated by the consistent community responses to threats of rural hospital closures or downgrades.[29] International studies have identified rural hospitals as important providers of healthcare that can benefit the health of rural populations by enhancing access to, and integration of, health services.[17–19] Although their role remains poorly understood, rural hospitals appear to be uniquely positioned to improve health equity for rural communities, particularly for Māori and Pacific peoples. Further research, strategy and policy at a national level is needed if they are to fully realise this potential.

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REFERENCES

1. Paremoer L, Nandi S, Serag H, Baum F. Covid-19 pandemic and the social determinants of health. BMJ. 2021;372:n129.
2. Pro G, Hubach R, Wheeler D, et al. Differences in US COVID-19 case rates and case fatality rates across the urban-rural continuum. Rural Remote Health. 2020;20(3):6074. doi: 10.22605/RRH6074 [published Online First: 2020/08/20]
3. Underwood A. COVID-19: A Rural US Emergency Department Perspective. Prehosp Disaster Med. 2021;36(1):4-5. doi: 10.1017/S1049023X20001417 [published Online First: 2020/11/05]
4. 50 new cases of Covid 19 in New Zealand. Ministry of Health news release. 25 March 2020 [cited 2021 Apr]. Available from: https://www.health.govt.nz/news-media/media-releases/50-new-cases-covid-19-new-zealand
5. Jefferies S, French N, Gilkison C, et al. COVID-19 in New Zealand and the impact of the national response: a descriptive epidemiological study. The Lancet Public Health. 2020;5(11):e612-e23. doi: 10.1016/s2468-2667(20)30225-5
6. First Death in New Zealand from Covid-19. Radio New Zealand News. 29 March 2020 [cited 2020 May]. Available from: https://www.rnz.co.nz/news/national/412864/coronavirus-first-death-in-new-zealand-from-covid-19
7. Locals frustrated as out-of-towners see out lockdown in Coromandel holiday homes. 1 News. 20 April 2020 [cited 2021 May]. Available from: https://www.tvnz.co.nz/one-news/new-zealand/locals-frustrated-towners-see-lockdown-in-coromandel-holiday-homes
8. Iwi lock down their rohe. Newsroom. 10 April 2020 [cited 2021 Apr]. Available from: https://www.newsroom.co.nz/iwi-lockdown-their-rohe-in-pictures
9. Statistics NZ [Internet]. Independent urban areas. Economic standard of living. Available from: http://archive.stats.govt.nz/browse_for_stats/Maps_and_geography/Geographic-areas/urban-rural-profile/independent-urban-areas/economic-standard-living.aspx
10. Statistics NZ [Internet]. Independent urban areas. People. http://archive.stats.govt.nz/browse_for_stats/Maps_and_geography/Geographic-areas/urban-rural-profile/independent-urban-areas/people.aspx
11. Mātātuhi Tuawhenua:Health of Rural Māori. Wellington. Ministry of Health. 2012.
12. The 1918 influenza pandemic. Uneven rates of Death. New Zealand History [2021 Apr]. Available from: https://nzhistory.govt.nz/culture/1918-influenza-pandemic/

death-rates

13. Steyn N, Binny RN, Hannah K, et al. Estimated inequities in COVID-19 infection fatality rates by ethnicity for Aotearoa New Zealand. N Z Med J. 2020;133(1521):28-39. [published Online First: 2020/10/01]
14. Janes R. Rural hospitals in New Zealand. N Z Med J. 1999;112(1093):297-9. [published Online First: 1999/09/24]
15. Blattner K, Stokes T, Nixon G. A scope of practice that works 'out here': exploring the effects of a changing medical regulatory environment on a rural New Zealand health service. Rural and Remote Health 2019;19(4). doi: 10.22605/rrh5442
16. Blattner K, Stokes T, Rogers-Koroheke M, et al. Good care close to home: local health professional perspectives on how a rural hospital can contribute to the healthcare of its community. N Z Med J. 2020;133(1509).
17. Nolte E, Corbett J, Fattore G, et al. Understanding the role of community hospitals: an analysis of experiences in five countries. European Journal of Public Health 2016;26(suppl_1). doi: 10.1093/eurpub/ckw164.069
18. Winpenny EM, Corbett J, Miani C, et al. Community Hospitals in Selected High Income Countries: A Scoping Review of Approaches and Models. Int J Integr Care. 2016;16(4):13. doi: 10.5334/ijic.2463 [published Online First: 2017/03/21]
19. Vaughan L, Edwards N. The problems of smaller, rural and remote hopsitals: Separating facts from fiction. Future Healthcare Journal. 2020;7(1):38-45.
20. Rural Hospital Medicine Training Programme Handbook. The Royal NZ College of General Practitioners. Wellington. 2020.
21. Webber J. Chair Royal NZ College of General Practitioners Rural Hospital Medicine Board of Studies. Personal communication. July 2021.
22. Lawrenson R, Reid J, Nixon G, et al. The New Zealand Rural Hospital Doctors Workforce Survey 2015. N Z Med J. 2016;129(1434):9-16.
23. Zoom Video Communications. San Jose, California, USA [cited 2020 May]. Available from: https://www.zoom.us/
24. Gale RC, Wu J, Erhardt T, et al. Comparison of rapid vs in-depth qualitative analytic methods from a process evaluation of academic detailing in the Veterans Health Administration. Implement Sci. 2019;14(1):11. doi: 10.1186/s13012-019-0853-y [published Online First: 2019/02/03]
25. Heslop C, Burns S, Lobo R. Managing qualitative research as insider-research in small rural communities. Rural and Remote Health. 2018;18(3).
26. Health and Disability System Review. 2019. Health and Disability System Review - Interim Report. Hauora Manaaki ki Aotearoa Whānui – Pūrongo mō Tēnei Wā.Wellington: HDSR [cited 2020 May]. Available from: www.systemreview.health.govt.nz/interim-report
27. Lawrenson R, Nixon G, Steed R. The Rural Hospital Doctors Workforce in New Zealand. Rural and Remote Health. 2011;11(1588). [published Online First: 19 April 2011]
28. Hauora Hokianga. Philosphy of Values [cited 2020 Apr]. Available from: http://www.hokianga-health.org.nz/HHET2017/base2.php?page=HHET_Philosophy
29. Barnett R, Barnett P. "If you want to sit on your butts you'll get nothing!" Community activism in response to threats of rural hospital closure in southern New Zealand. Health & Place. 2003;9(2):59-71. doi: 10.1016/s1353-8292(02)00019-9

Food, nutrition and cancer: perspectives and experiences of New Zealand cancer survivors

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ABSTRACT

AIM: This research sought to understand and describe cancer survivors' perspectives and post-diagnosis experiences of food and nutrition, with a particular focus on barriers to healthy eating, health equity, and Māori and Pacific perspectives.

METHOD: Data were collected using semi-structured interviews with cancer survivors from three different ethnic groups (Māori, Pacific Peoples, and New Zealand European). Thematic analysis was undertaken to identify both similar and contrasting experiences and perspectives in relation to topics of interest. Data analysis also sought to identify any trends indicating differences between ethnic groups.

RESULTS: Limited awareness of the role nutrition has in cancer recovery or prevention, combined with little or no access to nutrition advice/support, meant that healthy dietary change was not a focus for some cancer survivors in this study, whereas others invested considerable time and money accessing nutrition information and support outside of cancer care services. Financial limitations (eg, cost of healthy food and low income) and lack of practical support were also important barriers to post-diagnosis healthy eating.

CONCLUSION: There is a need for more widely available cancer-specific nutrition advice and support in New Zealand. Interventions to address financial barriers and increase access to cancer-related nutrition advice and support have the potential to improve cancer outcomes and reduce inequities in cancer outcomes.

The New Zealand Cancer Action Plan 2019–2029 recognises the need to consider a more holistic approach to cancer care, encourage and support healthy living, improve cancer survival, respond to the preferences and needs of our communities, and focus on achieving equitable cancer outcomes.[1] A healthy diet has an important role in a holistic approach to cancer care, with potential benefits including better health outcomes during treatment and improved cancer survival.[2–4] A detailed report by the World Cancer Research Fund International (WCRF) and the American Institute for Cancer Research (AICR) outlines growing evidence that dietary changes can improve cancer-related and non-cancer-related health outcomes for those with cancer.[2] In response to this evidence, the WCRF and AICR recommend that all cancer survivors receive dietary support from a trained professional.[2] Evidence also shows that many cancer survivors (defined as "people in a wide variety of circumstances beginning at diagnosis, through cancer treatment to the end of life"[2]) want to improve their health and wellbeing through diet, seek advice from a variety of sources about healthful diets, and make changes at various stages of their cancer experience.[5–10] In New Zealand, research shows that Māori and Pacific Peoples consider holistic and culturally appropriate healthcare essential for optimal health outcomes.[11,12] However, how that fits with nutrition in cancer care has not been explored.

Cancer accounts for around one third of all deaths in New Zealand.[13] There are important inequities in health status, with adverse health outcomes and multimorbidity more prevalent among Māori and Pacific Peoples.[11,13,14] Māori are 20% more

likely to get cancer than non-Māori and have substantially worse survival rates for cancer.[1] Pacific Peoples are more likely to get cancer and have higher mortality rates than New Zealand Europeans.[1] In addition, Māori and Pacific Peoples are disproportionately affected by material deprivation and poverty and have higher rates of food insecurity ("when the availability of nutritionally adequate and safe foods, or the ability to acquire such foods, is limited or uncertain"[15]) than non-Māori/non-Pacific New Zealanders.[15] Issues related to poverty, such as food insecurity, are a major barrier to healthy eating and increase the likelihood of chronic health conditions, with the resulting loss of income further exacerbating food insecurity.[16–18] This can lead to a cycle of increasing poverty and poorer health outcomes.[17] The extent to which lack of access to advice and support about healthy food, or lack of access to healthy and affordable food, contributes to gaps in health and wellbeing among cancer survivors in New Zealand is not known.

Although the ability to consume a healthy or normal diet can be directly impacted by cancer and cancer treatment,[19,20] many additional factors may impact on diet for cancer survivors. This research sought to understand and describe cancer survivors' perspectives and post-diagnosis experiences of food and nutrition, with a particular focus on barriers to healthy eating, health equity, and Māori and Pacific perspectives.

Method

Study design

This exploratory qualitative study took an interpretivist stance with a goal to understand participants' perspectives and experiences. The study design was informed by Māori and Pacific models of health and theories on the determinants of health.[21–23] Māori (eg, Te Whare Tapa Whā[22]) and Pacific (eg, Fonofale[21]) models of health are holistic models that encompass cultural, spiritual, and environmental elements in addition to physical and mental health, as well as emphasising whānau (extended family). Culture, poverty, and social/whānau/family support were important social determinants considered. Māori, Pacific, and New Zealand European members of the research team were actively involved throughout the planning, data collection, and data analysis/interpretation stages of the study. Ethical approval was obtained from the University of Otago Human Ethics Committee (Health), approval number H19/028.

Participant recruitment

Participants from three major ethnic groups (Māori, Pacific Peoples, and New Zealand European (NZE)) were recruited through Māori and Pacific healthcare providers, flyers and word of mouth. The purposeful sample included participants from different backgrounds (age, gender, ethnicity, type of cancer) to access a range of experiences and viewpoints. The inclusion criteria were: adults (18 years or older) who had completed the acute phase of cancer treatment within the past five years who were able to participate in a face-to-face English language interview.

Data collection

Participants took part in semi-structured interviews with a researcher from their ethnic grouping: Māori (CD, HT), Pacific (LM), NZE (RP). Interviews included questions with a focus on whānau (family), rongoā (traditional Māori therapies), cultural norms, and finances/cost. Participants were asked about their experiences of food and nutrition during and after their treatment for cancer, including the type of information they received about food and nutrition, any food or nutrition-related support they received during that time, and any dietary changes they made (refer to Table 1 for interview guide). The interviews were audio-recorded (with consent), transcribed verbatim by a transcription service, and checked for accuracy by the researchers.

Data analysis

RP, in collaboration with all other authors, led a thematic analysis[24] of the interview transcripts, which included both individual feedback from the other researchers and regular team meetings to discuss the themes. This included discussion of the themes/interpretation of the Māori and Pacific interview data with Māori and Pacific co-authors to ensure the themes accurately represented the data and that interpretations were appropriate. Manual coding was completed with the aid of the NVivo 12 software package (QSR International 2018).

Table 1: Interview guide (prompts shown in italics).

Can you share your story of cancer with me? *What cancer did you have? What treatment did you have? Length of treatment? Did you have other health problems that affected your cancer or that the cancer affected? Could you tell me about that?*
While you were having treatment, who supported you and your family with advice about kai/food and nutrition? *Dietitian? Nurse, practice nurse, general practitioner, hospital specialist? Whānau or health-worker? What about social media, personal trainer etc?*
What were you told about what to eat and drink? *Where else did you get information from (whānau, social media, internet...)?*
While you were having your treatment how did you manage your kai/food and nutrition? *Who did the cooking? Did you change what you ate? Complementary medicine/rongoā? Did you take dietary supplements? What about alcohol?*
Is there anything that made it hard to manage your kai/food and nutrition during this time? *Finances? Family circumstances? Treatment side effects? Lack of information?* • How did you get around these difficulties?
Is there anything that really helped you to manage your kai/food and nutrition during this time? *Whānau support? Support from health professionals? Financial support?*
Once your treatment had finished how did you manage your kai/food and nutrition? *Who did the cooking? Did you change what you ate? Complementary medicine/rongoā? Did you take dietary supplements? What about alcohol?*
Is there anything that made it hard to manage your kai/food and nutrition during this time? *Finances? Family circumstances? Treatment side effects? Lack of information?* • How did you get around these difficulties?
Is there anything that really helped you to manage your kai/food and nutrition during this time? *Whānau support? Support from health professionals? Financial support?*
What advice would you give someone else going through cancer treatment about managing their kai/food and nutrition?
What could be done in the health system to make it easier for people with cancer to manage their kai/food and nutrition? *Māori/Pacific providers; hospital; other agencies; Cancer Society.*
What other supports could be put in place to make it easier for people with cancer to manage their kai/food and nutrition?
Is there anything else you would like to tell us?

Passages were grouped based on the themes identified from the data that related to the research aims, with a focus on both similar and contrasting experiences or perspectives within the themes, as expressed by the participants. Representative quotes were identified and annotated according to ethnicity (Māori, M; Pacific Peoples, P; New Zealand European, NZE) and the participant number within the ethnicity grouping (eg, M3 refers to Māori participant 3).

Results

Participant characteristics

Participant characteristics are summarised in Table 2. The study participants (n=25) included cancer survivors from three ethnic groups: Māori (n=10), Pacific (n=5), and NZE (n=10). Participant age at interview ranged from 41 to 77 years and 68% of participants were female. Different cancer types were represented. The largest number were diagnosed with breast cancer (n=10), followed by gastrointestinal cancers (n = 4), gynaecological cancers (n = 4), prostate cancer (n=3), and then other cancers (n=4). Participants had undergone different treatments (including surgery, radiation, and chemotherapy). Self-reported co-existing health conditions were more common among Māori and Pacific participants, the most common being diabetes/prediabetes (Māori n=4, Pacific n=3), followed by high blood pressure (Māori n=2, Pacific n=1).

Theme 1: need for more nutritional information and support in cancer care

Our results indicate that cancer-related nutritional information or support is not commonly included as part of cancer treatment and follow-up care. Table 3 outlines the sub-themes and representative quotes related to this theme. Apart from a few participants who recalled being told to eat a healthy diet without being given specific information on how to achieve that, most participants received no advice about healthy eating. However, when advice was offered, it appears to have been well received.

> *"He said, 'I'm going to give you some advice', you know, 'If you want to stay healthy and not potentially ever have anything like breast cancer then you need to have a healthy diet, you need to look really carefully at what you eat and arm yourself for the future', he said. Yeah it was good advice, it was really good advice." – M10*

Often, when dietary information was provided, the focus was on the management of treatment side-effects (eg, maintaining hydration, eating small portions regularly, avoiding certain foods) or co-existing conditions (such as diabetes, obesity). A few participants with co-existing conditions were referred to dietitians for specialist

Table 2: Participant characteristics.

	Māori (n=10)	**Pacific (n=5)**	**NZ European (n=10)**
Age range	48–67	46–70	41–77
Gender			
Female	7	4	6
Male	3	1	4
Types of coexisting conditions			
Diabetes/prediabetes	4	3	
High blood pressure	2	1	
Other[a]	6		3

[a] Other conditions: arthritis, gout, angina, asthma, kidney disease, no gallbladder and spleen, mental health conditions.

Table 3: Sub-themes and quotes for theme 1: need for more nutritional information and support in cancer care.

Little/no nutritional information or support offered
"They don't provide you any information at all" NZE2 "No, not at all. I mean it was cut it out, kick 'em out, you're on your own." NZE6 "I feel like I'm very much doing it by myself." NZE8 "I had no guidance on nutrition." M4 "No, no, they just said to make sure you look after yourself and drink water." M6 "No one." P6 (when asked who supported them with advice about food and nutrition)
Just told to eat a healthy diet without information or support
"They basically just said, 'Maintain a healthy diet'." NZE2 "They said 'try and have a healthy diet', that was about all." M2
Dietary advice given was about managing cancer/treatment effects
"The radiation clinic gave us good sound advice about what to avoid, in terms of being ready for treatment." NZE1 "Keep up your liquids because you don't want to get dehydrated." NZE8 "There were foods that they did warn me about that could affect my insides due to the medicines they were giving me." M9
Wanting dietary support during and after treatment
"I kind of knew that there was a whole lot of information out there about food and what foods you should and shouldn't eat. Um, and... I wanted to be spoon-fed that information from my consultants rather than go falling down a rabbit hole on the internet." NZE2 "I would have liked to have spent time with a nutritionist. Because after the surgery, you know of course I had concerns you know in the back of my head that okay, maybe my diet was lacking, because I'm looking for the reason why I got the cancer. And I think well, if it is the diet, what should I be eating?" NZE5 "But I do know that kai [food] and cancer goes together and I would love to know more if I could." M2 "I think actually you should get more advice about that kind of stuff, you know, about the food." M10
Didn't realise diet was important because the medical practitioners didn't mention it
"There's been nothing about diet, so it can't be considered a, too much of a factor amongst the medical people"… "I would've thought if the food was going to make a difference, we would have been told about it, you know, by now. Like, as I've been discussing, I was never told anything"… "I'd definitely need to know about it [information about nutrition for cancer recovery/prevention] and I would follow it." NZE4 "I just ate normally. I didn't know about the nutrition"… "We didn't even know about this so if we had of known there was different foods, well we could of asked those questions. It's asking the right questions." M4 "I'm just thinking about all the different places that you become involved with when you go through the treatment and all of that, there's nothing there that talks about kai [food]. There's nothing at all"… "So I may suggest that may-be kai [food] is not that important a thing during that time [cancer treatment], cause there's nothing there." M10
Issues due to having to access own information
Not knowing what information to trust (misinformation and scare tactics) "There's a lot of information out there [on the internet] that you couldn't really call reliable, you know?" NZE1 "If no one's going to support me, I have to do the research myself. And then, of course you find things that scare you." NZE2 "There is a lot of information out there but sometimes when you go on the internet you get more than you bargain for and it just scares you, so that's why I don't go near the internet, just stayed right away from it." M10 "I didn't know where to look. You look on the internet, you get a thousand different answers." NZE5 *Concern about interference/interaction with cancer treatment* "But does that counteract or do something that it shouldn't be? You know?" NZE8 *Finding own information is too tiring (for already fatigued cancer patients)* "It's just me trying to work it out myself. That's what's really, really tiring." NZE3 *Having to access costly privately funded support* "I had to spend $95 to see the dietitian, and then I've seen her again and that was another $60." NZE3 "But that [dietary advice/support] was all privately funded." NZE10

dietary support for those conditions but not for cancer. Participants who did receive nutrition-related encouragement and support from healthcare workers or support services found that support helpful. Most of the participants reported not receiving any/enough support related to diet and nutrition as part of their care, but only a few asked their healthcare team for information or support if it was not offered. Compared to Māori participants, the NZE participants were more likely to have asked their oncology team for dietary information and support during their treatment, although it was not always provided, and they were more likely to actively seek out information from other sources (eg, internet searches, privately funded dietitian or nutritionist). Pacific participants did not report actively seeking out nutrition information. Several participants were not aware that nutrition can have a role in cancer recovery and prevention. Some had assumed diet/nutrition was not important because their oncology doctor did not mention it, expressed disappointment that they had not been informed, and suggested that they would have followed advice had it been given. Compared to both NZE and Māori participants, fewer Pacific participants were aware of a role for nutrition in cancer recovery and prevention.

Attempts to access nutrition information outside of the healthcare setting exposed participants to misinformation, scare tactics, and marketing of unproven expensive remedies, and placed an extra burden on their already low energy levels. Not knowing where to find correct up-to-date information and whether suggested foods/supplements might interfere or interact with their medical treatment were common concerns. These issues were often discussed in the context of wanting to have the important up-to-date dietary information provided to them by a trusted source (such as their oncologist or a dietitian accessible through oncology services) to reduce their burden at an already difficult time. Some participants paid to see a dietitian, nutritionist, or naturopath because this support was not available as part of their cancer care. However, privately funded dietary support was expensive and participants reported being constrained by their budget, especially while they were unable to work.

Theme 2: dietary changes during and after treatment

Table 4 outlines the sub-themes and representative quotes related to dietary changes. Many participants, largely Māori and Pacific Peoples, did not change their diets except in response to treatment side effects. In the absence of advice on nutrition, they did not explore diet as an option in their recovery. Keeping things normal during treatment and just getting through the cancer was the main focus for some of this group. Others believed their diet was already healthy and did not feel the need to make changes.

Participants who made changes to their diet that were not aimed at managing the effects of treatment did so to manage their weight or general health and/or to aid cancer recovery and reduce the risk of recurrence. Dietary changes commonly reported by participants included increasing their intake of fruit and vegetables, reducing red meat, and reducing processed foods and convenience foods such as takeaways and pre-prepared meals. Although less common, there were also some reports of more stringent diets as well as use of unproven supplements and remedies.

Theme 3: barriers to and enablers of healthy eating with cancer (during and after treatment)

Table 5 outlines the sub-themes and representative quotes related to barriers to and enablers of healthy eating with cancer. A major barrier to healthy eating with cancer was a general lack of awareness of the role that a healthy diet can have in cancer prevention and recovery. Awareness was associated with information seeking and attempts to make healthy dietary changes. However, implementing dietary changes was hampered by limited access to information about dietary recommendations and how to implement them, and the expense of food they believed was healthy (eg, fresh fruit and vegetables and fresh fish). Although some participants reported that they were lucky to not have their food choices limited by their budget, others had difficulty being able to afford the food they wanted. Some Māori and Pacific participants reported that low income was a barrier to accessing enough food, healthy or otherwise. Participants from all three ethnic groups

Table 4: Sub-themes and quotes for theme 2: dietary changes during and after treatment.

Carried on eating as normal
"Basically carried on eating the same foods as before because I was already, felt like I was already on a good diet." NZE5 "Just kept to what we usually eat or what was there." M4 "No didn't change my diet, didn't allow it to affect me. I think it was more of a mentality thing. Yeah, just carried on eating even if I didn't feel hungry." M9 "Nothing, no diet, just eat normal, whatever." P4
Managing the effects of cancer/treatment
"As a result of the treatment, I sort of avoid certain foods now." NZE1 "It was just about trying to get anything in." NZE3 "I couldn't eat so I tried really hard to drink and then after that people would bring me the things that I were craving for so that I would eat." M10 "I come home [after chemotherapy], I'm too tired and sleep all the time. Yeh, I can't eat, I can't drink." P1
Managing weight
"I needed to cut off something and try and lose a bit of weight." M4 "I'm trying to cut the way I eat, the eating. Just a little bit at night-time, and from now I lose weight." P4
Nutrition for cancer recovery and prevention
"It was about I can't have this happen again. What can I do naturally to build up my body and to make it stronger." NZE3 "It was sort of like feeling like you're doing something." NZE10 "I look at it [healthy food] as medicine." M8

reported difficulties changing established food preferences and habits as a barrier to healthy eating. These included wanting familiar foods (eg, traditional Pacific foods) and not knowing how to prepare/cook unfamiliar foods.

Short-term effects of cancer and cancer treatment presented barriers to healthy eating, with fatigue, feeling sick, and not being able to tolerate some foods being commonly reported factors influencing the types of food eaten. Food support from whānau (family) and friends enabled participants who were not feeling well to have better access to food, which saved them from having to prepare food while feeling unwell. However, this sometimes resulted in a loss of control over what food was eaten. Being alone or having no family support was a barrier to eating well. Some participants who were hospitalised as part of their treatment (eg, for surgery) felt that the food provided in hospital was poorly suited to their dietary needs and did not fit with healthy eating recommendations.

Theme 4: improvements to nutritional information and support

When asked for suggestions to improve services for cancer patients, most participants said that ongoing advice and support from a dietitian trained in cancer-related nutrition would be beneficial. One participant stated: "If there was a place where people could actually go and talk to some of these wonderful specialists… I think people may be more equipped to actually understand the value of eating properly" (M1). Some wanted personalised one-on-one support, whereas others suggested access to dietitian-led support groups or provision of reliable up-to-date written and/or online information. Such information should be easy to understand and concise, and practical advice on how to implement suggested dietary changes should be included. Other suggestions included offering courses on diet and how to prepare healthy meals, education of the general population to increase knowledge of healthy eating for cancer prevention, and hospital food that is better suited to cancer patients' needs. Many also suggested involving whānau/support people when information is provided, so they can better support the person with cancer, and providing written information for whānau/friends with hints on practical ways to help.

Many participants also acknowledged the increased financial burden that comes with a cancer diagnosis and suggested that some financial or practical support would be useful. Examples included enabling subsidised access to healthy pre-prepared meals and financial and practical help with food shopping and preparation. Further, participants suggested that all patients should be made aware of and actively encouraged to access these services, as many would otherwise not ask for help because, in the words of one participant, "there's a lot of proud people out there who will not put up their hand and say, 'I need help' [if that help were not offered]" (NZE8).

Discussion

This qualitative research identified a shortage of nutrition-related support for cancer survivors. Survivors' desire for more dietary information and support, either as part of a focus on health and wellbeing into the future, or as an important component of holistic healthcare during and after treatment, indicates an unmet need in the provision of cancer care and support in New Zealand. This research also indicates that a lack of dialogue about diet as part of cancer care is sometimes interpreted by patients as an indication that diet is not an important component of cancer care, recovery, and future health and wellbeing. This is of particular concern because belief in a connection between diet and cancer is predictive of successful healthful dietary change.[26,27] Our research indicates that more nutrition-related information and practical support is required to improve cancer outcomes and reduce inequities. This is consistent with international research,[25] but it is the first time this has been explored in a New Zealand context.

The WCRF/AICR report recommends that all cancer patients receive professional expert advice and support on diet and nutrition that is consistent with WCRF cancer prevention recommendations in order to improve survival, reduce risk of a new primary cancer, and minimise the impact of other non-communicable diseases.[2] However, our results indicate

Table 5: Sub-themes and quotes for theme 3: barriers to and enablers of healthy eating with cancer (during and after treatment).

Lack of awareness of nutrition and little/no nutritional information or support (see Table 3)
Financial limitations
"A lot of my food choices are actually dictated by price so it's a balance between what I want to do and what I can do." NZE1 "I was on sick leave last year, so I was getting paid. So I spread out, all the costs over my pays and haven't done anything this year." (talking about cost of accessing information/support) "The money is probably the biggest thing." "I've got to earn money first to be able to afford that stuff." NZE3 "Food's expensive"… "I live in a cold house but I eat veggies so, you know? It's sort of a balance, I guess. Balancing game." NZE7 "Finances have always been a bit of a barrier for me." M2 "You have to budget and those carbs do stretch your meals." M7 "Finances have been an issue because basically I haven't been able to do anything [work] for the last five or six months." M8 "It was hard to me to divided the money to go where it goes to but I want the bread and butter on the table for the kids." P2 "My finance is not very good." P3
Established food habits/preferences
"A lot of those processed meats and stuff that's bad for you actually does appeal to your taste buds." NZE1 "I love food, I love rich food." M3 **"**Especially I love eating takeaways [laughs] yeah I try to cut down"… **"**My family, husband love eating… so whatever I'm trying to cut the way I eat, I see my husband and kids [laughs]." P4
Effects of cancer/treatment
"I notice that when I get really tired, I eat, I eat more rubbish. I think it's just to compensate." NZE9 "The problem has been up until this week is that I haven't been able to eat. And so the food that I have been eating has been the food that I've been craving for so that at least I will eat." M10 "Yeah, can't eat like before." P3 "I was really scared that I would fall asleep [due to overwhelming fatigue] and I'd leave something on the stove"… "So that's why I didn't really cook a lot on the stove because I didn't want to set fire to the house." NZE9
Lack of support
"To try and get something out of WINZ [financial support] is hard and I just didn't have the energy to do it." M8 **"**I did not find 'the person' I was looking to find here who could support me." (talking about access to knowledgeable nutritional support for cancer recovery) NZE10 **"**And then, when you're out [after surgery] you just kind of fend for yourself." NZE7

that this is not currently available to cancer patients in New Zealand. There is increasing recognition that health literacy, which can be aided with dietary support, is an important component of holistic healthcare for cancer patients,[4] and there is evidence of a desire among cancer patients to pursue dietary changes as a way to improve their health (both in the current study and published research).[5–7,9,28] Consistent with other studies,[5,29] this study found that a major barrier to following WCRF recommendations is a lack of awareness that diet is important in cancer recovery.

Although dietitians were seen as the most reliable source of dietary support, participants identified that medical and other healthcare workers had an important role in highlighting the importance of diet in recovery and survival, something that is increasingly recognised internationally.[4] The current research suggests that the systematic incorporation of nutrition advice, information, and support into oncology care and support services would be beneficial for improving cancer-related outcomes and reducing cancer inequities in New Zealand. A comprehensive medical assessment at the time of cancer diagnosis, including attention to co-morbidity, has been suggested,[30] which could be an ideal time to introduce dietary support to help cancer patients during treatment and the post-treatment period.

In common with other evidence,[5] increasing the intake of fruit and vegetables and limiting convenience foods were highlighted by many in this study as dietary changes that were made or attempted. This is consistent with WCRF advice; however, specialist nutritional support would confer additional benefits, including support with how to achieve dietary goals (improved health literacy and self-efficacy),[31,32] information on other less well-known recommendations (such as increasing wholegrains), and recommendations specific to particular cancers and individual patient needs. Healthcare workers also have an essential role in accessing additional support for patients in the form of monetary assistance, food delivery, and referrals to specific support agencies. These forms of support will have an important role in addressing some of the barriers to dietary change and healthy eating identified from this research.

Inequalities in cancer outcomes by socioeconomic status and ethnicity persist in New Zealand and are due to a range of factors, including material deprivation, comorbidity, and health service factors (including institutional racism).[33–35] Differences in active information seeking between ethnic groups in this study are of concern and indicate that relying on patients to question healthcare workers and actively seek out their own information about nutrition may contribute to the gap in equitable cancer outcomes. Sociocultural barriers such as language proficiency, social/cultural norms, level of trust in the health system, stigma, and cultural taboos can limit information-seeking behaviour in disadvantaged and minority populations.[36–40] For example, listening quietly (as opposed to questioning) is common among both Māori and Pacific Peoples and demonstrates respect for someone of higher status such as a doctor.[41,42] In addition, a system that expects patients to ask for information and assumes patients know what questions to ask favours those who are already well informed.[43]

This research identified cost or finances as an important barrier to both accessing dietary support and implementing healthy dietary changes. Access to publicly funded dietitian support was unavailable to many, and support from a privately funded dietitian is financially untenable on a tight budget. The cost of healthy food and the difficulty balancing this with other financial pressures such as housing and family commitments were barriers to healthy eating, and some even struggled to access enough food because of financial or practical constraints. Food security is essential to maintaining a healthy diet at this time. Food insecurity impacts substantially on Māori, Pacific, and low-income families in New Zealand and is associated with increased psychological distress and decreased diet quality.[15,44] A diagnosis of cancer can result in reduced income or loss of employment, which impacts disproportionately on those already food insecure. The added costs of healthcare and time off work are often associated with financial stress and increased reliance on family and other support.[11,45] Financial as well as practical support will be essential for many cancer patients at this time. Providing all cancer patients with

access to dietary advice and support, as well as the means to achieve optimal nutrition, is an important component of equitable cancer care that is likely to contribute to more equitable cancer outcomes.[2]

The credibility of information found outside of standard cancer care services was questioned. This is consistent with other studies that show the availability of dietary information that is seen to be credible is important, especially for achieving persistent dietary change.[6,29] Dietary and other behaviour changes are often made by people looking to achieve greater agency over their prognosis and can be an important part of psychological support and improved quality of life during cancer treatment.[6,28] A recent New Zealand study with Māori and Pacific participants with multi-morbidities confirmed the importance of holistic and culturally competent healthcare for optimal health outcomes.[11] Nutritional recommendations must take into account both food preferences and cultural norms. Māori and Pacific healthcare providers have the potential to deliver such support in culturally appropriate ways. However, they would need to be well resourced and have support for appropriate capacity building.

Strengths and limitations

This study provides valuable insights into the nutrition-related experiences of New Zealand cancer survivors during and after acute cancer treatment. It includes participants from three ethnic groups in three regions of New Zealand in order to explore diversity of experiences, particularly as they relate to health and health service equity. Although this study provides valuable insight of similarities and differences in perspectives and experiences of Māori, Pacific, and New Zealand European cancer survivors, the lower number of Pacific participants and the use of English-language interviewing may have limited the depth of the Pacific participant data. The requirement for interviews to be in English may have contributed to difficulties recruiting Pacific participants. In addition, language barriers can impact on both understanding of the questions and the confidence to provide detailed (as opposed to succinct) answers.[46] This may have resulted in missing potentially important perspectives and limiting the depth of understanding.

Conclusions and recommendations

This research has exposed a need for more nutrition information and support for cancer patients during and after treatment. Cancer patients should be informed about the importance of nutrition and specific cancer-related nutrition recommendations, but provision of support (dietary, practical, financial) in a culturally appropriate context will also be necessary to ensure that those who wish to make dietary changes are able to do so. In addition to supporting cancer recovery with good nutrition, providing information and support has the potential to reduce stress introduced by having to search for information, and limit exposure to misinformation and expensive unproven remedies. A consistent and systematic approach to nutrition support that ensures all cancer patients have equal opportunity to benefit from good nutrition during and after treatment is important to support equity in cancer outcomes. Interventions to address financial barriers and increase access to cancer-related nutrition advice and support are needed to reduce inequities and improve cancer outcomes. A nationwide study to understand the provision of nutrition advice and support from the perspective of healthcare professionals (including barriers and enablers) will contribute to determining the best way forward to address this need. Further Pacific-led research with Pacific cancer survivors with the option to converse in their preferred language is recommended to gain an in-depth understanding of their specific nutrition information/support needs and how best to address those needs.

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REFERENCES

1. Ministry of Health. New Zealand Cancer Action Plan 2019-2029 - Te Mahere mo te Mate Pukupuku o Aotearoa 2019-2029. Wellington: Ministry of Health; 2019.
2. World Cancer Research Fund/American Institute for Cancer Research. Diet, nutrition, physical activity and cancer: a global perspective. Continuous update project expert report. 2018.
3. Guinter MA, McCullough ML, Gapstur SM, Campbell PT. Associations of pre- and postdiagnosis diet quality with risk of mortality among men and women with colorectal cancer. J Clin Oncol. 2018;36:3404-10.
4. Abrams DI. Milking the evidence: diet does matter. J Clin Oncol. 2014;32:2290-2.
5. Beeken RJ, Williams K, Wardle J, Croker H. "What about diet?" A qualitative study of cancer survivors' views on diet and cancer and their sources of information. Eur J Cancer Care. 2016;25:774-83.
6. Kassianos AP, Coyle A, Raats MM. Perceived influences on post-diagnostic dietary change among a group of men with prostate cancer. Eur J Cancer Care. 2015;24:818-26.
7. Tsay SL, Ko WS, Lin KP. The lifestyle change experiences of cancer survivors. J Nurs Res. 2017;25:328-35.
8. Avery KN, Donovan JL, Horwood J, et al. The importance of dietary change for men diagnosed with and at risk of prostate cancer: a multi-centre interview study with men, their partners and health professionals. BMC Fam Pract. 2014;15:81.
9. Patterson RE, Neuhouser ML, Hedderson MM, et al. Changes in diet, physical activity, and supplement use among adults diagnosed with cancer. J Am Diet Assoc. 2003;103:323-8.
10. Maskarinec G, Murphy S, Shumay DM, Kakai H. Dietary changes among cancer survivors. Eur J Cancer Care. 2001;10:12-20.
11. Signal L, Semper K, Stairmand J, et al. A walking stick in one hand and a chainsaw in the other: patients' perspectives of living with multimorbidity. N Z Med J. 2017;130:65-76.
12. Walker T, Signal L, Russell M, et al. The road we travel: Māori experience of cancer. N Z Med J. 2008;121:27-35.
13. Ministry of Health. Health loss in New Zealand

1990-2013: A report from the New Zealand burden of diseases, injuries and risk factors study. Wellington: Ministry of Health; 2016.

14. Statistics New Zealand. National population estimates: At 31 March 2020 - Infoshare tables. Statistics New Zealand; 2020. Available from: https://www.stats.govt.nz/information-releases/national-population-estimates-at-31-march-2020-infoshare-tables
15. University of Otago, Ministry of Health. A focus on nutrition: key findings of the 2008/09 New Zealand adult nutrition survey. Wellington; 2011.
16. Paolantonio L, Kim SY, Ramirez J, et al. Food purchasing behavior of food insecure cancer patients receiving supplemental food vouchers. Support Care Cancer. 2020;28:3739-46.
17. Tarasuk V, Mitchell A, McLaren L, McIntyre L. Chronic physical and mental health conditions among adults may increase vulnerability to household food insecurity. J Nutr. 2013;143:1785-93.
18. Patel KG, Borno HT, Seligman HK. Food insecurity screening: a missing piece in cancer management. Cancer. 2019;125:3494-501.
19. Virizuela J, Camblor-Alvarez M, Luengo-Perez L, et al. Nutritional support and parenteral nutrition in cancer patients: an expert consensus report. Clin Transl Oncol. 2018;20:619-29.
20. Vance V, Campbell S, McCargar L, et al. The voice of experience: diet and weight change in women with breast cancer associate with psychosocial and treatment-related challenges. Can J Diet Pract Res. 2017;78:74-80.
21. Pulotu-Endemann FK, Tu'itahi S. Fonofale: model of health. Fuimaono Karl Pulotu-Endemann; 2009.
22. Rochford T. Whare Tapa Whā: a Māori model of a unified theory of health. J Prim Prev. 2004;25:41-57.
23. Commission on Social Determinants of Health (CSDH). Closing the gap in a generation: health equity through action on the social determinants of health. Final Report of the Commission on Social Determinants of Health. Geneva: World Health Organization; 2008.
24. Braun V, Clarke V. Thematic analysis. In: Cooper H, editor. APA handbook of research methods in psychology, Vol 2: Research designs: quantitative, qualitative, neuropsychological, and biological. Washington: American Psychological Association; 2012.
25. van Veen MR, Mols F, Smeets L, et al. Colorectal cancer survivors' beliefs on nutrition and cancer; correlates with nutritional information provision. Support Care Cancer. 2020;28:1255-63.
26. Rabin C, Pinto B. Cancer-related beliefs and health behavior change among breast cancer survivors and their first-degree relatives. Psychooncology. 2006;15:701-12.
27. Patterson RE, Kristal AR, White E. Do beliefs, knowledge, and perceived norms about diet and cancer predict dietary change? Am J Public Health. 1996;86:1394-400.
28. Maunsell E, Drolet M, Brisson J, et al. Dietary change after breast cancer: extent, predictors, and relation with psychological distress. J Clin Oncol. 2002;20:1017-25.
29. Er V, Lane JA, Martin RM, et al. Barriers and facilitators to healthy lifestyle and acceptability of a dietary and physical activity intervention among African Caribbean prostate cancer survivors in the UK: a qualitative study. BMJ Open. 2017;7:e017217.
30. Signal V, Jackson C, Signal L, et al. Improving management of comorbidity in patients with colorectal cancer using comprehensive medical assessment: a pilot study. BMC Cancer. 2020;20:50.
31. Mosher CE, Fuemmeler BF, Sloane R, et al. Change in self-efficacy partially mediates the effects of the FRESH START intervention on cancer survivors' dietary outcomes. Psychooncology. 2008;17:1014-23.
32. Stoutenberg M, Sogor A, Arheart K, et al. A wellness program for cancer survivors and caregivers: developing an integrative pilot program with exercise, nutrition, and complementary medicine. J Cancer Educ. 2016;31:47-54.
33. Soeberg M, Blakely T, Sarfati D, et al. Cancer trends: trends in cancer survival by ethnic and socioeconomic group, New Zealand 1991–2004. Wellington: 2012.
34. Hill S, Sarfati D, Blakely T, et al. Survival disparities in Indigenous and non-Indigenous New Zealanders with colon cancer: the role of patient comorbidity, treatment and health service factors. J Epidemiol Community Health. 2010;64:117-23.
35. Jeffreys M, Sarfati D, Stevanovic V, et al. Socioeconomic inequalities in cancer survival in New Zealand: the role of extent

of disease at diagnosis. Cancer Epidemiol Biomarkers Prev. 2009;18:915-21.

36. Savolainen R. Approaches to socio-cultural barriers to information seeking. Libr Inform Sci Res. 2016;38:52-9.
37. Ludeke M, Puni R, Cook L, et al. Access to general practice for Pacific peoples: a place for cultural competency. J Prim Health Care. 2012;4:123-30.
38. Richardson A, Allen JA, Xiao HJ, Vallone D. Effects of race/ethnicity and socioeconomic status on health information-seeking, confidence, and trust. J Health Care Poor U. 2012;23:1477-93.
39. Southwick M, Kenealy T, Ryan D. Primary care for Pacific people: a Pacific and health systems approach. Wellington: Pacific Perspectives; 2012.
40. Sheridan NF, Kenealy TW, Kidd JD, et al. Patients' engagement in primary care: powerlessness and compounding jeopardy. A qualitative study. Health Expect. 2015;18:32-43.
41. Jansen P, Bacal K, Crengle S. He Ritenga Whakaaro: Māori experiences of health services. Auckland: Mauri Ora Associates; 2008.
42. Medical Council of New Zealand, Mauri Ora Associates. Best health outcomes for Pacific peoples: practice implications. Medical Council of New Zealand; 2007.
43. Sligo FX, Jameson AM. The knowledge–behavior gap in use of health information. J Am Soc Inf Sci. 2000;51:858-69.
44. Carter KN, Krus K, Blakely T, Collings S. The association of food security with psychological distress in New Zealand and any gender differences. Soc Sci Med. 2011;72:1463-71.
45. Longo CJ, Fitch MI, Banfield L, et al. Financial toxicity associated with a cancer diagnosis in publicly funded healthcare countries: a systematic review. Support Care Cancer. 2020;28:4645-65.
46. Premji S, Kosny A, Yanar B, Begum M. Tool for the meaningful consideration of language barriers in qualitative health research. Qual Health Res. 2020;30:167-81.

Breast cancer costs in New Zealand's public health system

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ABSTRACT

AIM: This study aims to estimate the mean costs of breast cancer in New Zealand's public health system.

METHOD: This study included women diagnosed with invasive breast cancer between 1 July 2010 and 30 June 2018 who received services in public hospitals. These patients were identified from the National Breast Cancer Register or the New Zealand Cancer Registry and linked with the Pharmaceutical Collection, National Minimum Dataset, National Non-Admitted Patient Collection and Mortality Collection.

RESULTS: 22,948 breast cancer patients were included. The mean public health cost of breast cancer was NZ$44,954 per patient for the period of three months preceding and five years following cancer diagnosis, with the treatment phase accounting for 70% of the cost and the follow-up phase accounting for the remaining 30%. During the treatment phase, surgery costs accounted for the biggest proportion (35%) of the total cost, followed by immunotherapy costs (18%), radiotherapy costs (17%) and costs of diagnostic test, scan and biopsy (16%). The costs decreased substantially with age, from $69,121 for women younger than 45 years old to $23,805 for those aged 80 or over.

CONCLUSIONS: The costs of breast cancer in New Zealand's public health system are substantial and have been increasing. However, outcomes of breast cancer have been improving. The results of this study can be used as a baseline of actual costs for comparing the costs of introducing new diagnosis and treatment modalities in the future.

Breast cancer is the most common cancer in New Zealand women and its incidence has been increasing steadily: from 2,799 cases in 2009 to 3,572 in 2018 (a 28% increase).[1] In contrast, mortality from breast cancer (in terms of both the number of deaths and the mortality rates) is declining in New Zealand,[2] with 80% of breast cancer patients now surviving for more than 10 years.[3] New Zealand has introduced and funded new treatments, such as trastuzumab , lapatinib, pertuzumab and ado-trastuzumab emtansine, fulvestrant, Palbociclib and zoledronic acid for adjuvant therapy.[4] Diagnostic tools have also been implemented in recent years, including breast MRI, PET-CT (for small number of patients applying well-defined criteria) and CT imaging for metastatic disease (initially three monthly, but now two monthly). The increasing incidence of breast cancer and advancements in diagnostics and therapeutic options have led to greater economic burden to the healthcare system.[5,6]

As reported in a 2008 Ministry of Health report, *The Price of Cancer*, breast cancer was the most expensive cancer to treat in New Zealand, with breast cancer diagnosis and treatments accounting for 15% of the total costs of cancer.[7] The report demonstrated that breast cancer cost the New Zealand healthcare system $76.8 million per year.[7] The very few studies on the economic burden of cancer in New Zealand[7,8] have focused on economic burden of all cancers in New Zealand, but with data collected a decade ago. Due to the rise in the number of patients diagnosed with breast cancer and evolving diagnostic and therapeutic options, the costs of breast cancer are changing. In order to guide future healthcare planning, an up-to-date and detailed report on the costs of breast cancer is needed.

By linking National Breast Cancer Register data with the national administrative datasets, this study aims to (1) estimate the mean costs of breast cancer in New Zealand's public health system, (2) calculate the proportion of different cost components in total costs and (3) examine the mean costs of breast cancer by age group.

Methods

Data sources

We identified women from the National Breast Cancer Register (NBCR) and the New Zealand Cancer Registry (NZCR) who were diagnosed with breast cancer between 1 July 2010 and 30 June 2018 and included only those who received healthcare services in public hospitals. We linked the eligible breast cancer cases with the Pharmaceutical Collection (PHARMS, which includes all publicly funded pharmaceuticals prescribed in both public and private hospitals), National Minimum Dataset (NMDS, which includes all publicly funded inpatient records), National Non-Admitted Patients Collection (NNAPC, which includes all publicly funded outpatient records), the Mortality Collection (MORT, coded mortality information) and death certificates (uncoded mortality information). The datasets were linked using National Health Index (NHI) numbers, which are unique identifiers for people using publicly funded health and disability services in New Zealand.

Cancer care pathway

We divided the cancer care pathway into two phases: (1) the treatment phase (TP, three months preceding and 12 months following diagnosis of breast cancer) and (2) the follow-up phase (second to fifth year following diagnosis). We further broke down the follow-up phase into the second (FU2), third (FU3), fourth (FU4) and fifth (FU5) years. We considered the date of death or the latest date of service (31 December 2019) available in the NNAPC, NMDS and PHARMS as the censor date (whichever was earlier). The estimation of costs for each phase only included patients who had follow-up time for that phase. For calculating the total cost of all phases combined, we only included patients who had follow-up time for all phases (ie, those who were still alive and not censored within five years post diagnosis).

Cost estimation and analysis

The cost estimation was from the perspective of the Ministry of Health and only included public medical costs, which were the costs of public outpatient services, of public inpatient services and of funded pharmaceuticals (prescribed by either public or private hospitals). Our clinical advisors (RL, MKH and IC) checked the definitions of purchase unit codes for outpatient services (in NNAPC), the definitions of surgery codes for inpatient services (in NMDS) and pharmaceuticals, and this study only included the inpatient, outpatient and pharmaceutical records that were relevant to breast cancer. Costs of diagnostic services such as radiology and pathology, and costs of treatment response assessment tools, were also included in the inpatient or outpatient costs. For pharmaceuticals, only relevant endocrine therapy, chemotherapy and therapies targeted at human epidermal growth factor receptor 2 (HER2) were included. Other medications, such as pain killers, were not included, because we could not identify whether these medications were breast cancer related; including all these medications would overestimate the costs. All cost estimations were based on 2019/2020 New Zealand dollars (NZ$).

Outpatient costs were estimated by multiplying the number of relevant outpatient visits recorded in the NNAPC with the unit cost of outpatient visits. The unit costs for the outpatient visits were based on district health board (DHB)-contracted purchase unit prices. Inpatient costs were estimated by multiplying the accumulated cost weights for all relevant events with the purchase unit price as set by the National Pricing Programme. The Ministry of Health calculates the cost weights, which provides resource utilisation information, for each diagnosis-related group (DRG) code using the weighted inlier equivalent separation (WIES) method and sets a purchase unit price for each year. The 2019/2020 cost-weight unit price was NZ$5,216.21.[9] The costs of publicly funded pharmaceuticals were estimated by multiplying the quantity of the pharmaceuticals dispensed by the unit prices for each pharmaceutical that appears in the Pharmaceutical Schedule.[10]

We estimated the mean of breast cancer in the public healthcare system during the treatment phase and the follow-up phase and described the proportions of different cost components in total costs. The mean costs of breast cancer during different phases were also compared by age group (<45, 45–59, 60–69, 70–79 and 80+ years) after stratification of the cancer cases by cancer stage (stage I, stage II, stage III and stage IV). The difference in costs by age group were examined by Kruskal–Wallis test. The proportions of cost components in total costs by age group were also explored.

Results

Between 1 July 2010 and 30 June 2018, 25,085 women were diagnosed with invasive breast cancer in New Zealand (Figure 1). We excluded 2,137 patients who did not have any treatment records in public hospitals. A total of 22,948 breast cancer patients received services in public hospitals. The number of patients in each phase decreased year by year because some patient died or censored. There were 13,312 patients with five-years follow-up time post diagnosis who were included in the cost estimation for FU5. The mean public health costs of breast cancer were $44,954 per patient (Table 1) for the TP–FU5. Over 70% of the costs were in the TP ($31,599), 14% in the FU2 ($6,181), 7% in the FU3 ($3,008), 6% in the FU4 ($2,721) and 5% in the FU5 ($2,364). The mean costs decreased with age. The costs for the TP–FU5 were from $69,121 for women under 45 years old to $23,805 for women aged 80 years or older (p-value<0.05 by Kruskal–Wallis test).

The proportion of each cost component varied in different phases (Figure 2). Surgery costs accounted for 35% of the total costs in the TP but only 22% in the FU2. In contrast, the immunotherapy costs comprised only 18% of the total costs in the TP and 47% in the FU2. Of the immunotherapy costs, 98% were trastuzumab costs in the TP and 95% in the FU2. During the TP, 16% of the breast cancer costs were for diagnostic test, scan or biopsy; 17% were for radiotherapy, 4% for medical oncology outpatient visit, 7% for chemotherapy (including delivery costs) and less than 1% for endocrine therapy.

Table 2 shows the mean public healthcare costs of breast cancer by age group and stratified by cancer stage. The mean costs of breast cancer decreased with age in all cancer stages, and the differences were significant in all subgroup costs (p-value<0.05 by Kruskal–Wallis test).

For stage I disease, the mean costs of the TP–FU5 were from $53,841 for women aged under 45 years to $22,816 for women aged 80 years or older; for stage II disease, the mean costs were from $57,905 for women aged under 45 years to $26,818 for women aged 80 years or older; for stage III disease, the mean costs were from $79,592 for women aged under 45 years to $27,536 for women aged 80 years or older; and for metastatic cancers, the costs were from $167,935 for women aged under 45 years to $27,902 for women aged 80 years or older.

The mean costs in different phases followed the same pattern. For example, during the TP for metastatic breast cancer, the mean costs decreased from $53,985 for those aged under 45 years to $13,757 for those aged 80 years or older.

The proportion of each cost component in different phases also varied by age group (Table 3). During the TP, the percentage of surgery costs and the percentage of costs of diagnostic test, scan or biopsy both increased with age, from 30% and 9% for women aged under 45 years to 57% and 22% for those aged 80 years or older. On the contrary, during the TP, the percentage of immunotherapy costs, the percentage of chemotherapy costs and the percentage of costs for medical oncology visits all decreased with age, from 27%, 11% and 6% for women aged under 45 years to 3%, 1% and 1% for those aged 80 years or older. During the TP, the percentage of radiotherapy costs increased from 14% for women aged under 45 years to 19% for women aged 60–69 years, and then decreased to 13% for those aged 80 years or older. During the FU2–FU5, the proportion of costs of chemotherapy all decreased with age, but the proportion of other cost components fluctuated.

Discussion

The number of new breast cancer cases has been increasing steadily in New Zealand.[1] The economic burden of breast cancer is also expected to be rising.[7,11]

Figure 1: Data cleaning flow chart.

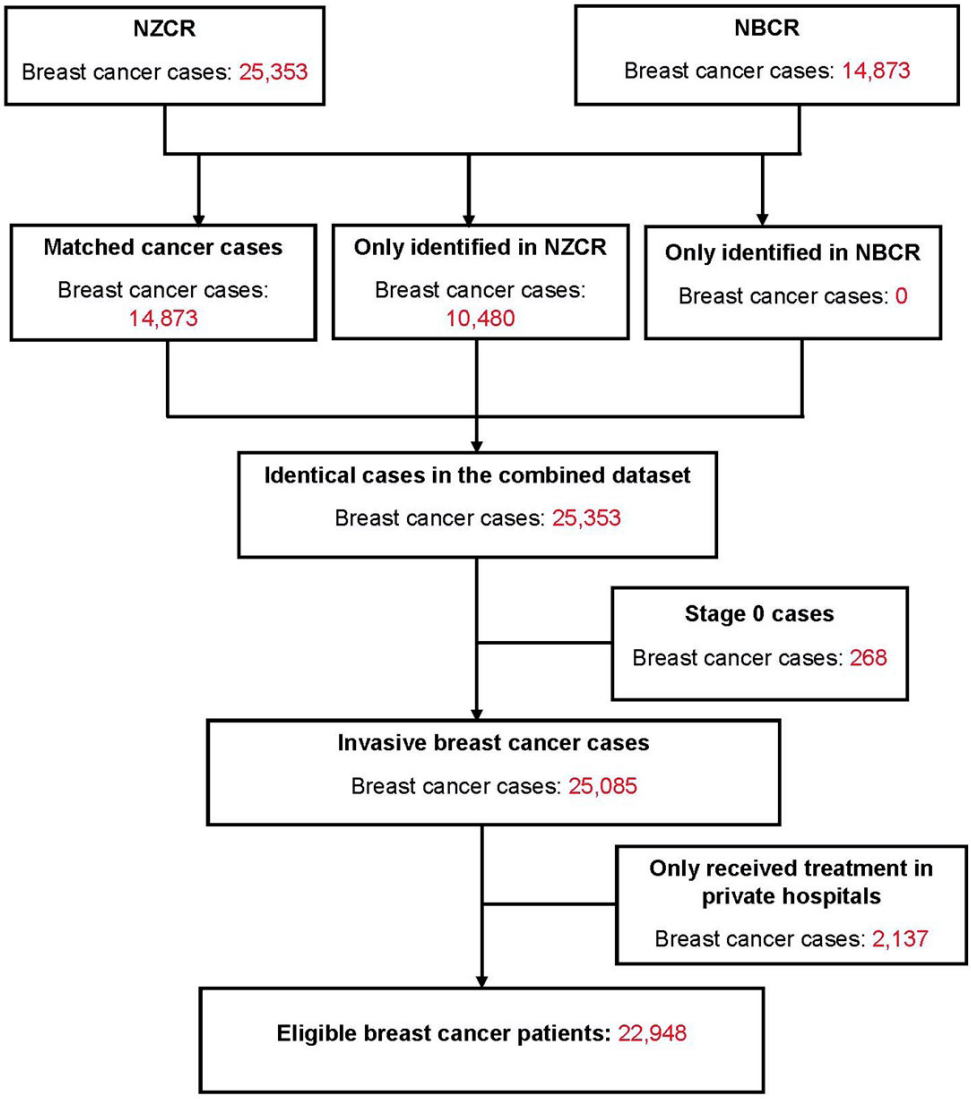

Table 1: Mean public health costs of breast cancer for eligible patients.

Phases	TP	FU2	FU3	FU4	FU5	All phases
Number of patients	22,948	22,204	19,918	16,527	13,312	13,312
Overall mean costs	$31,599	$6,181	$3,008	$2,721	$2,364	$44,954
Mean costs by age group						
<45 years	$44,189	$2,822	$5,705	$5,866	$4,268	$69,121
45–59 years	$35,268	$7,245	$3,434	$2,790	$2,434	$49,021
60–69 years	$29,801	$4,340	$1,972	$1,900	$1,935	$38,638
70–79 years	$25,297	$4,030	$2,383	$2,321	$1,841	$34,019
80+ years	$16,925	$1,976	$1,667	$1,145	$1,281	$23,805

Evolving diagnostic and therapeutic options will also increase the costs of breast cancer. The results of this study can be used as a baseline of actual costs for comparing the costs of introducing new diagnosis and treatment modalities in the future. For example, the results from this study can be used to examine the financial impact of introducing genomic testing in early breast cancer by comparing the costs of chemotherapy before (from this study) and after introducing genomic testing.[12]

Using data for patients diagnosed in 2003–2008, the 2008 Ministry of Health report *The Price of Cancer* showed that the diagnostic and treatment costs for breast cancer were $28,074 per patient from one year prior to diagnosis and five years post diagnosis.[7] In comparison, our study, based on data of patients diagnosed in 2010–2018, found that these costs of breast cancer have increased by 61% to $45,150. This increase can be partly attributed to newly funded pharmaceuticals that have become available during this period, including trastuzumab. From July 2007, PHARMAC agreed to fund trastuzumab for nine weeks for HER2 positive stage I–III breast cancer,[13] and from 1 July 2010 trastuzumab has been funded for up to 12 months for early-stage disease.[14] Publicly funded breast reconstruction has also been increasingly used in New Zealand, which would have increased the costs of breast cancer. However, breast conserving surgery is being used more and more commonly, and the use of breast reconstruction will be affected.[15] Though the costs of breast cancer have been increasing over time, the outcome of breast cancer has been improving.[3] Trastuzumab improved the breast cancer-specific survival for women diagnosed with HER2-positive disease by over 40%.[16]

Most of the costs of breast cancer were in the TP, which is in line with the findings of an Australian study.[17] This is because most of the treatments occur during the TP. In July 2012, the New Zealand healthcare system introduced faster cancer treatment indicators, including a 62-day indicator: patients referred urgently with a high suspicion of cancer receive their first treatment (or other management) within 62 days of the referral being received by the hospital.[18] The costs of breast cancer in our study are driven predominantly by costs of surgery, diagnostic test and immunotherapy. In contrast to the TP, the proportion of the costs for immunotherapy are the highest in the FU2. This might be because surgeries are typically performed in the first year after diagnosis, but the expensive HER2-targeted therapy trastuzumab (funded for 12 months) is still used into FU2.

Figure 2: Proportion of each cost component in different phases.

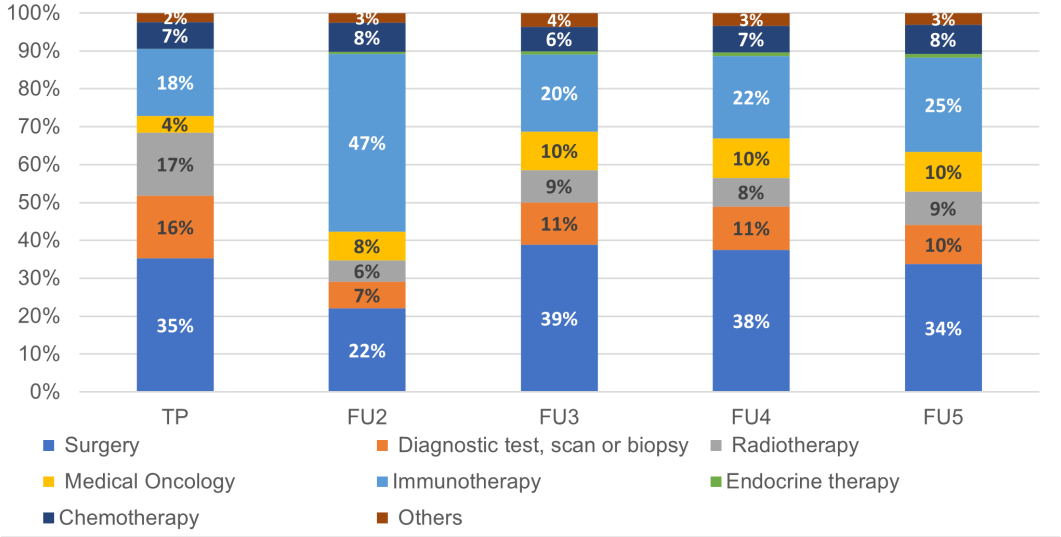

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Table 2: Mean public health costs of breast cancer by age group stratified by cancer stage.

Age group	TP	FU2	FU3	FU4	FU5	All years
Stage I						
<45	$34,423	$7,992	$2,706	$2,947	$3,625	$53,841
45–59	$28,687	$4,324	$1,838	$1,574	$1,891	$36,922
60–69	$26,074	$2,671	$1,294	$1,116	$1,333	$32,064
70–79	$22,229	$2,113	$1,084	$1,438	$998	$26,794
80+	$18,554	$1,272	$960	$984	$1,212	$22,816
Stage II						
<45	$41,744	$9,906	$3,941	$3,159	$1,972	$57,905
45–59	$35,214	$6,473	$2,626	$2,284	$1,926	$47,269
60–69	$30,423	$4,101	$1,422	$1,519	$1,331	$37,791
70–79	$26,166	$3,787	$2,369	$2,391	$2,306	$35,712
80+	$20,881	$1,343	$1,235	$1,331	$1,515	$26,818
Stage III						
<45	$49,407	$15,716	$6,450	$7,427	$4,896	$79,592
45–59	$42,893	$10,745	$4,676	$4,405	$3,484	$65,213
60–69	$38,277	$7,313	$3,147	$2,865	$2,913	$52,725
70–79	$30,843	$4,802	$3,467	$3,806	$1,923	$43,021
80+	$22,145	$3,093	$3,038	$1,339	$1,843	$27,536
Stage IV						
<45	$53,985	$30,360	$30,726	$30,371	$21,265	$167,935
45–59	$40,814	$25,555	$19,202	$16,245	$12,689	$98,527
60–69	$29,312	$17,729	$19,302	$21,300	$17,483	$102,292
70–79	$24,764	$14,276	$12,445	$6,677	$9,051	$53,348
80+	$13,757	$4,471	$3,826	$2,137	$3,751	$27,902

Table 3: Proportion of each cost component in different phases by age group.

Cost components	<45 years	45–59 years	60–69 years	70–79 years	80+ years
TP					
Surgery	30%	34%	35%	39%	57%
Diagnostic test, scan or biopsy	9%	15%	20%	20%	22%
Radiotherapy	14%	17%	19%	18%	13%
Medical oncology	6%	5%	4%	3%	1%
Immunotherapy	27%	19%	15%	13%	3%
Chemotherapy	11%	8%	5%	4%	1%
Endocrine therapy	0%	0%	0%	0%	0%
Others	3%	2%	2%	3%	3%
FU2					
Surgery	24%	22%	18%	22%	39%
Diagnostic test, scan or biopsy	5%	7%	8%	11%	17%
Radiotherapy	5%	5%	6%	8%	12%
Medical oncology	7%	7%	8%	9%	8%
Immunotherapy	49%	49%	48%	40%	13%
Chemotherapy	8%	8%	8%	7%	3%
Endocrine therapy	0%	0%	1%	1%	2%
Others	2%	2%	3%	3%	6%
FU3					
Surgery	41%	43%	30%	29%	42%
Diagnostic test, scan or biopsy	8%	11%	14%	11%	16%
Radiotherapy	6%	8%	11%	10%	12%
Medical oncology	10%	10%	12%	11%	6%
Immunotherapy	24%	18%	20%	27%	14%
Chemotherapy	8%	6%	6%	6%	3%
Endocrine therapy	0%	1%	1%	1%	2%
Others	2%	3%	5%	4%	5%

Table 3: Proportion of each cost component in different phases by age group (continued).

Cost components	<45 years	45–59 years	60–69 years	70–79 years	80+ years
FU4					
Surgery	44%	40%	27%	31%	33%
Diagnostic test, scan or biopsy	7%	11%	16%	14%	15%
Radiotherapy	6%	7%	9%	8%	14%
Medical oncology	9%	11%	11%	10%	7%
Immunotherapy	24%	20%	23%	25%	20%
Chemotherapy	8%	7%	7%	6%	4%
Endocrine therapy	0%	1%	1%	1%	2%
Others	2%	4%	4%	4%	4%
FU5					
Surgery	35%	34%	32%	28%	44%
Diagnostic test, scan or biopsy	7%	10%	12%	10%	22%
Radiotherapy	7%	9%	10%	9%	9%
Medical oncology	11%	11%	10%	11%	5%
Immunotherapy	29%	23%	24%	30%	14%
Chemotherapy	9%	8%	8%	7%	3%
Endocrine therapy	0%	1%	1%	1%	2%
Others	3%	3%	3%	3%	2%

Costs of breast cancer decreased with age. This is likely due to the fact that young woman are more likely to have advanced breast cancer and more likely to receive more treatments than older women.[19] The low chemotherapy and HER2-targeted therapy costs for older women (80+ years) is due to the fact that older women are less likely to receive chemotherapy and HER2-targeted therapies and there being fewer lines of treatment for advanced disease.[20] Increasing age was significantly associated with decreasing use of surgery, adjuvant radiotherapy, endocrine therapy and chemotherapy, even after adjustment for stage and level of co-morbidity.[20]

One of the strengths of this study is that, by combining the NBCR data with the NZCR, PHARMS, NMDS, NNAPC, MORT datasets and death certificates, we had comprehensive data on all breast cancer patients. Our clinical advisors helped us to identify the cancer-related events and therefore the estimated costs were more relevant to breast cancer. One of the limitations of this study is that, in order to calculate the pharmaceutical costs, we used the unit costs of drugs available in the Pharmaceutical Schedule. Using these unit costs might have led to an overestimation of the costs of cancer, because we did not know whether there were any confidential rebates for these drugs.[21] Another limitation is that we have only included endocrine therapy, chemotherapy and HER2-targeted therapy; including any other drugs would have caused underestimation of the total costs. Other drugs that might have been used for breast cancer (eg, pain killers and bisphosphonates) were not included in the cost estimation because we could not identify whether these drugs were used for breast cancer or other diseases (eg, arthritis and osteoporosis). The costs of complications of public chemotherapy, chemotherapy-induced short-term mortality and iatrogenic complication were not included in this study.

Conclusions

The costs of breast cancer in New Zealand's public health system are substantial and have been increasing. However, the outcomes of breast cancer have been improving. The results of this study can be used as a baseline of actual costs for comparing the costs of introducing new diagnosis and treatment modalities in the future.

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Competing interests:
Nil.
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REFERENCES

1. Ministry of Health. New cancer registrations 2018. Wellington, New Zealand.2020.
2. Ministry of Health. BSA New Zealand District Health Board Coverage Report: period ending 30 September 2018. Wellington: Ministry of Health; 2018.
3. Breast cancer in New Zealand. 2020 (cited 2021 Feb 12].
4. Breast Cancer Targeted therapy. 2021 [cited 2021 May 3]. Available from: https://www.breastcancerfoundation.org.nz/breast-cancer/treatment-options/targeted-therapy
5. Yabroff KR, Lund J, Kepka D, Mariotto A. Economic burden of cancer in the United States: estimates, projections, and future research. Cancer epidemiology, biomarkers & prevention : a publication of the American Association for Cancer Research, cosponsored by the American Society of Preventive Oncology. 2011;20:2006-14.
6. Financial Burden of Cancer Care. 2018 [cited 2019 Feb 26]. Available from: https://progressreport.cancer.gov/after/economic_burden
7. Ministry of Health. The Price of Cancer: The public price of registered cancer in New Zealand. Wellington: Ministry of Health. 2011.
8. Blakely T AJ, Kvizhinadze G, Wilson N, Davies A, Clarke P Patterns of cancer care costs in a country with detailed individual data. Medical care. 2015;53:302-9.
9. WIESNZ19 cost weights. 2020 [cited 2020 Nov 23]. Available from: https://www.health.govt.nz/nz-health-statistics/data-references/weighted-inlier-equivalent-separations/wiesnz19-cost-weights
10. Pharmaceutical Schedule. 2020 [cited 2020 Nov 23]. Available from: https://pharmac.govt.nz/pharmaceutical-schedule/
11. Mariotto AB, Robin Yabroff K, Shao Y, Feuer EJ, Brown ML. Projections of the Cost of Cancer Care in the United States: 2010–2020. JNCI: Journal of the National Cancer Institute. 2011;103:117-28.
12. Retèl VP, Byng D, Linn SC, et al. Cost-effectiveness analysis of the 70-gene signature compared with clinical

assessment in breast cancer based on a randomised controlled trial. Eur J Cancer. 2020;137:193-203.

13. Scott Metcalfe, Jackie Evans, Priest G. PHARMAC funding of 9-week concurrent trastuzumab (Herceptin) for HER2-positive early breast cancer. N Z Med J. 2007;120 (1256):1-20.
14. Tait M. Govt dodges Pharmac to fund full Herceptin courses. New Zealand Herald. 2008.
15. Campbell I, Lao C, Blackmore T, et al. Surgical treatment of early stage breast cancer in the Auckland and Waikato regions of New Zealand. ANZ Journal of Surgery. 2018;88:1263-8.
16. Lawrenson R, Lao C, Campbell I, et al. The use of trastuzumab in New Zealand women with breast cancer. Asia Pac J Clin Oncol. 2018;14:e152-e60.
17. Goldsbury DE, Yap S, Weber MF, et al. Health services costs for cancer care in Australia: Estimates from the 45 and Up Study. PLoS ONE. 2018;13.
18. Ministry of Health. Faster Cancer Treatment. 2018. Available from: https://www.health.govt.nz/our-work/diseases-and-conditions/cancer/previous-cancer-initiatives/faster-cancer-treatment
19. Bastiaannet E, Liefers GJ, de Craen AJM, et al. Breast cancer in elderly compared to younger patients in the Netherlands: stage at diagnosis, treatment and survival in 127,805 unselected patients. Breast Cancer Research and Treatment. 2010;124,:801-7.
20. Blackmore T, Lawrenson R, Lao C, et al. The characteristics, management and outcomes of older women with breast cancer in New Zealand. Maturitas 2018;112:64-70.
21. PHARMAC. Cost Resource ManualVersion3 - Pharmac. Wellington, New Zealand. 2018.

Use and results of systemic treatments for de novo and recurrent metastatic breast cancer: a population-based cohort study

Chunhuan Lao, Marion Kuper-Hommel, Ian Campbell, Mark Elwood, Ross Lawrenson

ABSTRACT

AIMS: To describe the systemic treatments in patients with de novo metastatic breast cancer (dnMBC, initial metastatic diagnosis) and recurrent metastatic breast cancer (rMBC).

METHODS: Women diagnosed with dnMBC and rMBC in 2010–2017 were identified. Adjusted odds ratios of receiving systemic treatments were estimated by logistic regression model. Cox proportional hazards regression was used to estimate adjusted hazard ratio of breast cancer-specific mortality by treatments.

RESULTS: The adjusted odds ratio of having chemotherapy and trastuzumab (for human epidermal growth factor receptor 2 positive (HER2+) disease) for Pacific women was 0.43 and 0.13 compared to European women. Patients receiving chemotherapy had improved survival for HER2+ non-luminal and triple negative metastatic breast cancer (MBC) (hazard ratios: 0.30, 0.66). Those with endocrine therapy was associated with better survival for luminal A and luminal B HER2+ MBC (hazard ratio: 0.25, 0.26). Trastuzumab was associated with superior survival in luminal B HER2+ and HER2+ non-luminal disease (hazard ratio: 0.34, 0.40).

CONCLUSIONS: Pacific women with MBC were less likely to receive chemotherapy and trastuzumab than non-Pacific women. Chemotherapy was associated with improved survival in HER2+ non-luminal and triple negative MBC. Endocrine therapy improved survival in luminal A and luminal B HER2+ disease. Trastuzumab was associated with improved survival in luminal B HER2+ and HER2+ non-luminal disease.

Breast cancer is the second most common cause of cancer death in New Zealand.[1] The prognosis for patients diagnosed with early breast cancer is excellent, but the prognosis for patients diagnosed with metastatic breast cancer (MBC) is poor.[2] Thanks to treatment advances over the last three decades, the survival of patients with MBC has improved.[3] New medications introduced for MBC in the last three decades include taxanes, vinca-alkaloids, pyrimidine analogs, capecitabine, human epidermal growth factor receptor 2 (HER2) targeted drugs and HER2 drug conjugates, aromatase inhibitors, selective estrogen receptor downregulators (SERDs) and CDK4/6 inhibitors.[3]

Multiple lines of chemotherapy, endocrine therapies, HER2-targeted therapies and immunotherapies are now available for MBC and have proven beneficial for specific breast cancer subtypes. It is known that women who have HER2 positive (HER2+) breast cancer have a poorer prognosis compared to women with HER2 negative (HER2-) disease.[4] Trastuzumab was first licensed by the US Food and Drug Administration (FDA) in 1998 for metastatic HER2+ breast cancer and was funded for metastatic HER2+ breast cancer in New Zealand since

2002 by PHARMAC, the national pharmaceutical funding agency.[5,6]

There are differences in the features and survival between patients with de novo MBC (dnMBC, initial metastatic diagnosis) and patients who develop recurrent MBC (rMBC) following an initial non-metastatic diagnosis.[7] For instance, more luminal A and triple-negative breast cancers are found among those with dnMBC compared to rMBC.[8] The median survival is 2–3 years for dnMBC but less than two years for rMBC.[2,7,9–11]

This observational study aims to describe the use and results of systemic treatments for patients with dnMBC and rMBC in New Zealand, and to examine the equity in access to systemic treatments by ethnic group. This study is an extension of an earlier study[7] that demonstrated the characteristics and survival of dnMBC and rMBC.

Methods

We included women diagnosed with dnMBC and women who developed rMBC during the period 2010–2017. Patients were identified from the New Zealand Breast Cancer Register (NZBCR). We linked patients via their National Health Index (NHI) numbers to the New Zealand Mortality Collection (including free-text mortality for more recent deaths not yet coded in the Mortality Collection) to obtain mortality data for survival analysis. The Pharmaceutical Collection dataset (PHARMS) was also linked to identify the use of endocrine therapy, chemotherapy and trastuzumab and was cross-checked with the NZBCR treatment data. From the combined dataset, the following data were collected: (1) patient characteristics: age, ethnicity and deprivation quintile; (2) tumour information: date of primary diagnosis, date of metastatic diagnosis, sites of metastases at diagnosis and biomarkers (estrogen receptor (ER), progesterone receptor (PR) and HER2); (3) treatments: surgery, radiotherapy, endocrine therapy, chemotherapy and trastuzumab; (4) outcomes: cause of death and date of death. The register records self-identified ethnicity collected as a part of the WBCR consent process, as per the Ministry of Health's Ethnicity Data Protocols. In accord with to the American Joint Committee on Cancer (AJCC) Cancer Staging Manual,[12] women who had presented with distant metastases at diagnosis or within four months of primary diagnosis were considered to have dnMBC, and women who had developed metastatic disease more than four months after a primary diagnosis were considered to have rMBC.

Based on the metastasis-free interval (MFI), which is the time between initial non-MBC diagnosis and diagnosis of rMBC, we stratified patients with rMBC into four groups: recurrent in <2 years, recurrent in 2–4 years, recurrent in 5–7 years and recurrent in 8+ years. First site(s) of metastases at metastatic diagnosis were classified into three groups: non-visceral (including bone and all nodal areas except ipsilateral axillary, internal mammary and supraclavicular areas), visceral (liver, lung, brain, pleura/peritoneum and others) and both (both visceral and non-visceral). The treatment option depended on subtype and the survival varies by subtype.[13–16] Breast cancer subtypes were categorised into five groups according to biomarker status, based on the modified St. Gallen Consensus recommendation, which excludes Ki67[13–16]: (1) luminal A: ER+, PR+ and HER2-; (2) luminal B HER2-: ER or PR+, HER2-; (3) luminal B HER2+: ER+ and/or PR+, HER2+; (4) HER2 non-luminal: ER-,PR-,HER2+; (5) triple negative: ER-, PR-, HER2-. In this study, HER2+ was defined as FISH amplified or 3+ staining on immunohistochemistry (IHC) according to the 2013 American Society of Clinical Oncology Guidelines.[17] As recommended in the 2001 St. Gallen Consensus, ER+ or PR+ was assessed as any degree of IHC positivity (at least 1+ intensity and 1% staining of nuclei).[18]

Characteristics of the study cohort and use of systemic treatments were compared between dnMBC and rMBC. The use of endocrine therapy was examined for ER+ or PR+ cases only, and use of trastuzumab was examined for HER2+ cases only. Adjusted odds ratios for receiving chemotherapy, endocrine therapy and trastuzumab were estimated by logistic regression model after adjustments for age, ethnicity, year of metastatic diagnosis, deprivation quintile, type of MBC (dnMBC and rMBC with different MFIs), site of metastases and biomarker subtype. Cox proportional hazards regression was used to estimate the adjusted hazard ratio of

breast cancer-specific mortality by treatments after adjustment for age, ethnicity, year of metastatic diagnosis, deprivation quintile, site of metastases and type of MBC, and after stratification by biomarker subtype. Analyses of breast-cancer-specific survival were censored at either date of death or 31 December 2018 (the last date of update of the Mortality Collection). All data analyses were performed in IBM SPSS 25 (New York, United States). Ethics approval for the study was granted through the Northern A Health and Disability Ethics Committee (reference: 19/CEN/14/AM01).

Results

We identified 2,177 patients diagnosed with MBC in 2010–2017, with 30.6% of cases (667) being de novo and 69.4% recurrent (1,510) (Table 1). Overall, 70.2% of the patients with MBC were New Zealand European and 47.7% were aged under 60 years. Among the dnMBC cases, 17.3% of them were luminal B HER2+ disease and 9.4% were triple-negative disease, compared to 9.5% and 19.6% in rMBC. Most of the rMBC cases were found within four years after the primary non-metatsatic diagnosis: 31.9% in less than two years, and 37.4% in 2–4 years.

Pacific women were the least likely to receive chemotherapy for MBC, and also the least likely to receive trastuzumab for HER2+ MBC (Table 2, Table 3), for both dnMBC and rMBC. After adjustment for age, year of metastatic diagnosis, deprivation quintile, type of metastases, site of metastases and biomarker subtype, the adjusted odds ratio of having chemotherapy was 0.43 (95% confidence interval (CI): 0.30–0.60, p-value<0.001) for Pacific women, and the adjusted odds ratio of having trastuzumab (for HER2+ disease only) was 0.13 (95% CI: 0.06–0.29, p-value<0.001) for Pacific women, compared to New Zealand European women. After adjustment, there was no significant difference in use of endocrine therapy for ER+ and/or PR+ MBC between different ethnic groups. The use of chemotherapy and endocrine therapy has been found to be decreasing over time, with adjusted odds ratios per year of 0.95 (95% CI: 0.91–0.99, p-value<0.05) and 0.90 (95% CI: 0.84–0.96, p-value<0.001).

Compared to those with dnMBC, patients with rMBC were less likely to receive endocrine therapy and trastuzumab. Patients with visceral metastases and patients with both visceral and non-visceral metastases were less likely to have endocrine therapy than patients with non-visceral metastases only (adjusted odds ratios: 0.34 (95% CI: 0.24–0.48, p-value<0.001) and 0.60 (95% CI: 0.41–0.87, p-value<0.01)). Compared to luminal A disease, patients with luminal B HER2+, HER2+ non-luminal and triple-negative disease were more likely to be treated with chemotherapy, with adjusted odds ratios of 1.67 (95% CI: 1.20–2.32, p-value<0.01), 2.50 (95% CI: 1.64–3.82, p-value<0.001) and 1.64 (95% CI: 1.22–2.20, p-value<0.001), respectively.

After adjustment for age, ethnicity, year of metastatic diagnosis, deprivation quintile, site of metastases and type of MBC, patients receiving chemotherapy showed improved survival for MBC patients with aggressive subtype disease after a median follow-up time of 16 months (adjusted hazard ratio of 0.30 (95% CI: 0.16–0.55, p-value<0.001) for HER2+ non-luminal and 0.66 (95% CI: 0.50–0.86, p-value<0.01) for triple-negative disease (Table 4). Patients with endocrine therapy had improved survival for patients with luminal A and luminal B HER2+ MBC, with an adjusted hazard ratio of 0.25 (95% CI: 0.20–0.31, p-value<0.001) and 0.26 (95% CI: 0.18–0.39, p-value<0.001). Patients with HER2+ disease treated with trastuzumab showed a substantial benefit, with adjusted hazard ratios of 0.34 (95% CI: 0.21–0.56, p-value<0.001) for luminal B HER2+ disease and 0.40 (95% CI: 0.24–0.68, p-value<0.001) for HER2+ non-luminal disease.

Discussion

This observational study found that systemic treatments are associated with differing MBC survival for different biomarker subtypes. Chemotherapy was associated with a significant survival benefit but only in HER2+ non-luminal and triple-negative disease. No significantly different outcomes in other subgroups were observed between those treated with and without chemotherapy where endocrine therapy and trastuzumab have benefits.

Table 1: Characteristics of metastatic breast cancer.

Subgroup	dnMBC		rMBC		P-value (Chi-square test)	Total	
Ethnicity							
European	435	(65.2%)	1093	(72.4%)		1528	(70.2%)
Māori	72	(10.8%)	159	(10.5%)		231	(10.6%)
Pacific	89	(13.3%)	132	(8.7%)	<0.001***	221	(10.2%)
Asian	42	(6.3%)	96	(6.4%)		138	(6.3%)
Others	29	(4.3%)	30	(2.0%)		59	(2.7%)
Age group							
<50	163	(24.4%)	378	(25.0%)		541	(24.9%)
50–59	125	(18.7%)	372	(24.6%)		497	(22.8%)
60–69	112	(16.8%)	286	(18.9%)	<0.001***	398	(18.3%)
70–79	149	(22.3%)	247	(16.4%)		396	(18.2%)
80+	118	(17.7%)	227	(15.0%)		345	(15.8%)
Deprivation quintile							
1 (least deprived)	71	(18.2%)	225	(19.0%)		296	(18.8%)
2	59	(15.1%)	201	(17.0%)		260	(16.5%)
3	78	(20.0%)	222	(18.7%)		300	(19.0%)
4	68	(17.4%)	236	(19.9%)	0.477	304	(19.3%)
5 (most deprived)	114	(29.2%)	301	(25.4%)		415	(26.3%)
Unknown	277		325			602	
Site of metastases							
Non-visceral	246	(39.1%)	551	(37.9%)		797	(38.2%)
Visceral	206	(32.8%)	528	(36.3%)		734	(35.2%)
Both	177	(28.1%)	376	(25.8%)	0.271	553	(26.5%)
Unknown	38		55			93	

Table 1: Characteristics of metastatic breast cancer (continued).

Subgroup	dnMBC		rMBC		P-value (Chi-square test)	Total	
Subtype							
Luminal A	276	(43.9%)	718	(49.3%)	<0.001***	994	(47.7%)
Luminal B HER2-	52	(8.3%)	69	(4.7%)		121	(5.8%)
Luminal B HER2+	109	(17.3%)	138	(9.5%)		247	(11.9%)
HER2+ non-Luminal	53	(8.4%)	103	(7.1%)		156	(7.5%)
Triple negative	59	(9.4%)	285	(19.6%)		344	(16.5%)
Unknown	118		197			315	
MFI							
<2 years	-		482	(31.9%)		-	
2–4 years			565	(37.4%)			
5–7 years			231	(15.3%)			
8+ years			232	(15.4%)			
Total	**667**	(30.6%)	**1,510**	(69.4%)		**2,177**	

dnMBC: de novo metastatic breast cancer; rMBC: recurrent metastatic breast cancer

* <0.05, **<0.01, ***<0.001; All p-values were estimated after excluding the unknown group.

Table 2: Treatment pattern for metastatic breast cancer.

Subgroup	Use of chemotherapy				Use of endocrine therapy (for ER+ and/or PR+ only)				Use of trastuzumab (for HER2+ only)			
	dnMBC		rMBC		dnMBC		rMBC		dnMBC		rMBC	
	n	%†	n	%	n	%	n	%	n	%	n	%
Ethnicity												
European	203	46.6%	586	53.7%	274	91.0%	594	78.3%	78	78.8%	91	57.2%
Māori	43	59.7%	90	56.6%	44	84.6%	94	81.0%	20	90.9%	25	73.5%
Pacific	39	43.8%	64	48.5%	60	87.0%	87	88.8%	15	65.2%	8	25.8%
Asian	26	61.9%	56	58.3%	23	79.3%	53	77.9%	9	81.8%	12	75.0%
Others	15	51.7%	17	56.7%	20	87.0%	15	65.2%	9	75.0%	3	75.0%
p-value	0.088		0.573		0.257		0.064		0.335		<0.001***	
Age group												
<50	125	76.7%	283	74.9%	109	90.8%	213	80.1%	61	89.7%	61	70.1%
50–59	86	68.8%	239	64.2%	75	87.2%	205	79.5%	25	86.2%	44	74.6%
60–69	56	50.0%	176	61.5%	67	88.2%	173	80.8%	27	79.4%	19	47.5%
70–79	51	34.2%	91	36.8%	100	86.2%	135	79.4%	17	63.0%	13	43.3%
80+	8	6.7%	24	10.6%	70	92.1%	117	75.0%	1	11.1%	2	7.1%
p-value	<0.001***		<0.001***		0.680		0.727		<0.001***		<0.001***	
Deprivation quintile												
1 (least deprived)	33	46.5%	133	59.1%	47	92.2%	130	79.3%	13	72.2%	19	54.3%
2	28	47.5%	116	57.7%	28	75.7%	109	76.2%	8	80.0%	14	48.3%
3	32	41.0%	129	58.1%	48	84.2%	137	83.0%	10	83.3%	25	62.5%
4	40	58.8%	132	55.9%	46	93.9%	147	83.1%	15	78.9%	16	51.6%
5 (most deprived)	53	46.5%	147	48.8%	78	86.7%	181	81.9%	22	78.6%	34	55.7%
Unknown	140	50.4%	156	48.1%	174	91.6%	139	71.6%	63	78.8%	31	64.6%
p-value	0.300		0.106		0.098		0.483		0.964		0.808	

Table 2: Treatment pattern for metastatic breast cancer (continued).

Subgroup	Use of chemotherapy				Use of endocrine therapy (for ER+ and/or PR+ only)				Use of trastuzumab (for HER2+ only)			
	dnMBC		rMBC		dnMBC		rMBC		dnMBC		rMBC	
	n	%†	n	%	n	%	n	%	n	%	n	%
Site of metastases at diagnosis												
Non-visceral	123	50.0%	291	52.8%	181	93.8%	387	87.2%	45	83.3%	39	50.0%
Visceral	109	52.7%	278	52.8%	104	83.9%	215	70.5%	49	81.7%	47	52.8%
Both	89	50.3%	228	60.6%	121	87.7%	221	80.1%	36	70.6%	50	69.4%
Unknown	5	13.2%	16	29.1%	15	78.9%	20	51.3%	1	50.0%	3	60.0%
p-value	0.804		0.030*		0.015*		<0.001***		0.221		0.034*	
Subtype												
Luminal A	112	40.4%	384	53.6%	253	91.3%	581	81.0%	-	-	-	-
Luminal B HER2-	19	36.5%	35	50.7%	48	92.3%	50	72.5%	-	-	-	-
Luminal B HER2+	80	73.4%	83	60.1%	89	81.7%	98	71.0%	82	75.2%	78	56.5%
HER2+ non-Luminal	44	83.0%	71	68.9%	-	-	-	-	45	84.9%	60	58.3%
Triple negative	44	74.6%	163	57.2%	-	-	-	-	-	-	-	-
Unknown	27	22.9%	77	39.1%	31	86.1%	114	81.4%	4	80.0%	1	33.3%
p-value	<0.001***		0.030*		0.017*		0.012*		0.160		0.788	
MFI												
<2 years	-		247	51.4%		-	218	77.0%	-		38	50.7%
2–4 years			342	60.5%			305	77.6%			79	64.2%
5–7 years			128	55.4%			155	81.2%			15	50.0%
8+ years			96	41.4%			165	83.8%			7	43.8%
p-value			<0.001***				0.232				0.133	
Total	326	48.8%	813	53.9%	421	88.8%	843	79.2%	131	78.4%	139	57.0%

dnMBC: de novo metastatic breast cancer; rMBC: recurrent metastatic breast cancer

* <0.05, **<0.01, ***<0.001; All p-values were estimated after excluding the unknown group.

† Percentage of patients having that systemic treatment over all dnMBC patients or over all rMBC patients.

Table 3: Adjusted odds ratios[†] of having treatment for metastatic breast cancer.

Factors	Chemotherapy	Endocrine therapy (for HR+ only)	Trastuzumab (for HER2+ only)
Age (continuous)	0.93 (0.93–0.94)***	1.00 (0.99–1.01)	0.93 (0.91–0.95)***
Ethnicity			
European	Reference	Reference	Reference
Māori	0.80 (0.57–1.11)	0.96 (0.61–1.53)	1.21 (0.51–2.85)
Pacific	0.43 (0.30–0.60)***	1.55 (0.91–2.65)	0.13 (0.06–0.29)***
Asian	0.77 (0.52–1.15)	0.83 (0.48–1.43)	1.12 (0.38–3.34)
Others	1.11 (0.61–2.03)	0.66 (0.31–1.37)	0.98 (0.25–3.85)
Year (continuous)	0.95 (0.91-–0.99)*	0.90 (0.84–0.96)***	1.04 (0.92–1.16)
Deprivation quintile			
1 (least deprived)	Reference	Reference	Reference
2	1.14 (0.77–1.67)	0.68 (0.41–1.13)	1.53 (0.57–4.12)
3	1.06 (0.73–1.54)	1.04 (0.62–1.76)	1.55 (0.60–3.95)
4	1.16 (0.80–1.68)	1.29 (0.76–2.20)	1.40 (0.55–3.56)
5 (most deprived)	0.78 (0.55–1.12)	0.94 (0.57–1.54)	1.78 (0.74–4.31)
Type of metastases			
De novo	Reference	Reference	Reference
Recurrent in <2 years	0.86 (0.65–1.14)	0.37 (0.24–0.56)***	0.26 (0.13–0.52)***
Recurrent in 2-4 years	1.22 (0.93–1.60)	0.40 (0.27–0.59)***	0.39 (0.20–0.73)**
Recurrent in 5-7 years	1.26 (0.89–1.79)	0.47 (0.29–0.77)**	0.22 (0.08–0.59)**
Recurrent in 8+ years	0.89 (0.62–1.28)	0.67 (0.39–1.16)	0.21 (0.06–0.70)*
Site of metastases			
Non-visceral	Reference	Reference	Reference
Visceral	1.08 (0.86–1.38)	0.34 (0.24–0.48)***	1.15 (0.63–2.11)
Both	1.27 (0.99–1.63)	0.60 (0.41–0.87)**	1.42 (0.75–2.68)
Subtype			
Luminal A	Reference	Reference	-
Luminal B HER2-	1.09 (0.70–1.70)	0.77 (0.46–1.29)	-
Luminal B HER2+	1.67 (1.20–2.32)**	0.50 (0.35–0.72)***	Reference
HER2+ non-Luminal	2.50 (1.64–3.82)***	-	1.27 (0.74–2.16)
Triple negative	1.64 (1.22–2.20)***	-	-

dnMBC: de novo metastatic breast cancer; rMBC: recurrent metastatic breast cancer

[†] All the above factors were included in the logistic regression model, and the respective odds ratios were adjusted for other factors.

* <0.05, **<0.01, ***<0.001

Table 4: Adjusted hazard ratios[†] of treatments on breast cancer-specific mortality by subtype.

Treatment	Luminal A (994)	Luminal B HER2- (121)	Luminal B HER2+ (247)	HER2+ non-luminal (156)	Triple negative (344)
Chemotherapy					
No chemo-therapy	Reference	Reference	Reference	Reference	Reference
Had chemo-therapy	1.11 (0.93–1.32)	0.61 (0.32–1.15)	0.82 (0.52–1.30)	0.30 (0.16–0.55)***	0.66 (0.50–0.86)**
Endocrine therapy					
No endocrine therapy	Reference	Reference	Reference		
Had endo-crine therapy	0.25 (0.20–0.31)***	0.60 (0.32–1.15)	0.26 (0.18–0.39)***	-	-
Trastuzumab					
No trastuzumab			Reference	Reference	
Had trastu-zumab	-	-	0.34 (0.21–0.56)***	0.40 (0.24–0.68)***	-

dnMBC: de novo metastatic breast cancer; rMBC: recurrent metastatic breast cancer.

[†] Adjusted for age, ethnicity, deprivation quintile, year of metastatic diagnosis, type of MBC (dnMBC and rMBC with different MFIs) and site of metastases.

* <0.05, **<0.01, ***<0.001.

As expected, trastuzumab was associated with improved outcome in HER2+ breast cancers, which confirms the outcomes of clinical trials[19–23] and that application in New Zealand reflects the positive clinical trial results.

Pacific women were less likely to have chemotherapy for MBC and less likely to have trastuzumab (for HER2+ disease only). Our previous paper investigating the use of trastuzumab for patients with stage I–III HER2+ breast cancer also found that Pacific women were less likely to receive trastuzumab.[13] This was partly because Pacific patients had more comorbidities[24] and were more likely to decline chemotherapy and trastuzumab.[13,25] Further research is needed to identify the reasons why Pacific women with metastatic breast cancer were less likely to receive treatments, and further efforts will be needed to ensure equal access to treatments. We did not find a significant difference in endocrine therapy and trastuzumab between Māori and New Zealand European women. These achievements are probably associated with the all advocations and efforts on reducing inequity for Māori patients with cancer in New Zealand.[26–28] There was a lower use of chemotherapies for Māori compared to European women, but this was probably because of the small number of patients and is likely insignificant; a larger sample size is needed for confimation.

We did not find any significant difference in survival between Māori and European women with MBC.[7] This is inconsistent with the Breast Cancer Foundation report for advanced breast cancer,[29] which found a 5% five-year survival rate for Māori and a 15% five-year survival rate for Europeans, and the viewpoint by Kereama-Royal et al [30] on wose outcome on MBC for Māori patients. This inconsistency may be because the Breast Cancer Foundation report included data from 2000 to 2015, whereas our study included data from 2010 to 2017. This study and our published study[7] show that equal outcomes for MBC have been achieved between Māori and Europeans in recent years.

There was less chemotherapy and endocrine therapy use recorded for patients diagnosed with MBC in 2016–2017 than in the previous years. This is probably because 19% of patients started their chemotherapy more than two yearsafter the metastatic diagnosis (based on the 2010–2015 data), and 18% of patients only started endocrine therapy more than two years after the metastatic diagnosis. We assumed that another 18–19% of patients diagnosed in 2016–2017 might have received chemotherapy and endocrine therapy more than two years after their metastatic diagnosis, but these data were not available when we conducted our study and therefore the use of chemotherapy and endocrine for patients diagnosed in 2016–2017 was underestimated. With the new targeted therapies being funded including pertuzumab (funded since January 2017) and trastuzumab emtansine (funded since December 2019), further research with a longer follow-up time is needed to find out the benefits of these new treatments.

We found that 78.4% of dnMBC HER2+ patients received trastuzumab, whereas only 57% of rMBC HER2+ patients received trastuzumab. The difference may be because 54% of rMBC HER2+ patients were treated with trastuzumab for their primary non-metastatic breast cancer. (Trastuzumab cannot be started at the time of the metastatic breast cancer diagnosis if the HER2+ breast cancer recurred within 12 months of completing adjuvant trastuzumab.) The Special Authority criteria by PHARMAC requires that interval between adjuvant and metastatic trastuzumab is more than 12 months. As expected, women with visceral metastases were significantly less likely to receive endocrine therapy (odds ratio of 0.34 for visceral metastases compared to non-visceral metastases). Previous literature has demonstrated both a greater chance of response and a more rapid response when chemotherapy is used for visceral disease.[31,32] In our study, compared to women with non-visceral metastases, women with visceral metastases and both metastases were slightly more likely to have chemotherapy, but the difference is not significant.

The strength of this work is that it is a population-based study with detailed data from the NZBCR, including biomarker status. Treatment information from NZBCR was cross-checked with the PHARMS data to make sure the treatment data

were relatively complete. However, as mentioned above, for patients diagnosed in 2016–2017, the short follow-up time available likely led to underestimation of treatments used. Also, our study was not based on randomised data, and patients were selected for each of these treatments based on a multitude of disease and patient factors, not all of which have necessarily been adequately adjusted for in our models. In our models, we have adjusted factors that were recorded in NZBCR, including age, ethnicity, deprivation quintile, year of metastatic diagnosis, type of MBC and site of metastases.

Conclusion

This observational population-based study found that Pacific women with MBC were less likely to receive chemotherapy and trastuzumab than other ethnic groups. Māori had equal access to systemic treatment as compared with Europeans. Chemotherapy was associated with improved survival in HER2+ non-luminal and triple negative MBC but not other subtypes. Endocrine therapy improved survival in luminal A MBC and luminal B HER2+ disease, and trastuzumab was associated with improved survival in luminal B HER2+ and HER2+ non-luminal disease.

Competing interests:
Nil.
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REFERENCES

1. Ministry of Health. Cancer: New registrations and deaths 2013. Wellington: Ministry of Health. 2016.
2. New Zealand Breast Cancer Foundation. Insights into living – and dying – with Advanced Breast Cancer in New Zealand. Auckland, New Zealand. 2018.
3. Caswell-Jin JL, Plevritis SK, Tian L, et al. Change in Survival in Metastatic Breast Cancer with Treatment Advances: Meta-Analysis and Systematic Review. JNCI Cancer Spectr. 2018;2:pky062-pky.
4. Slamon DJ, Clark GM, Wong SG, Levin WJ, Ullrich A, McGuire WL. Human breast cancer: Correlation of relapse and survival with amplification of the HER-2/neu oncogene. Science. 1987;235:177-82.
5. Ferrusi IL, Marshall DA, Kulin NA, Leighl NB, Phillips KA. Looking back at 10 years of trastuzumab therapy: What is the role of HER2 testing? A systematic review of health economic analyses. Personalized Medicine. 2009;6:193-215.
6. Metcalfe S, Evans J, Priest G. PHARMAC funding of 9-week concurrent trastuzumab (Herceptin) for HER2-positive early breast cancer. N Z Med J. 2007;120.
7. Lao C, Kuper-Hommel M, Elwood M, Campbell I, Edwards M, Lawrenson R. Characteristics and survival of de novo and recurrent metastatic breast cancer in New Zealand. Breast Cancer. 2021;28:387-97.
8. Malmgren JA, Mayer M, Atwood MK, Kaplan HG. Differential presentation and survival of de novo and recurrent metastatic breast cancer over time: 1990-2010. Breast Cancer Res Treat. 2018;167:579-90.
9. den Brok WD, Speers CH, Gondara L, Baxter E, Tyldesley SK, Lohrisch CA. Survival with metastatic breast cancer based on initial presentation, de novo versus relapsed. Breast Cancer Res Treat. 2017;161:549-56.
10. Lobbezoo DJ, van Kampen RJ, Voogd AC, et al. Prognosis of metastatic breast cancer: are there differences between patients with de novo and recurrent metastatic breast cancer? Br J Cancer. 2015;112:1445-51.
11. Howlader N, Noone A, Krapcho M, et al. SEER Cancer Statistics Review, 1975-2012. Bethesda, MD. USA: National Cancer Institute. 2015.
12. Kalli S, Semine A, Cohen S, Naber SP, Makim SS, Bahl M. American Joint Committee on Cancer's Staging System for Breast Cancer, Eighth Edition: What the Radiologist Needs to Know. Radiographics : a review publication of the Radiological Society of North America, Inc. 2018;38:1921-33.
13. Lawrenson R, Lao C, Campbell I, et al. The use of trastuzumab in New Zealand women with breast

cancer. Asia Pac J Clin Oncol. 2018;14:e152-e60.

14. Coates AS, Winer EP, Goldhirsch A, et al. Tailoring therapies--improving the management of early breast cancer: St Gallen International Expert Consensus on the Primary Therapy of Early Breast Cancer 2015. Annals of oncology: official journal of the European Society for Medical Oncology. 2015;26:1533-46.
15. Lawrenson R, Lao C, Campbell I, et al. The impact of different tumour subtypes on management and survival of New Zealand women with Stage I–III breast cancer. N Z Med J. 2018;131(1475):51-60.
16. Lawrenson R, Lao C, Campbell I, et al. Treatment and survival disparities by ethnicity in New Zealand women with stage I-III breast cancer tumour subtypes. Cancer causes & control : CCC 2017;28:1417-27.
17. Wolff AC, Hammond ME, Hicks DG, et al. Recommendations for human epidermal growth factor receptor 2 testing in breast cancer: American Society of Clinical Oncology/College of American Pathologists clinical practice guideline update. Journal of clinical oncology : official journal of the American Society of Clinical Oncology. 2013;31:3997-4013.
18. Thuerlimann B. International consensus meeting on the treatment of primary breast cancer 2001, St. Gallen, Switzerland. Breast Cancer. 2001;8:294-7.
19. Perez EA, Romond EH, Suman VJ, et al. Trastuzumab plus adjuvant chemotherapy for human epidermal growth factor receptor 2 - Positive breast cancer: Planned joint analysis of overall survival from NSABP B-31 and NCCTG N9831. Journal of Clinical Oncology. 2014;32:3744-52.
20. Smith I, Procter M, Gelber RD, et al. 2-year follow-up of trastuzumab after adjuvant chemotherapy in HER2-positive breast cancer: a randomised controlled trial. Lancet. 2007;369:29-36.
21. Piccart-Gebhart MJ, Procter M, Leyland-Jones B, et al. Trastuzumab after adjuvant chemotherapy in HER2-positive breast cancer. New England Journal of Medicine. 2005;353:1659-72.
22. Marty M, Cognetti F, Maraninchi D, et al. Randomized phase II trial of the efficacy and safety of trastuzumab combined with docetaxel in patients with human epidermal growth factor receptor 2-positive metastatic breast cancer administered as first-line treatment: The M77001 study group. Journal of Clinical Oncology. 2005;23:4265-74.
23. Yin W, Jiang Y, Shen Z, Shao Z, Lu J. Trastuzumab in the adjuvant treatment of HER2-positive early breast cancer patients: a meta-analysis of published randomized controlled trials. PLoS One. 2011;6:e21030.
24. Brown C, Lao C, Lawrenson R, et al. Characteristics of and differences between Pasifika women and New Zealand European women diagnosed with breast cancer in New Zealand. N Z Med J. 2017;130:50-61.
25. Seneviratne S, Campbell I, Scott N, et al. Adherence to adjuvant endocrine therapy: Is it a factor for ethnic differences in breast cancer outcomes in New Zealand? Breast. 2015;24:62-7.
26. Cormack D, Purdie G, Ratima M. Access to cancer services for Maori: A report prepared for the Ministry of Health. Wellington, New Zealand. 2005.
27. Gurney J, Campbell S, Jackson C, Sarfati D. Equity by 2030: achieving equity in survival for Māori cancer patients. N Z Med J. 2019;132:66-76.
28. Hobbs M, Ahuriri-Driscoll A, Marek L, Campbell M, Tomintz M, Kingham S. Reducing health inequity for Māori people in New Zealand. Lancet. 2019;394:1613-4.
29. Breast Cancer Foundation New Zealand. "I'm still here": Insights into living and dying- with Advanced Breast Cancer in New Zealand. Auckland, New Zealand. 2018.
30. Kereama-Royal I, Jones S, Wijohn EL, Doole C, Burgess EL, Came H. Resisting ethnic inequities in advanced breast cancer: a call to action. N Z Med J. 2019;132:83-9.
31. Pronzato P, Rondini M. First line chemotherapy of metastatic breast cancer. Annals of oncology : official journal of the European Society for Medical Oncology 2006;17 Suppl 5:v165-8.
32. Hernandez-Aya LF, Ma CX. Chemotherapy principles of managing stage IV breast cancer in the United States. Chinese Clinical Oncology 2016;5:13.

Barriers to physical activity in prostate cancer survivors

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ABSTRACT

AIMS: Despite the benefits of regular physical activity (PA), many prostate cancer (PCa) survivors are not engaging in sufficient PA to achieve health-related gain. This qualitative study sought to gain further insight regarding barriers to PA in older-aged PCa survivors.

METHODS: Sixteen participants were individually interviewed, and data were analysed using an inductive thematic approach.

RESULTS: Six main themes affecting perceived barriers for PA post diagnosis were identified: the effects of the PCa and PCa treatments on PA, urinary incontinence and bowel control, pre-existing comorbid conditions, increased age, time constraints and lack of proximity to PA or exercise venues.

CONCLUSIONS: Only two of the six barriers identified directly related to having had PCa. With an increase in PCa survivorship, an active focus needs to be placed on the role that PA can have in helping maintain and improve both the physical and psychological health-related outcomes of PCa survivors.

Prostate cancer (PCa) is the most common male cancer in many countries.[1] With advancements in both screening procedures and treatment options, men are living longer post diagnosis, and more focus is now being placed on survivorship in relation to maintaining and improving the health-related outcomes of PCa survivors.[1,2] Because of the prolonged disease course and ongoing treatment associated with PCa, the terms "survivor" and "survivorship" encompass men who are in remission and treatment free as well as men who have incurable PCa and are receiving intermittent or ongoing treatment for their PCa, such as hormone suppression treatment.[3]

Physical activity (PA) is a modifiable behaviour that can help improve both the physical and psychological health of PCa survivors during all stages of the PCa continuum, from diagnosis and treatment through to remission and survivorship.[1,2,4] Engagement in regular PA has been associated with lower prostate specific antigen (PSA) levels, a delay in the use of hormone suppression therapy and a lower risk of cancer progression and recurrence.[1,2,5]

Physical activity can protect men who are currently receiving treatment for their PCa.[2,4] This is especially the case for men undergoing hormone-suppression treatment in the form of androgen deprivation therapy (ADT).[1,2,4] Physical activity, especially in the form of aerobic and resistance exercise, can help counteract some of the negative treatment-related side-effects associated with ADT. Specifically, these forms of PA may counteract the increases in body fat accumulation (predominately in the abdominal region), which increase the risk for both type 2 diabetes and metabolic syndrome, as well as loss in muscle and bone mass that can become a risk factor for osteoporosis and reduced physical function.[1,2,4] Physical activity can also help counteract cancer-related fatigue and depression, which can be more prevalent in men on ADT.[1,2,4]

Despite the benefits of regular PA, the majority of PCa patients and survivors are not engaging in sufficient PA to achieve health-related gain.[4,5–8] The American College of Sports Medicine (ACSM) roundtable on exercise guidelines for cancer survivors recommends 150 minutes of moderate-intensity PA per week.[9] More research is required to identify and examine the barriers to PA that survivors may encounter.[6] Limited New Zealand-based research has focused on qualitatively

identifying perceived barriers to PA in a cross-section of PCa survivors, such as men who are in remission and treatment free but live with long-term post-treatment related side-effects (ie, urinary incontinence), as well as men who are currently receiving treatment for their PCa. A qualitative approach can provide greater insight into these men's perceptions of how their PCa diagnosis, and their experience of treatment-related side-effects, impacted on their post-diagnosis and post-treatment PA. The aim of the present study is to qualitatively identify and examine barriers to PA in 16 older-aged PCa survivors who would be more representative of the typical PCa survivor, in relation to their older age and experience of multiple PCa treatments.

Methods

Participants

Men with any stage or grade of PCa, including those in remission, were eligible to participate in the present study. There were no criteria relating to pre-cancer PA levels. We pre-determined a sample of 16 participants, as other qualitative studies that examined various aspects of PA engagement in PCa survivors had similar sample sizes.[10–12] At recruitment, 10 participants had not received chemotherapy or radiation or undergone prostate-related surgery within the past 12 months. Six men were on ADT at recruitment. All 16 participants lived in the Auckland region. A summary of the participants involved in the study is presented in Table 1.

Measure

Members of the research team developed an interview schedule for the present study. Questions were based on relevant literature relating to barriers to PA that PCa patients and survivors can encounter. Questions were open-ended and designed to facilitate discussion. The two main questions were:

1. How do your levels of physical activity or exercise differ to before you were diagnosed with prostate cancer?
2. What barriers to physical activity have you experienced since your diagnosis?

Procedure

Information pertaining to the larger study (via a participant information sheet) was included in the content of three of the monthly newsletters that the Prostate Cancer Foundation of New Zealand email to their members. The majority of participants (n=14) were recruited through the Prostate Cancer Foundation. The remaining

Table 1: Participant characteristics and prostate cancer treatments that participants had undergone.

Characteristic	
Age in years (mean, SD)	57–88 years of age (71.3±7.4)
Time since diagnosis in years (mean, SD)	1–17 years (6.5±5.6)
Prostate cancer treatment type in counts	
Radical prostatectomy	9
ADT	9
Chemotherapy treatment	2
Radiation treatment	4
Time on ADT in years (mean, SD)	1–17 years (5.3±5.8)
Men on ADT at time of recruitment	6

Some participants received more than one type of treatment.

ADT: Androgen deprivation treatment

two participants were recruited via word of mouth by members of the research team. Men who were interested in taking part in the study contacted the first author by email or phone. Once contact had been made and their eligibility to participate confirmed, an interview time and location were arranged. Participants were individually interviewed by the first author at their home, their place of work or the university. All interviews were audiotaped, with the average length of interviews being 40 minutes. Prior to the commencement of each interview, informed written consent was obtained from each participant. Ethics approval for this study was obtained from Northern A Health and Disability Ethics Committee (reference number: 13/NTA/241/AM01).

Data analysis

Interviews were transcribed verbatim and analysed using an inductive thematic approach based on Auerbach and Silverstein's approach to thematic analysis.[13] Four main steps were involved in the analysis process:

1. Reading and re-reading each transcript several times for each question within a topic area.
2. Identifying repeating ideas (ie, discursive commonalities in the interview transcripts) in response to a particular question. This involved identifying segments of text whereby participants had used similar words or experiences to convey the same idea.
3. Coding and naming the repeating ideas. This resulted in the generation of themes. A theme can be defined as an organisation of repeating ideas that is given a name that tries to communicate what participants are trying to convey in their response to a particular research question.[13]
4. Verifying the trustworthiness of the study findings and reduce individual researcher bias. The first author initially analysed the data and identified themes. Both co-authors then independently read the transcripts to validate or invalidate themes. This ensured that participant quotes matched the categories of themes identified.

Results

Data were examined under the main topic area designed to identify barriers to PA post diagnosis. Six main themes were identified:

1. The effects of the PCa and PCa treatments on PA
2. Urinary incontinence and bowel control
3. P-existing comorbid conditions
4. Increased age
5. Time constraints
6. Lack of proximity to PA or exercise venues.

The main themes are outlined below, and direct quotes are provided that illustrate participants' experiences and views.

Theme 1: The effects of the prostate cancer and prostate cancer treatments on physical activity

This theme involved a number of participants discussing how their PA was affected by their PCa diagnosis and the associated side-effects of their various PCa treatments, which predominantly resulted in loss of strength and increased fatigue. This in turn resulted in a decrease in PA or cessation of PA during the active treatment process:

> *"Physical activity is curtailed considerably. You can't be as physical as you were before. You feel so weak when you've got prostate cancer. There is no strength left in you." – Participant 4, Chemotherapy, ADT*

> *"Before [the prostate cancer] I had a lot more strength. I felt as weak as a baby at times. I was told that it had something to do with losing my male hormone count." – Participant 16, Radiation, ADT*

> *"Over the four-year treatment, there's been periods when I've felt unwell. My level of activity has been up and down. There have been periods when I have been physically inactive because of the medical treatment." – Participant 1, Radical Prostatectomy, Radiation, Chemotherapy, ADT*

> *"Not exercising because of what was going on with the hormone*

treatment. I put on weight. I was always an exercise person, that's why the extra weight didn't sit comfortably for me." – Participant 3, Radical Prostatectomy, ADT

Theme 2: Urinary incontinence and bowel control

Physical activity post treatment was also negatively affected by issues relating to incontinence and bowel control. Participants gave accounts of how their PA engagement was reduced or limited as a result of long-term, treatment-related side-effects that continued to result in incontinence:

"I have problems with leakage. I can only walk for a couple of hours now. There was a time I used to walk a lot further. It's just that I'm wet through with the pad." – Participant 12, Radical Prostatectomy

"I do have to be careful with my mid-section exercises. I have to be careful that I don't promote a leakage if I'm exercising that sort of way." – Participant 3, Radical Prostatectomy, ADT

"Loose bowel motions. When I first had the treatment it was terrible. If I had to go to the toilet, I had to go to the toilet and there was no ifs or maybes. I'm involved at the Maritime Museum taking people sailing. I've had to refuse going on some offshore sailing trips." – Participant 16, Radiation, ADT

Theme 3: Pre-existing comorbid conditions

A number of participants discussed how other health conditions not related to having had PCa acted as barriers to engagement in certain types of PA:

"A physical barrier not to do with the prostate cancer but the heart bypass. There's more physical barriers with that than the prostate cancer."– Participant 16, Radiation, ADT

"Arthritic problems. Runner's knee. A bad back is my biggest problem at the moment. I would still run if it wasn't for my back and knees." – Participant 7, Radiation

"I have back problems." – Participant 12, Radical Prostatectomy

Theme 4: Increased age

A number of participants discussed how increased age was a factor in their declining PA levels. Participants cited examples of physical factors, such as reduced balance and flexibility, that affected their ability to engage in certain physical activities. There was also a perception that increased age equated with less need to engage in regular PA:

"I would probably do less now because of my age. I don't run now, I just walk. It's nothing to do with the prostate cancer, its old age." – Participant 7, Radiation

"There is still limit to how much I want to do at 72. I play golf at least once a week with blokes younger than me who can't walk. I am probably more active than any of my other friends." – Participant 6, ADT

"I can't do much in the way of helping in the garden. If I bend down, I'm likely to fall over. So, I don't do that. My balance is not as good as it used to be." –Participant 13, currently on ADT

"Getting older, I can't do all the things I used to because I don't have the flexibility to do some of the things." – Participant 14, Radical Prostatectomy

Theme 5: Time constraints

The following quotes illustrate how time constraints acted as barriers to regular PA engagement regardless of whether participants were retired or semi-retired:

"The only barrier would be time. I have to do other things and I haven't always got time available. That would be the only reason." – Participant 5, ADT

"The fact is the day gets filled up very quickly." – Participant 13, ADT

"Time to do it is the barrier. I lead a pretty busy life even though I'm eighty percent retried. There's a lot going on and I don't always get the time." – Participant 14, Radical Prostatectomy

Theme 6: Lack of proximity to physical activity and exercise venues

Lack of proximity to a PA or exercise venue was also identified as being a barrier to engaging in certain types of PA that seemed to best suit the individual needs of certain participants:

> *"Close proximity to somewhere where we get something like tai chi. It would help if there was something local." – Participant 13, ADT*

> *"If I lived closer to a gym, I would go to the gym. But I'm 40 [kilometres] from the gym." – Participant 15, Radiation, ADT*

Discussion

The present study identified a number of barriers to PA that PCa survivors can encounter, even when they are more than 12 months post chemotherapy, radiation or prostate-related surgery. Only two of the six barriers identified directly related to having had PCa. The two PCa-specific barriers were (1) the effects of PCa and PCa treatments on PA and (2) urinary incontinence and bowel control, which were long-term, post-treatment-related side-effects. A salient barrier to PA engagement in the context of PCa was the effect of the PCa itself and PCa-treatment-related side-effects on an individual's ability to engage in regular PA.[10,11,14,15] A number of participants in the present study discussed how their PA was affected by both their PCa diagnosis and the treatment-related side-effects of their various (and in most cases multimodality) PCa treatments (eg, a combination of chemotherapy, radiation, prostate-related surgery and ADT). This in turn resulted in fatigue, feeling weak and having no strength, which resulted in either a decrease in PA or cessation of PA.

A number of previous studies have also cited the effects of the cancer- and various cancer-treatment-related side-effects as being the most salient barriers to PA in both newly diagnosed individuals and in those receiving active treatment.[11,16,17] Side-effects of cancer treatments also impact PA engagement in individuals who are in remission and treatment free, as treatment-related side-effects can linger.[18] A growing body of evidence-based research has found PA to be both safe and beneficial along the cancer continuum, from diagnosis and active treatment through to remission and survivorship.[2,5,9] Engagement in PA, regardless of cancer type, stage or grade, has been found to be beneficial in maintaining and improving physical function and psychological wellbeing and alleviating treatment-related side-effects, such as cancer-related fatigue.[1,2,4,5]

Evidence of the benefits of PA for cancer survivorship is now relatively well understood by health professionals. Australasian cancer nurses are actively involved in the promotion of PA to their cancer patients.[19] Healthcare practitioners who treat PCa patients and see PCa survivors on a regular basis for the monitoring of PSA levels and for other conditions are well placed to provide advice or referral for PA and PA programmes. [20]

Urinary incontinence and bowel control also affect men's PA, potentially for many months or years post treatment.[13,15,9] Some studies have reported that urinary incontinence and lack of bowel control have acted as barriers to PA, as men were worried and fearful about possible leakage during PA, or they had experienced embarrassment due to incontinence when engaging in PA.[15,17,21] However, other studies have reported that urinary incontinence was experienced at a minor degree, and hence was a minor barrier to PA.[10,22]

This was also the case in the present study. Some participants discussed how their PA was reduced (eg, less walking activity because one's pad becomes more saturated with activity), or how they had to limit other types of PA (eg, sailing) due to bowel-control issues, even if they didn't completely cease these activities. The findings of the present study highlight how long-term post-treatment-related side-effects can still affect PA more than 12 months after the cessation of certain PCa treatments or prostate-related surgeries. Physical activity in the form of pelvic floor muscle training, as well as aerobic exercise and resistance training before and after prostate-related surgery, can positively influence continence in men following a radical prostatectomy.[23]

Some participants in the present study had pre-existing comorbidities, and it was these, not the PCa itself, that were identified as barriers to PA. A number of participants discussed how other condi-

tions (eg, arthritis, back problems) inhibited them from engaging in certain activities. Pre-existing comorbid conditions have also been identified as being barriers to PA in both PCa and other cancer populations, as well as in community-dwelling older adults.[10,11,15,18,24] Men with PCa are more likely to have comorbid conditions, which further reinforces the need to better support PCa survivors to become and remain physically active.[1–3]

Increased age, like pre-existing comorbidities, was identified as a factor that contributed to a decline in PA for some participants, irrespective of whether they had PCa. A number of participants discussed how physical factors associated with ageing, such as loss of balance, fear of falling, reduced flexibility and increased tiredness, limited their PA engagement. There was also a perception held by some participants that increased age equated with less need to engage in regular PA. These findings are similar to the results of an earlier study that examined factors that influenced PA in 18 PCa survivors, and a study designed to examine quality of life and PA engagement in 14 PCa survivors.[10,12] A scoping review designed to identify key facilitators and barriers to PA change in PCa survivors also found increased age to be a barrier to PA.[15]

Time constraints is one of the most cited barriers to PA in PCa populations,[7,8,11,15] in other cancer populations[14,9] and in healthy older adult populations.[24] In the present study, a number of participants discussed how time constraints acted as a barrier to PA regardless of their work status (eg, retired, semi-retired or in full time employment). It has been suggested that strategies for changing behaviour could be employed to emphasise the importance of PA. One such strategy could be the use of motivational interviewing to increase adherence to PA by focusing on barriers related to time management.[21]

Clifford and colleagues suggested that readily accessible local exercise facilities could be important for helping to counteract time constraints for PA.[21] This is consistent with the results of the present study: for example, the oldest participant discussed how he would have liked to have attended tai chi classes that would have aided his balance, though lack of proximity to an organised tai chi venue became a barrier to engaging in this type of activity. Lack of proximity to PA and exercise venues have also been cited as a barrier to PA in both PCa survivors and in other cancer survivor populations.[14,15,17,25,26]

A potential limitation of the present study is the small sample size, which may limit the generalisability of our findings. However, other qualitative studies that examined various aspects of PA engagement in PCa survivors had similar sample size.[10–12] PCa survivors living in rural New Zealand may encounter more barriers to PA in relation to lack of proximity to PA or exercise venues compared to those who live in urban areas, such as Auckland. There was no ethnic variance in our study; all participants identified as New Zealand European.

A strength of the present study is that a qualitative interview-based approach provided insights regarding barriers to PA that PCa survivors can experience. Employing a cross-section of PCa survivors (ie, men in remission who are treatment free and men who are currently receiving treatment for their PCa in the form of ADT) highlighted that men who are in remission and treatment free can still live with long-term, post-treatment-related side-effects. Treatment-related side-effects, such as urinary incontinence and bowel-control issues, affected participants' PA more than 12 months after the cessation of certain PCa treatments and prostate-related surgeries.

Conclusions

The present study identified a number of barriers to PA that PCa survivors who are at least one year post cancer treatment can still encounter. Two barriers related to PCa-treatment-related side-effects, and the remining four barriers to PA that have already been reported in the literature as being experienced by older male populations who have not had PCa. With an increase in survivorship, there needs to be an active focus on the role that modifiable behaviours, such as PA, can have in helping maintain and improve both the physical and psychological health-related outcomes of PCa survivors. The findings from this study, combined with existing literature, can be used to develop strategies and programmes that help facilitate and maintain regular PA engagement in PCa survivors.

Competing interests:
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REFERENCES

1. Campos C, Sotomayor P, Jerez D, Gonzalez J, Schmidt CB, Schmidt K, et al. Exercise and prostate cancer: From basic science to clinical applications. Prostate. 2018;78:639-45.
2. Newton RU, Galvao DA. Exercise medicine for prostate cancer. Eur Rev Aging Phys Act. 2013;10:1041-5.
3. Narayan V, Harrison M, Cheng H, Kenfield S, Aggarwal R, Kwon D, et al. Improving research for prostate cancer survivorship: A statement from the Survivorship Research in Prostate Cancer (SuRECaP) working group. Urol Oncol. 2020;38:83-93.
4. Galvao DA, Newton RU, Gardiner RA, Girgis A, Lepore SJ, Stiller A, et al. Compliance to exercise-oncology guidelines in prostate cancer survivors and associations with psychological distress, unmet supportive care needs, and quality of life. Psychooncology. 2015;24:1241-9.
5. Friedenreich CM, Wang Q, Neilson HK, Kopciuk, KA, McGregor SE, Courneya KS. Physical activity and survival after prostate cancer. Eur Urol. 2016;70:576-85.
6. Keogh JWL, Shepherd D, Krageloh CU, Ryan C, Masters J, Shepherd G, et al. Predictors of physical activity and quality of life in New Zealand prostate cancer survivors undergoingandrogen-deprivation therapy. NZ Med J. 2010;123(1325):20-9.
7. Ottenbacher AJ, Day RS, Taylor WC, Sharma SV, Sloane R, Snyder DC, et al. Exercise among breast and prostate cancer survivors – what are their barriers? J Cancer Surviv. 2011;5:413-9.
8. Weller S, Oliffe JL, Campbell KL. (2019). Factors associated with exercise preferences, barriers and facilitators of prostate cancer survivors. Eur J Cancer Care. 2019;28(5)-e13135.
9. Schmitz KH, Courneya KS, Matthews C, Demark-Wahnefried W, Galvao DA, Pinto BM, et al, (2010). American College of Sports Medicine Roundtable on Exercise Guideline, Cancer Survivors. Med Sci Sports Exerc. 2010;42(7):1409-26.
10. Craike MJ, Livingston PM, Botti M. An exploratory study of the factors that influence physical activity for prostate cancer survivors. Support Care Cancer. 2011;19:1019-28.
11. Keogh JWL, Patel A, MacLeod RD, Masters J. Perceived barriers and facilitators to physical activity in men with prostate cancer: Possible influence of androgen deprivation. Eur J Cancer Care. 2014;23:263-73.
12. Keogh JWL, Patel A, MacLeod RD, Masters J. Perceptions of physically active men with prostate cancer on the

role of physical activity in maintaining their quality of life: Possible influence of androgen deprivation therapy. Psychooncology. 2013; 22:2869-75.

13. Auerbach C, Silverstein L. Qualitative data. An introduction to coding and analysis. New York: New York University Press; 2003.
14. Min J, Yoo S, Kim MJ, Yang E, Hwang S, Kang M, et al. Exercise participation, barriers, and preferences in Korean prostate cancer survivors. Ethn Health. 2019. DOI: 10.1080/13557858.2019.1634184
15. Yannitsos D, Murphy RA, Pollock P, Di Sebastiano KM. Facilitators and barriers to participation in lifestyle modification for men with prostate cancer: A scoping review. Eur J Cancer Care. 2020;29(1):e13193.
16. Catt S, Sheward J, Sheward, Harder H. Cancer survivors' experiences of a community-based cancer-specific exercise programme: results of an exploratory survey. Support Care Cancer. 2018;26:3209-16.
17. Sheill G, Guinan, E, O'Neil LO, Hevey, D, Hussey J.The views of patients with metastatic prostate cancer toward physical activity: a qualitative exploration. Support Care Cancer. 2018;26:1747-54.
18. Blaney JM, Lowe-Strong A, Rankin-Watt J, Campbell A, Gracey JH. Cancer survivors' exercise barriers, facilitators and preferences in the context of fatigue, quality of life and physical activity participation: a questionnaire-survey, Psychooncology. 2013;22:186-94.
19. Keogh JWL, Puhringer P, Olsen A, Sargeant S, Jones LM, Climstein M. Physical activity promotion, beliefs, and barriers among Australasian oncology nurses. Oncol Nurs Forum. 2017;44(2):235-45.
20. Patel A, Schofield G, Keogh J. Influences on health-care practitioners' promotion of physical activity to their patients with prostate cancer: a qualitative study. J Prim Health Care. 2018;10(1):31-38.
21. Clifford BK, Mizrahi D, Sandler CX, Barry BK, Simar D, Wakefield, CE, et al. Barriers and facilitators of exercise experienced by cancer survivors: a mixed methods systematic review. Support Care Cancer. 2018;26:685-700.
22. Bohn SKH, Fossa SD, Wisloff T, Thorsen L. Physical activity and associations with treatment-induced adverse effects among prostate cancer patients. Support Care Cancer. 2019;27:1001-11.
23. Mungovan SF, Carlsson SV, Gass GC, Graham PL, Sandhu JS, Akin O, Scardino PT, Eastham JA, Patel MI. Preoperative exercise interventions to optimize continence outcomes following radical prostatectomy. Nat Rev Urol. 2021;18:259-81.
24. Patel A, Schofield GM, Kolt GS, Keogh WL. Perceived barriers, benefits, and motives for physical activity: Two primary-care physical activity prescription programs. J Aging Phys Act. 2013;21:85-99.
25. Blaney J, Lowe-Strong A, Rankin J, Campbell A, Allen J, Gracey J. The cancer rehabilitation journey: Barriers to and facilitators of exercise among patients with cancer-related fatigue. Phys Ther. 2010;90(8):1135-47.
26. Robertson L, Richards R, Eagan R, Szymlek-Gay. Promotion and support of physical activity among cancer survivors: a service provider perspective. Psycho-Oncol. 2013;22:441-44.

He Pikinga Waiora Kimi Ora lifestyle programme: case study of a successful community-based Indigenous diabetes intervention

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ABSTRACT

AIM: To co-design and implement a whānau-centred, community-based lifestyle programme (Kimi Ora) intended to ensure no worsening of HbA1c and to improve wellbeing for Māori whānau and communities with diabetes or pre-diabetes.

METHODS: Māori healthcare providers, community members, research advisors and wider stakeholders used a co-design process underpinned by He Pikinga Waiora to collaboratively develop and implement Kimi Ora Control group comparisons and participants were recruited from Te Kōhao Health. Multi-method monitoring and collection captured individual, whānau and community data.

RESULTS: Kimi Ora was run in two communities in Aotearoa New Zealand. In total, there were 35 participants who took part in an eight-week programme offered five times alongside a comparison group comprising 21 participants. Kimi Ora resulted in significant improvements on all biomedical measures compared to baseline, and participants had gains relative to the comparison group for variables including weight, BMI, blood pressure and waist measurement. Of particular note was the 100% retention rate and sustained community support for Kimi Ora.

CONCLUSIONS: Outcomes from Kimi Ora demonstrate this programme, which was actively tailored for and worked with Māori communities in a responsive and flexible manner, resulted in successful biomedical outcomes, high engagement and high retention.

Diabetes is being experienced at epidemic rates and is disproportionately affecting Indigenous peoples.[1] In Aotearoa New Zealand, diabetes age-standardised prevalence is 1.6–2.4-times higher for Māori compared to those of European ethnicity.[2,3] This is associated with significant complications from the burden of diabetes, with increased rates of cardiac complications, renal failure and amputation[3] and, most importantly, avoidable mortality for Māori.[4] Overall, Māori have a 1.8-times greater health burden than non-Māori and a nine-year lower average life expectancy.[3] Research into the different rates point towards obligations under Te Tiriti o Waitangi as a fundamental driver of the unequal distribution of the determinants of health and inaction in the face of need.[5,6]

Treatment of type 2 diabetes mellitus (T2D) seeks to reduce blood glucose levels through diet, exercise, lifestyle changes and, where necessary, the use of medication. In New Zealand's current primary care environment, treatment is heavily focused on medicine. Diet, exercise and lifestyle prescriptions in primary care achieve mixed results, suggesting there may be an "unknown" factor. Although it is well established that glycaemic control is closely

linked to development of diabetes-related complications, elevated glycaemic control indicates a reduced adherence to treatment measures and/or the necessary lifestyle changes (eg, diet care, physical activity, use of medication, blood glucose monitoring).[5] Treatment inertia and undertreatment are also associated with individuals not reaching target levels.[7] Adequate T2D management among Indigenous populations in particular has been identified as a challenge that requires urgent attention.[9–11] Barriers experienced by Indigenous peoples with T2D relating to glycaemic control include an obesogenic environment, geographic isolation and fragmented services,[12,13] ongoing impacts of colonisation, political and social challenges[14] and cultural differences between health services, medical professionals and Indigenous communities.[11,14] These structural-level barriers have a cumulative effect on Indigenous peoples. Indigenous communities have had little ability to contribute to the nature and quality of services provided.

Interventions have been implemented to assist with and promote diabetes management for Indigenous communities internationally.[8,13,15] In New Zealand, despite the steep rise in obesity and diabetes rates for Māori,[5,16] there has been a limited array of interventions specifically designed for Māori communities with T2D. Examples of interventions offered include health navigators, health communication tools,[17,18] culturally tailored interventions[19,20] and, most recently, a multi-pronged programme.[8] A key feature within these interventions is the relevance of a Māori approach. Collectively they acknowledge a holistic view of health, comprise a co-design or community partnership aspect, Māori knowledge, language[24] and leadership and a multi-disciplinary approach to intervention development and delivery. Across the Māori interventions noted, socioeconomic costs (such as for households, transport and healthy food) were indicated but not investigated.

It is imperative that initiatives aim to observe no worsening of HbA1c are designed and implemented in a way that contributes to better health for Māori.[21]

This article describes a community-based participatory approach to improve outcomes for whānau Māori with T2D by describing the co-design process employed by Kimi Ora and an overview of the health outcomes. Kimi Ora is part of the broader He Pikinga Waiora project.[22]

Kimi Ora is a whānau-centred lifestyle intervention based in the community focused principally on improving health outcomes for Māori with pre-diabetes or T2D. Kimi Ora was co-designed by several groups: a marae-based service provider (Te Kōhao Health Ltd), locals at participating sites (Melville and Raglan), researchers from the University of Waikato and wider stakeholders (community health and education providers such as school, district health board (DHB) and Ministry of Health staff). The initial design took 18 months to develop.[21] Iterative refinement meant that Kimi Ora was continually reshaped as issues were identified, new evidence came to light and participant feedback was evaluated.[23,24]

Implemented in two communities (a suburb of Hamilton and a rural Waikato township), Kimi Ora comprises 2–3 interactions per week over an eight-week period, with screening and evaluation activities during the weeks at either end. The screening and evaluation weeks are undertaken within a group context, with opportunities for one-on-one interaction between the participant and community facilitator. Regular interactions allow opportunities to form and reinforce culturally relational engagements,[25] as well as to monitor participant involvement, troubleshoot individual and whānau concerns, respond to queries and share successes. Examples of the many resources include week-to-week meal planning that reflect of whānau budgets to allow for incorporation of discount items at local grocery stores; trialling recipe variations for improved nutrition; guidance reading nutritional labels; and discussing alternatives to fast food. These resources ensure participants can integrate learnings into their home environment. Additionally, tailored physical activities were designed to enhance cultural knowledge and provide opportunities to improve their sense of community belonging and their health and wellbeing (eg, exercise sessions and guided walks to cultural sites were open to participants their whānau and the wider community).

Methods

Participants of Kimi Ora were initially identified through the client database as service-users registered with Te Kōhao Health (TKH) who had either pre-diabetes or T2D. Invitations were sent to those who met the criteria (Māori adults with pre-diabetes or T2D). Given the focus on a whānau-centred approach and the poor uptake of interventions that focus on individuals while ignoring the family/household situation, Kimi Ora looked to impact people in the same household; as such, potential participants were also encouraged to include whānau (whether in the same household or not).

There were three cohorts from within TKH, and two cohorts were later recruited from a rural township located outside of Hamilton. A control group was recruited through the TKH database. This group received the standard diabetes care through their usual primary care team, with members followed-up at approximately eight weeks after their first assessment. At the end of each eight-week round of delivery, control group members (n=21) were invited to participate in the next Kimi Ora cohort.

Kimi Ora was co-designed with regards to its approach, design and measures. The team of service provider staff, clinicians, academics, researchers and whānau advisors settled on a non-randomised pre-intervention/post-intervention design and intervention/control with multi-method data collection. The four areas of focus were: clinical measures selected to capture individual biometric measures of glycaemic control, including glycated haemoglobin (HbA1c), blood pressure, weight, body mass index (BMI) and waist circumference; individual self-reporting, which captured physiological features with known links to weight problems (such as perceived energy levels, hours of sleep,[26] fruit/vegetable servings); whānau engagement, which enabled reflections on household/whānau activities; and community activities, which utilised participant-observation recording of wider community (multiple households) healthy lifestyle, health education activities.

Formal data collection began prior to the eight-week programme and then again at completion. To assist organising data and assessments, the He Pikinga Waiora framework[22] was used by the research team. Ethical approval was received by the University of Waikato Management School Ethics Committee (15/202).

Baseline measures, including HbA1c, blood pressure, health rate, weight, waist circumference and height, were collected prior to starting and at follow-up at the completion of the programme (post-intervention) for both the participants and the control group. Demographic details were analysed using frequencies or mean/standard deviations. Descriptive statistics of key clinical outcomes included frequencies and charts. All items used the original scale. Data analysis for the outcome measures pre-intervention to post-intervention utilised paired sample t-tests. Analysis for the comparison between intervention and comparison group used independent sample t-tests of the pre/post difference scores. All analyses were completed with SPSS 25.0 (released 2017, Armonk, NY: IBM Corp).

For the self-report and whānau engagement elements, participants completed an interviewer-assisted questionnaire with a community researcher at TKH. The questionnaire was administered to all enrolled participants, including the control group, and covered topics such as self-reported measures of overall feelings of health, food and nutrition, physical activity, lifestyle knowledge and demographic information.

In addition to the use of measures for statistical reporting, interviews with whānau and key stakeholders contributed understanding perceptions, attitudinal shifts and socioeconomic contexts. Lastly, observations at three key community events were held as part of assessing uptake of Kimi Ora.

Results

There were 35 participants who started and completed an eight-week programme. One participant was excluded from some analyses measures due to pregnancy. Most participants were female (n=31, 89%). Participant ages ranged between 20 and 69 years old (two did not report age). All participants (Kimi Ora and the control group) were of Māori ethnicity. Post-intervention

gains are observed on most variables in the initial analysis of Kimi Ora outcomes (Table 1). Improvement on all clinical measures include median weight loss of 4.71 kg, BMI reduction of 1.80 kg/m^2 and HbA1c reduction (mmol/mol) by 8% of initial level. The latter reduced the sample median from pre-diabetic to normal (44 to 40mmol/mol). Further information, including a descriptive exploration of key outcome variables along with charts to illustrate the changes, is available in the supplementary material.

Food, activity and lifestyle questionnaires showed differences at both individual and whānau level. After the programme, there were minimal changes in hours of sleep, fried foods eaten and dollars spent per week on food. In all other variables, a significant difference was observed over the eight-week period of the programme.

Pre and post measures had to be available in order to be reported. Some results reported have less than 35 participants. The absent individual biomedical measure is the result of a pregnancy exclusion. Although everyone was encouraged to complete all areas of individual self-report, a large number of participants felt uncomfortable reporting their estimated total weekly minutes active (n=13). Missing data from whānau engagement reflect the exclusion of children (under 12 years of age) and missed appointments where measures were recorded for the study.

A second analysis compared the difference in pre-intervention and post-intervention scores between the Kimi Ora participants and the control group (Table 2). Members of the control group were less likely to have all measures done (eg, HbA1c), so the response rates within categories vary. Comparison results observe changes in Kimi Ora participants that are not seen in the control group. Differences in the measures for weight, waist, and BMI show significant improvement in Kimi Ora participants.

Kimi Ora retained 100% of participants. Significant results for median reductions of weight (4.7kg), waistline measures (9.1cm) and BMI (1.8 kg/m^2) reflect strong impacts for individual Kimi Ora participants when compared to control group participants who observed a median increase in weight, waistline and BMI (-0.2kg, -0.4cms and -0.1 kg.m^2 respectively). Additional to individual and whānau level engagement, community activities were created to encourage social interaction. Community events such as a community kai, local sports day and a tree planting event were organised as part of Kimi Ora and reflect stakeholder engagement:

The community kai was held at the local primary school. Community members were invited to have food, engage in activities and receive information from seven different sponsoring organisations. There were 200 meals served. The event was so well attended that the food ran out with 30 minutes remaining in the event.

The local sports day was open to the whole community to come and have an enjoyable day “giving it a go.” A free barbeque was available and a range of fun games was offered. The day included a range of stallholders and organisations to assist and guide youth and whānau into future career and lifestyle pathways.

With support and tree donations from the local city council, fruit trees and a vegetable garden were established in the community. The intention of the community garden was to provide low income whānau with free access to fruit and vegetables. This initiative involved engagement and education on planting, growing and maintaining the trees.

Discussion

This article discusses the design, implementation and outcome evaluation of the Kimi Ora community-based lifestyle intervention for Māori with T2D. The overall aim of Kimi Ora was to improve HbA1c levels for Māori with pre-diabetes and T2D while making lifestyle changes. results indicate that participants did improve their HbA1c levels. Two variables that could be interpreted as negative results were that fruit servings went down (from 1.56 to 0.91, albeit with an associated increase in servings of vegetables) and processed meat went up (from 2.68 to 3.16). These changes were expected because of the low carbohydrate diets of the participants. Although the increased processed meat intake is not recommended long term, the biomedical measures indicate positive gains in overall health for the short term while participants were monitored by medical support staff from TKH.

Table 1: Pre-intervention/post-intervention outcomes for Kimi Ora (N=35).

Outcome	N	Pre		Post	
		M	SD	M	SD
Individual biomedical measures					
Weight (kg)	34	109.2	22.4	***104.4	21.8
Waist (cm)	34	124.7	19.3	***115.6	18.2
BMI (kg/m^2)	34	40.1	7.2	***38.3	7.1
BP systolic (mmHg)	35	131.9	12.0	**128.3	9.3
BP diastolic (mmHg)	35	84.3	6.7	***81.1	6.0
Resting heart rate (beats per minute)	30	78.0	8.8	*75.8	7.5
HbA1c (mmol/mol)	33	43.9	10.4	***40.3	8.9
Individual self-report					
Physical health (1 = highest level)	34	2.6	1.2	**1.9	0.9
Energy (1 = highest level)	34	3.4	0.7	***2.1	0.5
Emotional problems (1 = highest level)	33	2.3	1.3	**1.6	0.7
Hours of sleep	32	7.8	1.3	7.9	1.3
Fruit servings (5 = highest level)	32	1.6	1.1	**0.9	0.5
Vegetable servings (5 = highest level)	32	1.9	0.9	***3.1	0.9
Water intake (5 = highest level)	32	2.6	1.5	**3.4	1.2
Check nutritional labels (5 =highest level)	32	0.8	1.3	***4.3	1.0
Total weekly minutes active	21	71.2	101.6	**146.9	121.5
Whānau engagement					
Knowledge of physical activity benefits (3 = highest level)	26	1.9	0.7	**2.5	0.5
Knowledge of healthy eating benefits (3 = highest level)	26	1.9	1.0	***2.9	0.4
Knowledge of types of activities (3 = highest level)	24	1.9	0.9	***2.7	0.5
Processed meat (0 = highest level)	25	2.7	0.7	*3.2	1.0
Fast food (0 = highest level)	25	2.3	0.9	**1.6	0.6
Fruit juices (0 = highest level)	25	1.6	1.2	**0.6	0.7
Fried foods (0 = highest level)	26	1.8	0.6	1.5	0.7
Soft drinks (0 = highest level)	25	2.2	1.5	***0.6	0.8
Sweets (0 = highest level)	25	2.2	1.0	***0.8	0.6
Average weekly food spend ($)	20	210.0	91.9	227.0	84.7
Knowledge of community activism (4 = highest level)	20	1.3	1.0	***2.3	0.6

***p<.001; **p<.01, *p<.05

Table 2: Intervention vs control group.

Outcome	Kimi Ora			Control		
	n	M change	SD	n	M change	SD
Individual biomedical measures						
Weight (kg)	34	***4.7	3.2	21	-0.2	1.0
Waist (cm)	34	***9.1	6.2	16	-0.4	18.2
BMI (kg/m^2)	34	***1.8	1.4	21	-0.1	.3
BP systolic (mmHg)	35	**3.6	6.1	6	-0.8	2.0
BP diastolic (mmHg)	35	3.2	3.8	6	-4.3	15.6
Heart rate (beats per minute)	30	2.2	4.7	7	0.4	3.8
Individual self-report						
Physical health	34	***0.6	1.0	9	-0.2	0.8
Energy	34	**1.2	0.8	9	0.0	0.9
Emotional problems	33	0.7	1.0	9	-0.2	1.9
Fruit servings	32	-0.7	1.2	8	0.0	0.8
Vegetable servings	32	***1.2	1.1	8	0.0	0.5
Water intake	31	**0.8	1.3	9	-1.1	1.5
Check nutritional labels	32	***3.4	1.5	9	0.1	0.3
Whānau engagement						
Knowledge of physical activity benefits	26	0.6	0.8	6	0.0	0.6
Knowledge of healthy eating benefits	26	*1.0	0.9	6	0.2	0.4
Knowledge of types of activities	24	0.8	0.9	6	0.2	0.8
Processed meat	25	*-0.5	0.9	6	0.3	0.5
Fast food	25	**0.6	1.0	6	0.0	0.0
Fruit juices	25	*1.0	1.5	6	0.2	0.4
Soft drinks	25	1.6	1.6	6	0.7	1.2
Sweets	25	*1.4	1.2	6	0.2	1.5
Knowledge of community activism	20	1.0	1.0	4	0.5	0.6

***p<.001; **p<.01, *p<.05

Kimi Ora participants report improvements in their feelings of physical health, energy levels and their intake of vegetables and water. Nutritional education was a key component of the weekly cooking sessions where participants were able to discuss menus, taste-test a variety of unfamiliar foods and learn new skills, such as interpreting nutritional labels. A difference with regards to checking nutritional labels suggests key learning was transferred to participants through these sessions. Another area of suggested correlation is observed with the doubling of weekly activity minutes (71.2 minutes to 146.9 minutes) and an increase in observed average weekly spend on food (+$17 per week).

The strong stakeholder relationships that support co-designed programmes such as Kimi Ora are difficult to establish within the usual funding timeframes (of 36 months): project planning and formal relationship building took six months, co-designing Kimi Ora took 18 months of relational engagements and recruitment of the first cohort took three months: that's a total of 27 months. In the remaining project time (five months), delivery of four more cohorts took place alongside the development of systems to support adequate reporting.

Despite approaching clients within a marae-based service provider, it was initially difficult to recruit participants for an unknown and unproven programme through usual channels (primary care doctors, hospital, other providers). Slow initial recruitment engagement indicates that distrust of research among Māori still remains. A strategy to mitigate recruitment reluctance is to foster research relationships with whānau recruits. Their involvement, in addition to highly engaged stakeholder groups across multiple interests, will impact the pace of the programme. Decision-making processes and access to resources were difficult conversations to navigate at times. Future programmes similar to Kimi Ora will need to factor such delays into project planning or risk non-delivery. By the time systems were agreed upon and organised to record changes, the first cohort had nearly finished the eight-week programme. Observed gains quickly spread by word of mouth among other TKH clients. Subsequent recruitment became easier. The high demand for in-person interactions and the provision of support needed to undertake research components (obtain biomedical measures, survey assistance and project evaluation) meant participant cohort numbers were intentionally kept small.

Initiatives aiming to improve health outcomes for Māori need to be co-designed and co-produced with communities and key stakeholders in a manner that reflects the realities of the intended communities.[29] Kimi Ora was implemented in communities with many low-income households. The high cost of healthy food[19, 30] is a known barrier to maintaining a healthy diet for Indigenous peoples. Thus, the meal planning component of Kimi Ora was tailored to be flexible and responsive to participants' incomes and what was on special at the supermarket on a week-to-week basis. The reflexive process within Kimi Ora helped to ensure the programme was relevant and remained engaging for participants. When barriers or challenges emerged, adjustments became necessary to ensure Kimi Ora remained fit for purpose. Incorporating community voices during and after design and delivery contributed to feelings of control. For instance, pre-pilot interviews with service users highlighted key issues for whānau. Strategies to navigate key issues were then integrated into the programme design.[24,25]

Health service providers and governments tend to adopt a top-down, dictatorial approach to healthcare interventions, essentially inviting Māori along on a journey designed by, for and with another group, rather than creating a space for partnership. Key points of note from this study are the positive outcomes for participants involved in the intervention compared to the comparison group. Although the improvement in biomedical measures assessed cannot be overlooked, particularly when considering the impact of diabetes and its complications, the retention rate of Kimi Ora signals added contributing factors to the success. The outcomes of Kimi Ora highlight how actively tailoring programmes for and working with participants can function to increase engagement and retention of the intervention while achieving health gains. As this and similar projects demonstrate,[9,20,29] community-based, community-owned health initiatives that are responsive and flexible

to the needs of the people involved can improve the health of participants, enable greater rates of engagement and retention, allow for a sense of ownership, cultivate participants supporting and championing the programme and have broader benefit to the community beyond the participants alone.

This research highlights that a community-based, participatory and co-design process that truly involves the community is vital to ensure greater uptake of the resulting intervention. Health research consultation includes a snapshot of people's experiences regarding a particular issue to design a service or intervention that is then implemented in that community. However, a consultation approach does not reflect genuine and effective engagement with communities.[21] Rather, a community-based, participatory and co-design approach involves a relationship of partnership and reciprocity between researchers and the community throughout the research.[23,28] Such an approach to research can ensure effective implementation, dissemination, uptake and sustainability.[27] These two key features speak to the overall positive outcomes and, as such, are vital to consider when designing and implementing health interventions, particularly with Indigenous communities.

Competing interests:
Nil.

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REFERENCES

1. Rice K, Te Hiwi B, Zwarenstein M, Lavallee B, Barre DE, Harris SB; FORGE AHEAD program team. Best Practices for the Prevention and Management of Diabetes and Obesity-Related Chronic Disease among Indigenous Peoples in Canada: A Review. Can J Diabetes. 2016 Jun;40(3):216-25. doi: 10.1016/j.jcjd.2015.10.007. Epub 2016 Apr 7. PMID: 27066857.
2. Ministry of Health (published online 30 September 2020) Virtual Diabetes Register [Internet]. Available from: https://www.health.govt.nz/our-work/diseases-and-conditions/diabetes/about-diabetes/virtual-diabetes-register-vdr
3. Ministry of Health. 2013/2014 New Zealand Health Survey2014 2 Dec 2020 [Internet]. Available from: https://www.health.govt.nz/our-work/populations/maori-health/tatau-kahukura-maori-health-statistics/nga-mana-hauora-tutohu-health-status-indicators/diabetes
4. Walsh M, Grey C. The contribution of avoidable mortality to the life expectancy gap in Māori and Pacific populations in New Zealand-a decomposition analysis. N Z Med J. 2019 Mar 29;132(1492):46-60. PMID: 30921311
5. Coppell K, Mann J, Williams SM, Jo E, Drury PL, Miller J, Parnell W. Prevalence of diagnosed and undiagnosed diabetes and pre-diabetes in New Zealand: findings from the 2008/09 Adult Nutrition Survey. NZ Med J 2013;126(1370):23-42.
6. Waitangi Tribunal. Hauora: Report on Stage One of the Health Services and Outcomes Kaupapa Inquiry (Report no. WAI 2575). Wellington, New Zealand: Waitangi Tribunal; 2019. Available from: https://www.waitangitribunal.govt.nz/news/report-on-stage-one-of-health-services-and-outcomes-released/
7. Giugliano D, Maiorino MI, Bellastella G, Esposito K. Clinical inertia, reverse clinical inertia, and medication non-adherence in type 2 diabetes. J Endocrinol Invest. 2019 May;42(5):495-503. doi: 10.1007/s40618-018-0951-8. Epub 2018 Oct 6. PMID: 30291589.
8. Harwood M, Tane T,

Broome L, Carswell P, Selak V, Reid J, et al. Mana Tū: a whānau ora approach to type 2 diabetes. N Z Med J. 2018;131(1485):76-83.

9. Herman WH, Zimmet P. Type 2 diabetes: an epidemic requiring global attention and urgent action. Diabetes Care. 2012 May;35(5):943-4. doi: 10.2337/dc12-0298. PMID: 22517937; PMCID: PMC3329834.
10. Howard H. Politics of Culture in Urban Indigenous Community-Based Diabetes Programs. American Indian Culture and Research Journal. 2014;38(1):49-72.
11. Jacklin KM, Henderson RI, Green ME, Walker LM, Calam B, Crowshoe LJ. Health care experiences of Indigenous people living with type 2 diabetes in Canada. Canadian Medical Association Journal. 2017;189(3):E106.
12. Yashadhana A, Fields T, Blitner G, Stanley R, Zwi AB. Trust, culture and communication: determinants of eye health and care among Indigenous people with diabetes in Australia. BMJ Glob Health. 2020 Jan 9;5(1):e001999. doi: 10.1136/bmjgh-2019-001999. PMID: 32133172; PMCID: PMC7042588.
13. St Clair M, Murtagh D, Kelly J, Ford PL, Wallace R. Telehealth: A Game Changer - Closing the Gap in Remote Indigenous Health in Three Remote Homeland Communities in the Laynhapuy Homelands, East Arnhem, Northern Australia. Stud Health Technol Inform. 2018;252:132-8. PMID: 30040695.
14. Janssen J, Nelson K. Meeting the needs of Māori with diabetes: Evaluation of a nurse-led service. Nurs Praxis NZ. 2014;30(3):6-18.
15. Tag H, Kalita P, Dwivedi P, Das AK, Namsa ND. Herbal medicines used in the treatment of diabetes mellitus in Arunachal Himalaya, northeast, India. J Ethnopharmacol. 2012 Jun 14;141(3):786-95. doi: 10.1016/j.jep.2012.03.007. Epub 2012 Mar 13. PMID: 22433536.
16. Sellman D, Schroder R, Deering D, Elmslie J, Foulds J, & Frampton C. Psychosocial enhancement of the Green Prescription for obesity recovery: a randomised control trial. NZ Med J. 2017;130(1450). Available from: https://www.nzma.org.nz/journal-articles/psychosocial-enhancement-of-the-green-prescription-for-obesity-recovery-a-randomised-controlled-trial
17. Farmer A, Edgar T, Gage J, Kirk R. "I Want to Walk with My Moko." The Application of Social Cognitive Theory in the Creation of a Diabetes Prevention Documentary with New Zealand Māori. J Health Commun. 2018;23(3):306-12. doi: 10.1080/10810730.2018.1442531. Epub 2018 Feb 22. PMID: 29469669.
18. Farmer A, Gage J, Kirk R, Edgar T. Applying Community-Based Participatory Research to Create a Diabetes Prevention Documentary with New Zealand Māori. Progress in community health partnerships: research, education, and action. 2016;10(3):383-90.
19. Murphy E, McAuley KA, Bell D, McLay RT, Chisholm A, Hurley R, et al. A new approach to design and implement a lifestyle intervention programme to prevent type 2 diabetes in New Zealand Maori. Asia Pac J Clin Nutr. 2003;12(4):419-22. PMID: 14672865.
20. Coppell KJ, Tipene-Leach DC, Pahau HL, Williams SM, Abel S, Iles M, et al. Two-year results from a community-wide diabetes prevention intervention in a high risk indigenous community: the Ngati and Healthy project. Diabetes Res Clin Pract. 2009 Aug;85(2):220-7. doi: 10.1016/j.diabres.2009.05.009. Epub 2009 Jun 13. PMID: 19525026.
21. Harding T, Oetzel J. Implementation effectiveness of health interventions for indigenous communities: a systematic review. Implement Sci 2019 Aug 5;14(1):76. doi: 10.1186/s13012-019-0920-4. PMID: 31382994; PMCID: PMC6683565.
22. Oetzel J, Scott N, Hudson M, Masters-Awatere B, Rarere M, Foote J, Beaton A, Ehau T. Implementation framework for chronic disease intervention effectiveness in Māori and other indigenous communities. Global Health. 2017 Sep 5;13(1):69. doi: 10.1186/s12992-017-0295-8. PMID: 28870225; PMCID: PMC5584010.
23. Rarere M, Oetzel J, Masters-Awatere B, Scott N, Wihapi R, Manuel C, Gilbert R. Critical reflection for researcher-community partnership effectiveness: the He Pikinga Waiora process evaluation tool guiding the implementation of chronic condition interventions in Indigenous communities. Aust J Prim Health. 2019 Nov;25(5):478-485. doi: 10.1071/PY19022. PMID: 31506161.
24. Oetzel J, Rarere M, Wihapi R, Manuel C, Tapsell J. A case study of using the He Pikinga Waiora Implementation Framework: challenges and successes

in implementing a twelve-week lifestyle intervention to reduce weight in Māori men at risk of diabetes, cardiovascular disease and obesity. Int J Equity Health. 2020;19(1):103.

25. Masters-Awatere B, Rarere M, Gilbert R, Manuel C, Scott N. He aha te mea nui o te ao? He tāngata! (What is the most important thing in the world? It is people!). Aust J Prim Health. 2019 Nov;25(5):435-42. doi: 10.1071/PY19027. PMID: 32171366.
26. Patel, S., & Hu, F. (2008) Short sleep duration and weight gain: A systematic review. Obesity (Silver Spring). 2008 Mar;16(3):643-53. doi: 10.1038/oby.2007.118. Epub 2008 Jan 17. PMID: 18239586; PMCID: PMC2723045.
27. Teng A, Blakely T, Scott N, Jansen R, Masters-Awatere B, Krebs J, Oetzel, J. What protects against pre-diabetes progressing to diabetes? Observational study of integrated health and social data. Diabetes Res Clin Pract. 2019 Feb;148:119-29. doi: 10.1016/j.diabres.2018.12.003. Epub 2019 Jan 8. PMID: 30633935.
28. Smith, LT. Decolonizing methodologies: Research and indigenous peoples. 2021. Zed Books Ltd.
29. Tipene-Leach DC, Coppell KJ, Abel S, Pahau HL, Ehau T, Mann JI. Ngati and healthy: Translating diabetes prevention evidence into community action. Ethn Health. 2013;18:402-14. doi: 10.1080/13557858.2012.754406. Epub 2013 Jan 29. PMID: 23360172.
30. Moeke-Pickering T, Heitia M, Heitia S, Karapu R, Cote-Meek S. Understanding Māori food security and food sovereignty issues in Whakatāne. MAI Journal [Internet]. 2015; 4(1). Available from : http://www.journal.mai.ac.nz/content/understanding-m%C4%81ori-food-security-and-food-sovereignty-issues-whakat%C4%81ne.

Addressing equity: a 10-year review of strabismus surgery in 0–19-year-olds in the New Zealand public health system

Cheefong Chong, Alexandra Lawrence, Dan Allbon

ABSTRACT

BACKGROUND: This study aimed to identify the relationship between the incidence of strabismus surgery, ethnicity and socioeconomic deprivation in the New Zealand public health system. Secondary outcomes explored the association between re-operation rate for surgical failures, ethnicity and socioeconomic deprivation.

METHOD: Cases receiving operative management for strabismus were retrieved from the National Minimum Dataset. The incidence of surgery was correlated to patient demographics by ethnicity and socioeconomic deprivation and compared to population profiles for 0–19-year-olds constructed from the 2013 census.

RESULTS: There were 4,476 strabismus surgeries recorded over a 10 year period from 1 January 2005 to 31 December 2014 included in the study. There was a lower incidence of strabismus surgery performed in Māori, Pacific Peoples and the least socioeconomically deprived cohort. There were significant inter-regional variations in the incidence of strabismus surgery. The European ethnic group was 1.4 times as likely to receive subsequent procedures following a primary procedure than either Māori or Pacific Peoples.

CONCLUSION: Disproportionately fewer strabismus surgeries were performed in Māori, Pacific Peoples and New Zealanders from the lowest deprived group in the New Zealand Public Health System. Minority ethnic groups are less likely to receive secondary operations following a primary procedure when compared to a European cohort. Further research is needed to directly compare health outcomes between these high-needs and lower-needs groups.

Strabismus is a common paediatric eye disorder occurring in 1–3% of children. However, it can present at any age.[1,2] Strabismus can be defined as any misalignment of the visual axes and is often referred to as a squint. Strabismus may be congenital or acquired and results from any abnormality along the ocular and oculomotor neural pathways.

In children, risk factors for strabismus include a family history of strabismus, prematurity and low birth weight.[3] Comorbid ocular conditions, including any cause of vision deprivation, neuromuscular disorders such as cerebral palsy and any systemic disease affecting the extraocular muscles of the eye, are also associated with a higher incidence of strabismus.

The goals of treatment are to improve ocular alignment and to preserve binocular vision, including stereopsis. Operative and non-operative interventions are used in the treatment of strabismus, and management is dependent on the subtype and etiology.[3] Surgical intervention for the purposes of this study include resection, recession or trans-

position of the extraocular muscles, as well as the application of botulinum toxin to any of the extraocular muscles.

There is a large body of evidence that demonstrates differences in health outcomes between population groups in New Zealand, with a specific focus placed on Māori, Pacific Peoples and high socioeconomic deprivation. This study aims to support the mandate of the New Zealand Government to deliver equitable health outcomes for all New Zealanders by building an understanding of how ophthalmic surgical services are distributed in the New Zealand public health system.

Strabismus is an important condition to explore in the context of equity due to the potential functional and psychosocial impacts of strabismus on children. Children with strabismus experience visual field defects and impaired binocular vision, and they are at higher risk of vision loss, which has serious implications for their education and future opportunities.[4] A review of the psychosocial, quality-of-life and health impacts of strabismus found that children with strabismus suffer from headaches, eye strain and increased incidences of mental illness such as anxiety, social phobia and learning disorders. Buffenn et al also described a continuation of a decreased quality of life into adulthood and negative attitudes and preconceptions regarding intelligence and trustworthiness towards individuals with strabismus.[4]

Methods

A retrospective analysis of all surgical strabismus procedures within the New Zealand public health sector between 1 January 2005 and 31 December 2014 was performed. Surgical strabismus data for the time period were retrieved from the National Minimum Dataset (NMDS)[5].

The NMDS is a national collection of public and private hospital discharge information, including coded clinical data for inpatients and day patients for publicly funded events. Data are provided by public and the larger private hospitals in a standardised electronic file format. Publicly funded hospital events are required to be loaded onto the NMDS within 21 days after the month of discharge.[5] Data are coded according to the International Statistical Classification of Diseases and Related Health Problems (ICD-10) classification system. There is no single ICD-10 code for a primary diagnosis of strabismus or for a strabismus procedure. A number of codes have been identified to represent the variety of subtypes and operations performed (Appendix Figure 1, Appendix Figure 2).

All cases retrieved from the NMDS with a recorded strabismus-related procedure and an associated diagnosis of any subtype of strabismus between the ages of 0 and 19 years were included in the study. Cases retrieved with incomplete data for ethnicity or deprivation index were excluded from the study. Data entries with a primary diagnosis of diplopia were also excluded due to ambiguity of diagnosis.

Ethnicity data recorded in the NMDS is self-reported at the time of admission for the given procedure. The cases were grouped according to the New Zealand census groupings of European, Māori, Pacific Peoples, Asian and Middle Eastern/Latin American/African (MELAA).

The New Zealand Index of Deprivation (NZDep13) is an area-based measure of socioeconomic deprivation derived from census data: it combines census data relating to income, family structure, education, employment, housing, home ownership and access to transport and communications. Socioeconomic deprivation is estimated by geographical location according to the NZDep13[6] and recorded in the NMDS. NZDep13 groups deprivation by deciles giving a score from 1 to 10 for each meshblock in New Zealand. An NZDep13 value of 1 represents the least deprived 10% of areas, whereas a value of 10 represents most deprived 10% of areas in New Zealand. For the purposes of this study, socioeconomic deprivation deciles were further grouped 1–3, 4–7 and 8–10 to respectively represent low, medium and high deprivation.

Data retrieved from the NMDS were then compared to regional demographic profiles, constructed from the 2013 census data. In the analysis, district health boards (DHBs) were grouped according to census DHB groupings under four corresponding regions: Northern, Midlands, Central and South Island.

Results

Six thousand and ninety-five cases from the 10-year period were retrieved from the NMDS: 1,563 cases were 20 years of age or older, and a further 56 cases had incomplete ethnicity or socioeconomic data and therefore did not meet the inclusion criteria. The final analysis included 4,476 cases. The median age was 5 years and there was a 50:50 split of cases by sex.

The distribution of cases by key ethnic groups were 71.4% European, 15.6% Māori and 4.9% Pacific Peoples. Thirty-four percent of procedures were in cases from the highest socioeconomic deprivation group, 41% of cases were from medium deprivation and 25% from the lowest deprivation group.

Over the 10-year period, the national incidence of strabismus surgery was 3.38 per 1,000 aged 0–19 years. The incidence of strabismus surgery in the South Island was 4.85 per 1,000 aged 0–19 years, more than double that of the Midlands region at 2.24 surgeries per 1,000. The inter-regional variation in procedural incidence may represent inter-regional disparities in access to surgical ophthalmic services.

There was a higher incidence of surgeries performed in the European ethnic group: 4.1 surgeries per 1,000 aged 0–19 years. When compared to the incidence of priority ethnic groups of Māori and Pacific Peoples, Europeans were respectively 1.5 times and 2.6 times as likely to receive surgical intervention for strabismus.

The most socioeconomically deprived group had the highest incidence of strabismus procedures over the 10-year period at 3.87 per 1,000. There appears to be a relationship between increasing incidence of strabismus surgery and higher socioeconomic deprivation. However, when stratifying the distribution of strabismus procedures by NZDep13 deciles (Figure 2), there is a notable under-representation of the most deprived 10% of the population when compared to the cases from deciles 8 and 9, which also make up the highest deprivation group.

Re-operation rate for surgical failures

The re-operation rate was calculated on a population level by dividing the number of secondary or subsequent procedures by the total number of primary procedures for each ethnic and socioeconomic deprivation cohorts. The national re-operation rate over the 10-year period was 11.8%.

The European ethnic group had the highest rate of re-operation, with 13.0% receiving subsequent procedures following a primary procedure. The re-operation rate was lowest in the MELAA cohort at 2.6%. In comparison to the European cohort, Māori, Pacific Peoples and Asian ethnic groups were also less likely to receive subsequent procedures following the primary procedure, with respective re-operation rates of 8.4%, 9.4% and 9.2%.

When compared to the re-operation rate in the most deprived socioeconomic group (9.2%), the low and medium deprivation groups were 1.46 and 1.43 times as likely to receive subsequent procedures following a primary operation.

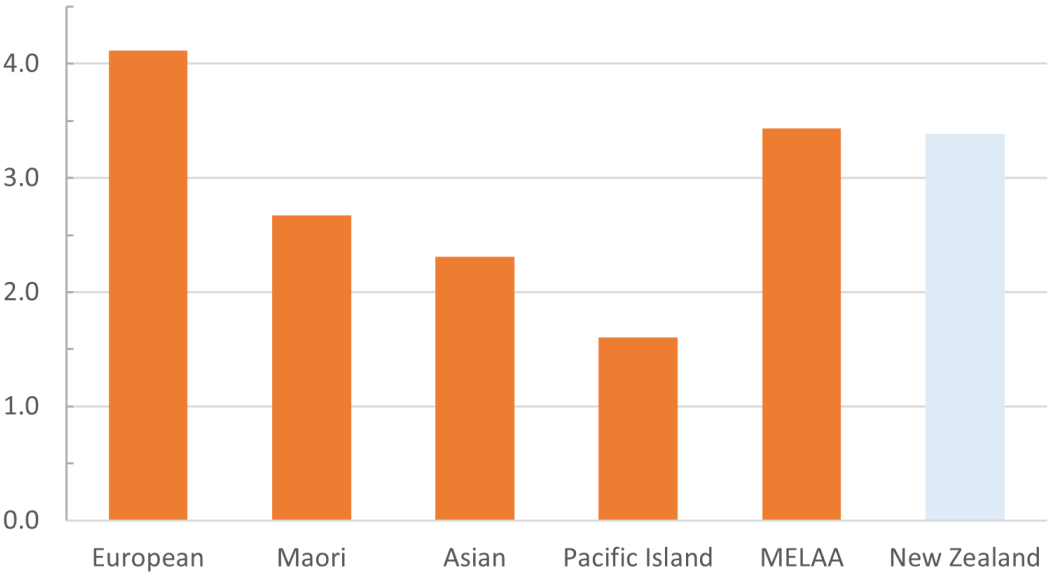
Table 1: Cases by ethnicity and socioeconomic deprivation, n (%).

	Low	Medium	High	Grand total
European	933 (20.8%)	1,379 (30.8%)	883 (19.7%)	3,195 (71.4%)
Māori	66 (1.5%)	250 (5.6%)	382 (8.5%)	698 (15.6%)
Pacific Island	13 (0.3%)	58 (1.3%)	148 (3.3%)	219 (4.9%)
Asian	77 (1.8%)	134 (3.0%)	99 (2.2%)	310 (6.9%)
MELAA	12 (0.3%)	17 (0.4%)	25 (0.5%)	54 (1.2%)
Grand total	1,101 (25%)	1,838 (41%)	1,537 (34%)	4,476

*MELAA: Middle Eastern/Latin American/African.

Figure 1: Incidence of strabismus surgery per 1000 aged 0–19 years.

Figure 2: Incidence of strabismus surgery per 1,000 population aged 0–19 years.



*MELAA: Middle Eastern/Latin American/African.

Figure 3: Incidence of strabismus surgery per 1,000 youth population aged 0–19 years.

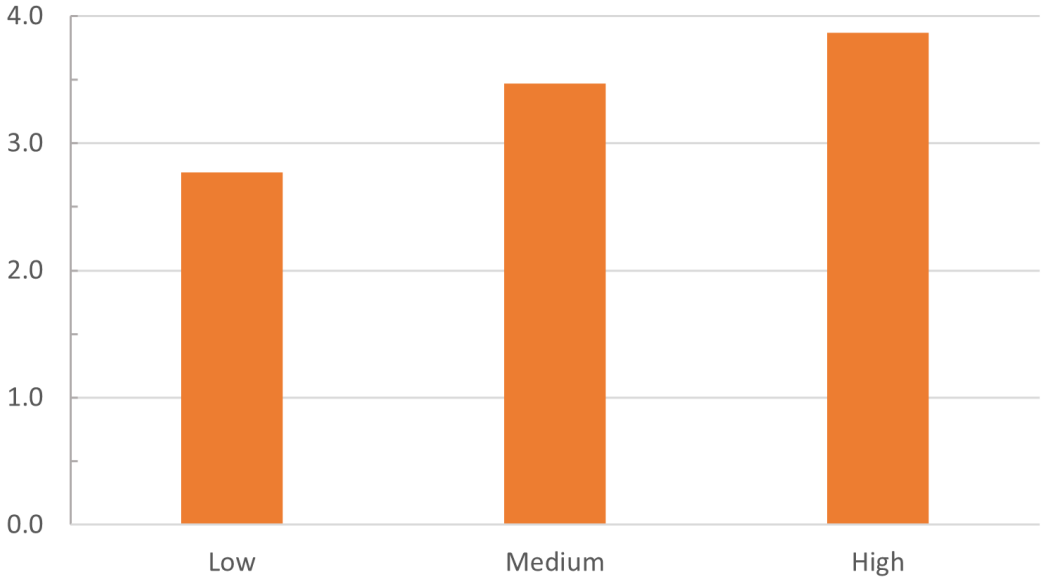
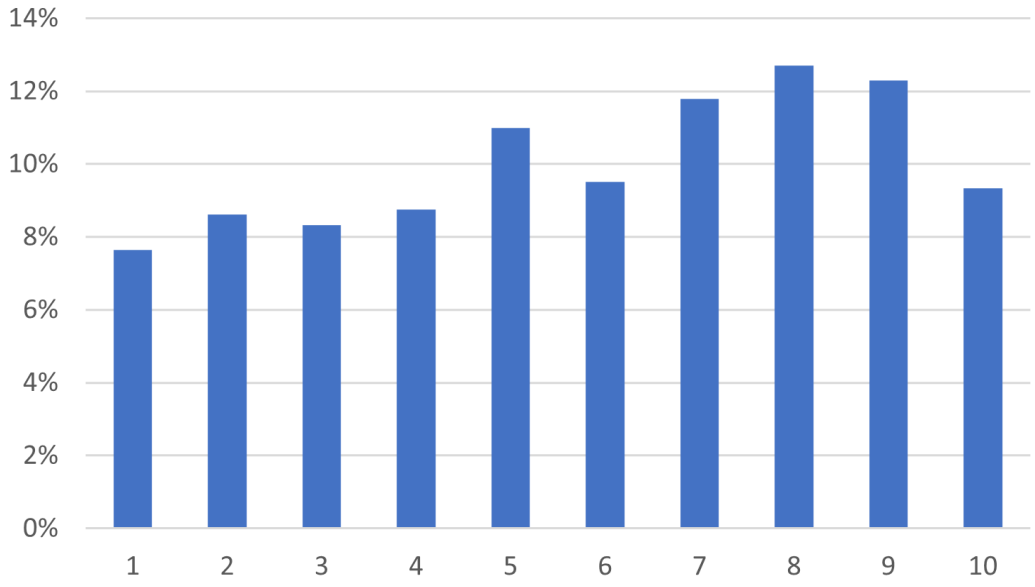


Figure 4: Distribution of cases of strabismus surgery by NZDep13.



Early intervention

The distribution of strabismus procedures by ethnicity were stratified further by age group for cases under the age of 19 years and then compared to the ethnic distribution of the youth population in the 2013 census. There was a higher representation of the European ethnic group across all three age categories. The degree of over-representation of the European ethnic group was found to be most pronounced in the 0–4-years age group, representing 75% of all procedures despite only comprising 59% of the population 4 years or younger. Minority ethnic groups were found to be under-represented across almost all age-groupings when compared to their census population distribution, with the Pacific Peoples ethnic group being most greatly under-represented. These findings could suggest earlier access to surgical services for Europeans when compared to all minority ethnic groups.

Discussion

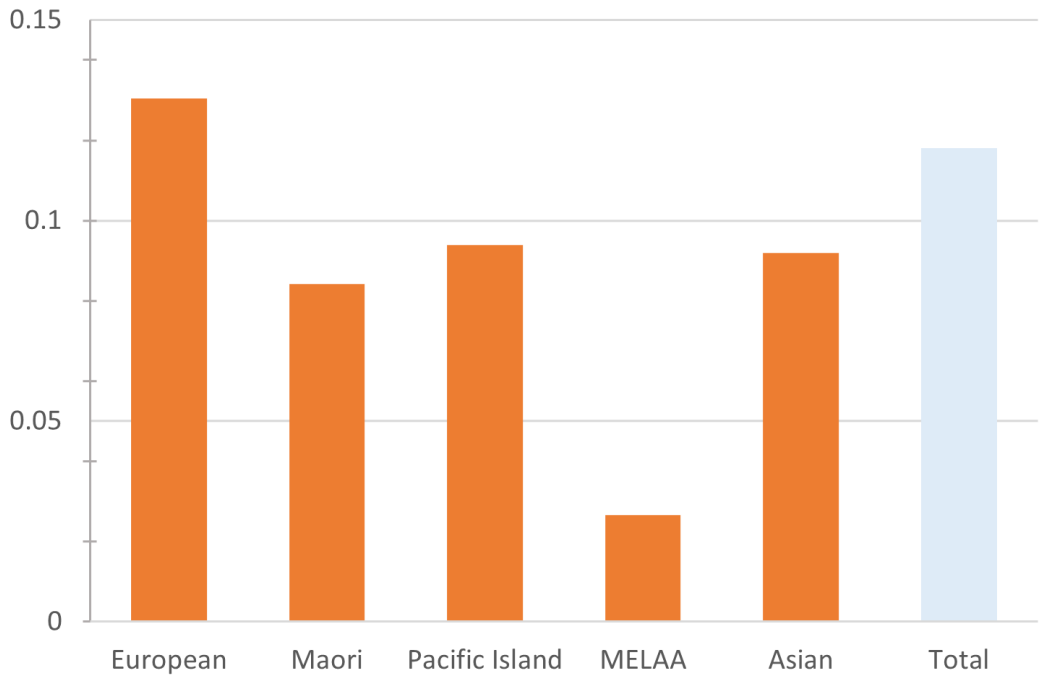
This is the first population-based study to explore the association between the incidence of strabismus surgery, ethnicity and socioeconomic status in New Zealand. The over-arching aim of this study was to explore access to surgical intervention in the New Zealand public health system, with a specific focus on the surgical specialty of ophthalmology.

There is a body of evidence that demonstrates reduced access to care and poorer health outcomes for Māori, Pacific Peoples and those who experience greater socioeconomic deprivation. Few studies have directly compared access to surgical intervention with socioeconomic deprivation and ethnicity in New Zealand. Key strengths of the study were its large population-base of data analysed over a 10-year time period with over 97% of data complete for ethnicity and deprivation index.

Limitations of the study include inconsistencies in the NMDS data entries and collection; the use of NZDep13 to estimate socioeconomic status; self-reported ethnicity; and the unavailability of data for procedures performed in the private surgical healthcare setting.

A number of different ICD-10 codes had been used to represent various sub-types as the diagnosis for strabismus and operation

Figure 5. Reoperation rate by ethnicity



*MELAA: Middle Eastern/Latin American/African.

Figure 6: Re-operation rate by deprivation group.

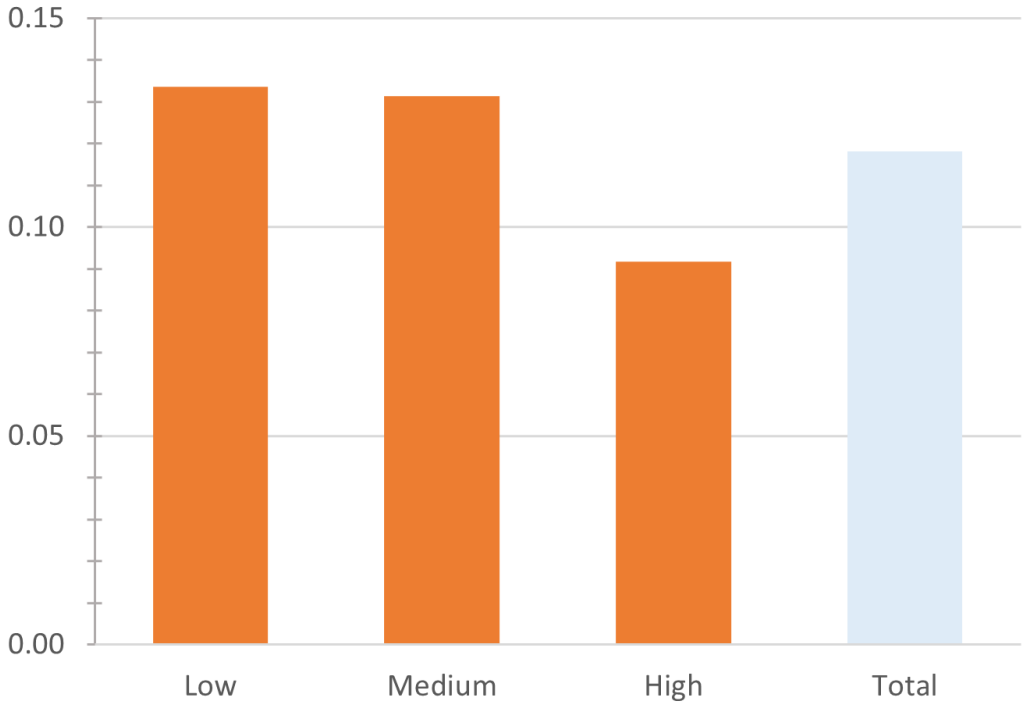


Table 2: Distribution of strabismus surgery by age group compared with 2013 census distribution of youth population.

	Ethnicity				
Age group	**European**	**Māori**	**Pacific Peoples**	**Asian**	**MELAA**
0–4 yrs	**75.0%**	13.9%	4.0%	6.1%	1.0%
5–9 yrs	67.3%	**18.3%**	5.5%	7.6%	1.4%
10–19 yrs	71.0%	14.0%	**5.9%**	**7.6%**	**1.4%**
Grand total	71.4%	15.6%	4.9%	6.9%	1.2%
2013 census population ethnic distribution (0–19 years)	**58.6%**	**19.7%**	**10.3%**	**10.1%**	**1.2%**

*MELAA: Middle Eastern/Latin American/African.

type in the retrieved NMDS. On entering the data, clinicians were also required to enter a written diagnosis and/or operation. Few inconsistencies were found in the entries of written diagnoses or operation types requiring clarification between stated written entries and ICD-10 codes. However, ICD-10 codes were reliable overall, with no significant inconsistencies in the ICD-10 coding for diagnosis or operation type.

The NMDS includes discharge information from all public and larger private hospitals, including day stay facilities for publicly funded events. There are potentially missing entries for publicly funded procedures performed at smaller private and day-stay surgeries in New Zealand. There is a nominal three-hour threshold of admission for reporting events to NMDS. If a case doesn't meet this threshold for reporting, it may not be reported by same-day eye facilities. Outpatient data for publicly funded surgical procedures may also be reported to the National Non-Admitted Patient Collection (NNPAC), but the reported data do not include diagnostic or procedural data, which were therefore not explored further for the purposes of this study. A large majority of publicly funded ophthalmic procedures are performed in public hospitals in New Zealand. There are three private day surgeries in New Zealand contracted by their DHBs to routinely provide publicly funded ophthalmic surgeries. Two of these do not provide general anaesthetic and therefore are unsuitable for most eye procedures in children; the third facility was contacted and consistently reports their day-stay data to the NMDS. The authors consider the data retrieved from the NMDS to be a reasonable representation of the publicly funded procedures for strabismus over the 10-year period.

NZDep13 is an area-based measure of socioeconomic deprivation, as estimated by a participant's address, and therefore might not be a true reflection of a person's socioeconomic status. Ethnicity recorded in the NMDS and the 2013 New Zealand census are both self-reported. However, in the census an individual may be able to be represented under a number of different ethnic groups, and in the NMDS only one primary ethnicity can be recorded.

The data retrieved from the NMDS represented publicly funded strabismus procedures from 1 January 2005 to the 31 December 2014, but population profiles were constructed from a static point in time at the 2013 census. There are small variations between regional age, ethnic and socioeconomic deprivation distributions between the 2006, 2012 and 2018 censuses. The overall trends in population distribution remain consistent between the three most recent censuses and thus the 2013 census is considered to be a reasonable estimate of the population profile over the study period.

A larger proportion of surgeries were performed in the highest deprivation cohort when compared with the lowest deprivation cohort. This demonstrates a greater distribution of public health services for New Zealanders who are more socioeconomically deprived. It is worth noting that procedures performed privately are not required to be reported to the NMDS. Therefore, it is possible that there was bias towards private surgical care for lower deprivation groups, who can more likely afford private healthcare or health insurance. A greater uptake of surgical procedures in a private setting for more affluent New Zealanders could be another possible explanation for a lower incidence of strabismus procedures in the least socioeconomically deprived group. It is also possible that children from less-deprived homes receive non-operative care earlier and thus have a lower need for surgical intervention.

It is possible that the lower incidence of surgeries performed in Māori and Pacific Peoples is due to a lower population prevalence of strabismus and therefore a reduced need for surgery. A retrospective analysis of the electronic records of 846,477 patients with strabismus in the United States found a higher prevalence of strabismus in non-Hispanic Whites: 2.9% compared with 2.4% for African American and 2.0% for Native Hawaiian.[7] Interestingly, the prevalence of strabismus was found to be greatest in bi-racial/multi-racial ethnicity at 3.3%.[7] However, this large US study included patients of all ages, with different risk factors and aetiology of strabismus in adults than in children. The Sydney Paediatric Eye Disease Study also demonstrated ethnic variation in the prevalence of strabismus

in children 6–72 months, with 4% in South Asian, 3.5% in European Caucasian and 3.3% in other ethnicities.[8] Although global studies have showed some ethnic variation in the prevalence of strabismus, there is no current evidence to support a higher prevalence of strabismus in New Zealand European's than in Māori or Pacific Peoples. The disparity in the incidence of strabismus surgeries between ethnic groups in this study is too large to account for a difference in ethnic prevalence alone and more likely reflects a component of differing access to health services. Further research is required to determine the specific ethnic variation of common ophthalmic conditions such as strabismus in a New Zealand context.

The national re-operation rate was estimated on a population level to be 11.8%. This was further explored by ethnicity and socioeconomic deprivation. Re-operation rates in this study were similar to those in a large population-based study in the United States with estimated re-operation rates for strabismus procedures between 6.7% and 11.5% across all age groups.[9] We found that Māori, Pacific Peoples and those in the highest deprivation grouping had lower rates of re-operation. Although the MELAA ethnic group was found to have an incidence of strabismus surgery similar to the national incidence, the rate of re-operation in the cohort was less than quarter of the national rate at 2.7%. This can be interpreted either as lower operative failure rates in these cohorts, or as a reduced access to subsequent procedures following an unsuccessful primary procedure. Strabismus procedures can be performed for both cosmetic and functional corrections of misalignment. Factors affecting the likelihood of re-operation for strabismus include the type of strabismus, case complexity, patient age, the experience of the surgeon, the surgical method and patient satisfaction. While appreciating the complexity of factors influencing reoperation rate, we still expect reasonable randomisation of these effects between groups given the large size of our sample. It is possible that the observed variation in re-operation rates may reflect intrinsic cohort characteristics, with European and less socioeconomically deprived groups being more likely to seek further medical attention if a primary operation was perceived as unsatisfactory.

The findings in this study suggest earlier access to surgical intervention for a European cohort when compared to all other ethnic groups. There appears to be a trend across all minority ethnic groups of an increasing incidence of procedures with increasing age. The greatest incidence of surgeries by ethnicity peak at 0–4 years for European, 5–9 years for Māori and 10–19 years for Pacific Peoples, Asian and MELAA ethnic groups.

For the purposes of this study, having received surgical intervention for strabismus was used as an estimate of a population's access to healthcare. To further assess access to ophthalmic services in the New Zealand public health system, the number of referrals made to ophthalmology services and alternative treatment options offered by ethnicity and socioeconomic status could also be explored. By using an event of surgical intervention as an end point, this study did not directly compare health outcomes. Further research is required to explore long-term visual outcomes between these population groups and assess the clinical significance of these reported variations in surgical intervention for strabismus.

Conclusion

This research shows that disproportionately fewer strabismus surgeries are performed in Māori, Pacific Peoples and those in the lowest deprivation group.

Our findings also suggest that access to subsequent secondary procedures in minority ethnic and higher deprivation groups may also be reduced. Further research is needed to directly compare health outcomes between these higher-needs and lower-needs groups.

Appendix

Appendix Table 1: ICD-10 strabismus sub-type codes.

Subtype	Code
Third [Oculomotor] Nerve Palsy	H490
Fourth [Trochlear] Nerve Palsy	H491
Sixth [Abducent] Nerve Palsy	H492
Paralytic Strabismus, Unspecified	H499
Convergent Concomitant Strabismus	H500
Divergent Concomitant Strabismus	H501
Vertical Strabismus	H502
Intermittent Heterotropia	H503
Heterotropia	H504 / H505
Other Specified Strabismus including Duane's, Dysthyroid and Mechanical Strabismus	H506 / H508
Other Strabismus unspecified includes unilateral and bilateral	H509 / H518
Amblyopia	H530

Appendix Table 2: ICD-10 strabismus procedure codes.

Procedure	Code
Administration Of Botulinum Toxin For Strabismus	4283000
Strabismus procedure involving 1 or 2 muscles, 1 eye	4283300
Strabismus procedure involving 1 or 2 muscles, bilateral	4283301
Reoperation Of Strabismus Procedure Involving 1 Or 2 Muscles,1 Eye, Second Procedure	4283302
Reoperation Of Strabismus Procedure Involving 1 Or 2 Muscles, Both Eyes, Second Procedure	4283303
Re-Operation Strabismus Procedure Involving 1 Or 2 Muscles, 1 Eye, Third Or Subsequent Procedure	4283600
Reoperation Strabismus Procedure Involving 1 Or 2 Muscles, Both Eyes, Third or subsequent procedure	4283601
Strabismus Procedure Involving 3 Or More Muscles, 1 Eye	4283900
Strabismus Procedure Involving 3 Or More Muscles, Bilateral	4283901
Reoperation Of Strabismus Procedure Involving 3 Or More Muscles, Unilateral, Second Procedure	4283902
Reoperation Of Strabismus Procedure Involving 3 Or More Muscles, Both Eyes, Second Procedure	4283903
Re-Operation Of Strabismus Procedure Involving 3 Or More Muscles, 1 Eye, Third Or Subsequent Procedure	4284200
Reoperation Of Strabismus Procedure Involving 3 or more muscles, Both Eyes, Third Or Subsequent Procedure	4284201
Readjustment Of Adjustable Sutures Following Previous Surgery For Correction Of Strabismus, Unilateral	4284500
Readjustment Of Adjustable Sutures Following Prev Surgery For Correction Of Strabismus, Bilateral	4284501
Muscle Transplant For Strabismus	4284800
Reoperation Of Muscle Transplant Procedure For Strabismus	4284801

Competing interests:
Nil.

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REFERENCES

1. Torp-Pedersen T, Boyd HA, Skotte L, Haargaard B, Wohlfahrt J, Holmes JM, Melbye M. Strabismus Incidence in a Danish Population-Based Cohort of Children. JAMA Ophthalmol. 2017 Oct 1;135(10):1047-53. doi: 10.1001/jamaophthalmol.2017.3158. PMID: 28859196; PMCID: PMC5710488.
2. Hashemi H, Pakzad R, Heydarian S, Yekta A, Aghamirsalim M, Shokrollahzadeh F, Khoshhal F, Pakbin M, Ramin S, Khabazkhoob M. Global and regional prevalence of strabismus: a comprehensive systematic review and meta-analysis. Strabismus. 2019 Jun;27(2):54-65. doi: 10.1080/09273972.2019.1604773. Epub 2019 Apr 23. PMID: 31012389.
3. Williams C, Northstone K, Howard M, Harvey I, Harrad RA, Sparrow JM. Prevalence and risk factors for common vision problems in children: data from the ALSPAC study. Br J Ophthalmol. 2008 Jul;92(7):959-64. doi: 10.1136/bjo.2007.134700. Epub 2008 May 14. PMID: 18480306.Ono H, Mapp AP. A restatement and modification of Wells-Hering's laws of visual direction. Perception. 1995;24(2):237-52. doi: 10.1068/p240237. PMID: 7617427.
4. Angela N. Buffenn, The impact of strabismus on psychosocial heath and quality of life: a systematic review, Survey of Ophthalmology. Available from: https://doi.org/10.1016/j.survophthal.2021.03.005
5. Ministry of Health [Internet]. Data and Statistics National Minimum Dataset (Hospital Events) (NMDS). 2010. Available from: http://www.moh.govt.nz/moh.nsf/indexmh/dataandstatistics-collections-nmds
6. Atkinson J, Salmond C, Crampton P. 2014. NZDep2013 Index of Deprivation. Dunedin: University of Otago.
7. Repka M, Lum F, Burugapolli B. Strabismus and strabismus surgery in the United States: analysis from the IRIS registry. Journal of American Association for Pediatric Ophthalmology and Strabismus. 2018;22(4):e6.
8. S. Sharbini. Prevalence Of Strabismus & Associated Risk Factors: The Sydney Childhood Eye Studies. The University of Sydney. 2015 Oct.
9. Repka MX, Lum F, Burugapalli B. Strabismus, Strabismus Surgery, and Reoperation Rate in the United States: Analysis from the IRIS Registry. Ophthalmology. 2018 Oct;125(10):1646-53. doi: 10.1016/j.ophtha.2018.04.024. Epub 2018 May 18. PMID: 29779683.

A distance-based approach to rurality and remoteness in health: concept, methodology and correlates of a patient-centred health services spatial accessibility index

Emmanuel Jo, Chris Lane, Keri McArthur, Fei Xu

ABSTRACT

AIM: To develop a distance-based index of patients' spatial accessibility to healthcare services as a quantifiable basis for analysing health services and health outcomes in urban, rural and remote locations.

METHOD: A distance score was calculated based on each primary health organisation enrollee's shortest distance to the nearest primary care facility and to the nearest secondary or tertiary hospital. The distance scores were then grouped into ten distance deciles (DDs).

RESULTS: When these DDs are compared with Stats NZ's urban-rural indicator, "small urban areas" fall mainly along with rural and remote areas into the two DDs (DD9 and DD10) based on the greatest distance scores. When compared with Stats NZ's urban accessibility classification, the same two DDs correspond mainly to the most rural and remote areas. In both the North and South islands, 25% or more of enrollees in DD9 and DD10 are aged 60+. Of enrollees in DD10 in the North Island, 32% are Māori and 33% live in highly deprived areas (NZDep2013 deciles 9 and 10).

CONCLUSION: The results provide an initial validation of the patient-centred health services spatial accessibility index as a measure of rurality and remoteness for analysis of health service provision and health outcomes.

Concern about the provision of health services to rural and remote populations in New Zealand continues,[1–5] but relevant analyses of health service provision and health outcomes have been hampered by a lack of a clear and consistent framework for distinguishing urban, rural and remote locations from a health perspective. It is possible to routinely analyse health conditions, health-related behaviours and health outcomes by age, gender, ethnicity and socioeconomic deprivation, but not by urban, rural or remote locations. At the Health Workforce Directorate (the Directorate) of the Ministry of Health (the Ministry), we provide funding for the training of general practitioners (family physicians, GPs) and have sought to make sure that GP trainees gain experience in serving rural and remote communities. More broadly, the Directorate has also sought to understand the distribution of primary care practices and their patients in rural and remote communities. In 2018, the Analytics and Intelligence section in the Directorate developed an approach to rurality and remoteness that focuses on "spatial access."[6] This has improved our understanding of differences among primary care practices and contributed to analysing the placement of resources

for general practice training. This approach was updated in 2020 to provide a flexible tool for analysis and forecasting, which we have incorporated (along with regional and patient demographic variables) in a model for forecasting future demand for primary care services in rural and remote areas. This spatial accessibility index has been developed independently of the Geographic Classification for Health[7] and is complementary to it.

This paper describes the development of the patient-centred health services spatial accessibility index in terms of the concept, the data used and the calculation of the index. This index is then compared with two of Stats NZ's indicators of rural-urban differences, and use of the index is illustrated in terms of how it relates to other factors potentially linked to health outcomes.

Defining urban and rural

Since 2001, Stats NZ has had two general approaches to classifying urban and rural areas: one based on population density, and the other based on patterns of travel or potential travel. More specifically, the first approach distinguishes urban areas by their total population and rural areas by whether there are local concentrations of population ("rural settlements").

The earliest version of the second approach was the urban-rural experimental profile (UREP).[8] This was based on patterns of commuting between home and work addresses found in census data.

Both classifications have been assessed as a basis for identifying rural as opposed to urban. Both have also been found to be problematic from the perspective of analysing healthcare.[9] One issue relates to small urban areas that are relatively distant from larger urban areas but where the health services cater for a largely rural population. This is not well accounted for in either classification. Fearnley, Lawrenson and Nixon proposed a modification to UREP to better represent urban and rural health provision, but even with this modification, we have found UREP unsatisfactory because it does not take into account the actual locations of hospitals and other health facilities.

Stats NZ recently released a new travel-based "urban accessibility" classification, this time based on driving times to larger urban areas from locations outside them.[10] This classification is considered in more detail below in comparison with the spatial accessibility index.

At the time of developing the spatial accessibility index, there was an existing Rural Ranking Scale (RRS) for general practitioners, based on their on-call duties, their coverage of peripheral clinics and three distance-based measures: travelling time to a major hospital, travelling time to the nearest GP colleague's place of work and travel time to the most distant practice boundary.[11] These distance-based measures were based on the location of each general practice, rather than the locations of their patients.

Method

The Health Workforce Directorate of the Ministry of Health sought a measure of rurality/remoteness that reflects where patients live rather than where general practitioners work. So, we adapted the hospital-distance and distance-to-practice measures in the RRS to ones that apply to patients. As a result, the Directorate developed a measure of the spatial accessibility of health services based on the distance of primary health organisation (PHO) enrollees' locations from the nearest secondary/tertiary hospital and from the nearest primary care facility (this category includes general practices led by GPs and by nurse practitioners, urgent care clinics, primary hospitals, hauora Māori/Māori health providers, Pacific health providers and tertiary education student health centres).

The Ministry of Health retains data on healthcare facilities and on enrollees (identified by their National Health Index numbers (NHIs)) in which locations are specified on a longitude (X) and latitude (Y) grid. As Ministry employees, we had access (under the provisions of the Health Information Privacy Code[12,13] allowing use for statistical purposes) to data on 4.7 million New Zealanders enrolled in PHOs. This was reduced to an analysis dataset of 4.6 million validated PHO enrollees after removing invalid NHIs and those without valid X and

Y coordinates. We put our use of this data in front of the Health and Disability Ethics Committees, Ministry of Health, and were advised that as "an Audit or related activity it does not require HDEC review."[14] We used a PHO enrollee dataset extracted from the National Enrolment Service (NES) at March 2020.[15] We measured the distance "as the crow flies" between each enrollee's location and the nearest primary care facility and the nearest secondary or tertiary hospital (these are hospitals with the capacity (24 hours a day, seven days a week) to provide acute surgery under general anaesthesia and to regularly undertake Caesarean sections: the 24 such hospitals are listed in Appendix Figure 1). We then calculated a distance score by adding the home-to-nearest-primary-care straight-line distance and the home-to-nearest-hospital straight-line distance in a weighted proportion. The simplification to straight-line distances was required so that the necessary billions of calculations would be tractable.

The main weighting we have used is 30% primary care distance and 70% hospital distance, which is approximately in line with the weighting of practice distance and hospital distance in the RRS. That weighting is the basis of the analyses explored later in the paper. We compared this weighting with two other potential weightings (10%/90% and 50%/50%) on a national scale and found only small differences in the relative ordering of the distance scores and in the way that distance scores group into deciles, because whatever the weighting, the hospital distance accounts for most of the difference in distance scores.

The straight-line distances used will underestimate the actual travel distances for enrollees, but the point of calculating the distance scores is to estimate enrollees' relative distances from health facilities.

As of March 2020, we had counted 1,063 primary care facilities and 24 secondary and tertiary hospitals in New Zealand. Therefore, calculation of the distance score involved (4.6 million x 1,063) + (4.6 million x 24) = 5 billion distance calculations. SAS® 9.4 was used for the calculation of distance score and distance decile and further analysis.

The distance scores provide a patient-centred health services accessibility measure for each enrollee—"accessibility" here refers to spatial accessibility rather than financial, social or cultural accessibility. We grouped enrollees' distance scores into deciles (with 10% of enrollees in each, by definition) to produce a "distance decile" measure as a way of representing spatial accessibility. The distance decile approximates an urban-rural/remote continuum, with distance decile 1 being the most urban and distance decile 10 the most rural or remote. The boundaries between deciles (using a 30%/70% weighting) are shown in Table 1. The maximum distance scores are for enrollees in the Chatham Islands/Rēkohu/Wharekauri.

The average (mean) distance score of each primary care practice's enrollees was also calculated to produce a practice distance score, and then these practice distance scores were grouped into practice distance deciles.

The distance scores and distance deciles for enrollees and for primary practices were then available for analysis and modelling, together with demographic and health variables for enrollees and practice and practitioner characteristics for primary practices.

Table 1: Distance Decile lower and upper boundaries.

Distance decile	1	2	3	4	5	6	7	8	9	10
Lower distance score	0	1.6	2.4	3.2	4.1	5.3	6.7	10.7	18.7	32.7
Upper distance score	1.6	2.4	3.2	4.1	5.3	6.7	10.7	18.7	32.7	720.2

As a check on the distance-score measure, we took a random sample of 200 enrollees and compared their straight-line distance scores with distance scores calculated using road distances obtained from OpenStreetMap. Overall, the relationship between the road and straight-line distance scores was linear, with a correlation coefficient of 0.99. The ratios of road distance scores to straight-line distance scores were variable for small distance scores but more consistent for larger scores. For straight-line distance scores over 10.7 (ie, distance deciles 8, 9 and 10), the average ratio was 1.28 with a standard deviation of 0.15, compared with an average ratio of 1.49 and standard deviation of 0.33 for distance deciles 1 to 7. In distance deciles 8 to 10, there was one anomalous ratio of 1.88 where the road route to hospital had to skirt a mountain range. But for distance deciles 8 to 10 in general, the straight-line distance score represented a fairly consistent proportion of the road distance score.

The processes of extracting the enrollee data and calculating distance deciles are visualised in Figure 1.

Results

As an initial test of the spatial accessibility index, we compared the distance deciles with two of Stats NZ's urban-rural classifications and used the distance deciles to analyse the distribution of health-related factors in the North and South islands.

Distance decile compared with Stats NZ's urban-rural indicator

We compared our distance decile with Stats NZ's urban-rural indicator (IUR 2020). The urban categories in IUR 2020 are defined by population size: major urban (100,000+), large urban (30,000–99,999), medium urban (10,000–29,999) and small urban (1,000–9,999). Figure 2 shows the percentages of validated PHO enrollees in March 2020 in each IUR category within each distance decile (for the purposes of direct comparison, both classifications are defined on 2013 meshblocks, the geographical units used for the 2013 census).

The PHO enrollees at the greatest distance from secondary/tertiary hospitals and primary care practices are in distance deciles 9 and 10, and these enrollees are largely in rural or small urban areas.

For the purposes of analysing health services accessibility, distance deciles 9 and 10 can be taken as approximately equivalent to "rural/remote." Similarly, rural/remote can be more loosely approximated by the IUR 2020 categories "small urban area," "rural settlement" and "rural other."

Distance decile compared with Stats NZ's urban accessibility classification

Stats NZ recently (September 2020) released the urban accessibility classification, which is focused on rural areas and small urban areas and based on how long it takes to drive from those areas to the nearest larger urban areas (ie, major, large or medium urban areas, as defined for the urban-rural indicator).[10] The categories are:

- High urban accessibility (high UA): up to 15 minutes from a major urban area
- Medium urban accessibility: not high UA but up to 25 minutes from a major or large urban area, or up to 15 minutes from a medium urban area
- Low urban accessibility: not high or medium UA, but up to 60 minutes from a larger urban area
- Remote: 60 to 120 minutes from a larger urban area
- Very remote: more than 120 minutes from a larger urban area

Figure 3 shows the estimated percentages of validated PHO enrollees at March 2020 in each urban accessibility category within each distance decile. (The urban accessibility classification is defined over a 2018 census geographical base, whereas the distance deciles were calculated over 2013 census meshblocks. The geographical classifications for the two censuses differ somewhat due to population growth, hence the comparison between the urban accessibility classification and distance deciles is approximate.)

In terms of the urban accessibility classification, distance deciles 1 to 7 are largely urban, and distance decile 8 is mainly a mix of large and medium urban and high, medium and low urban accessibility. A large part of distance decile 9 (77%) consists

Figure 1: Data analysis and distance decile calculations.

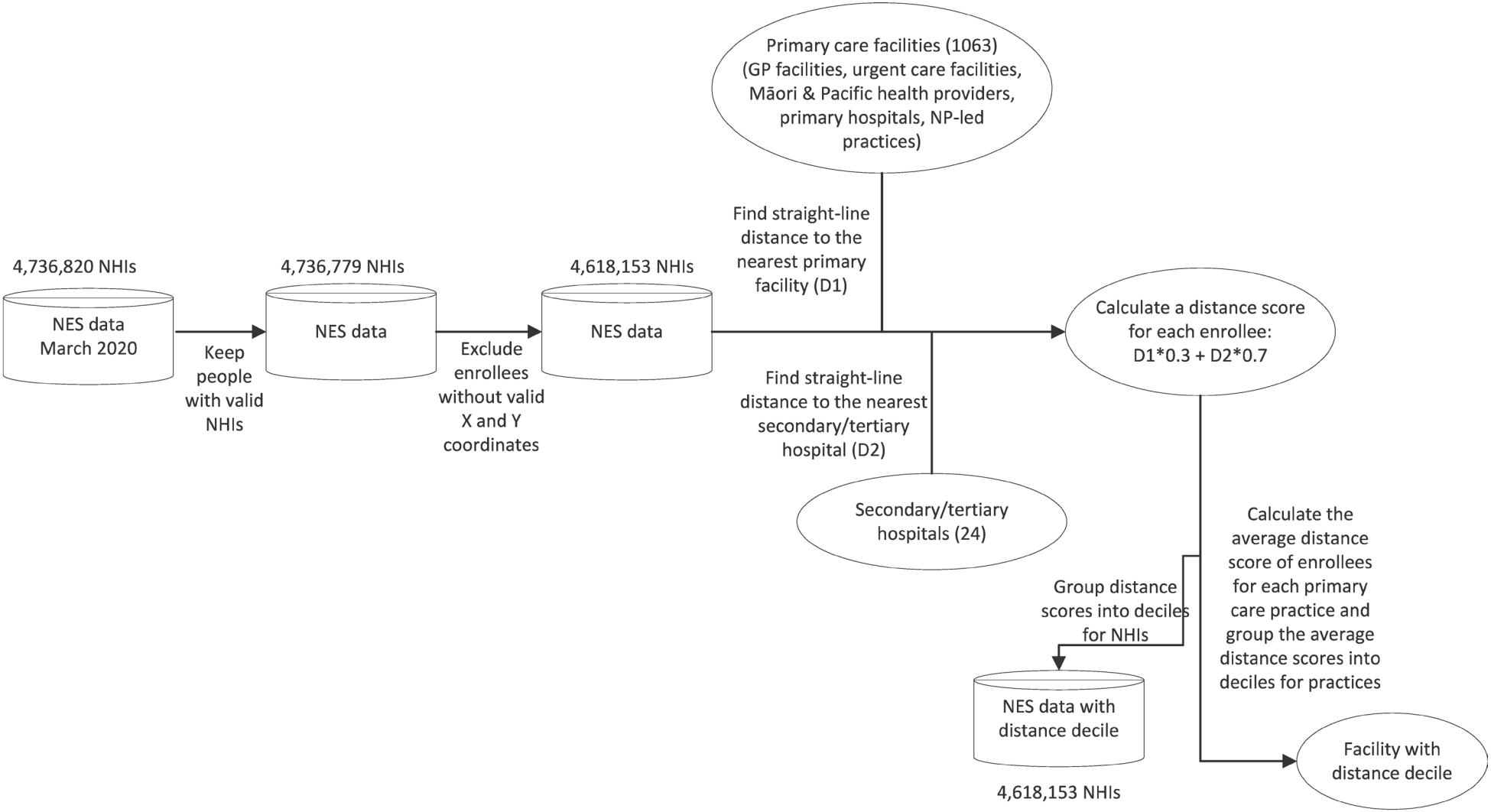

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Figure 2: Percentage of validated PHO enrollees at March 2020 in Stats NZ's urban-rural indicator categories (IUR 2020) in each distance decile (30%/70% weighting).

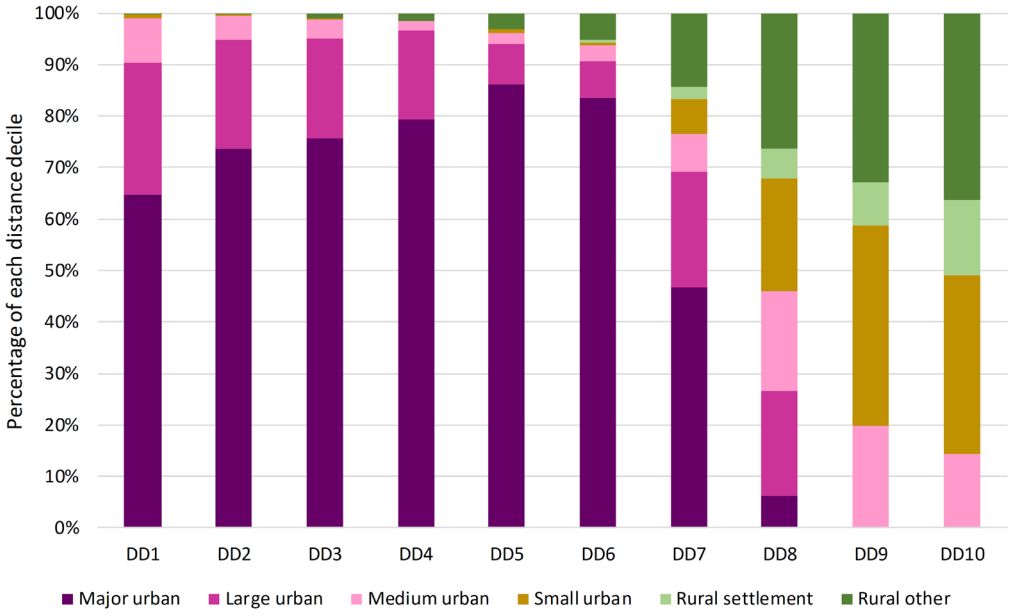
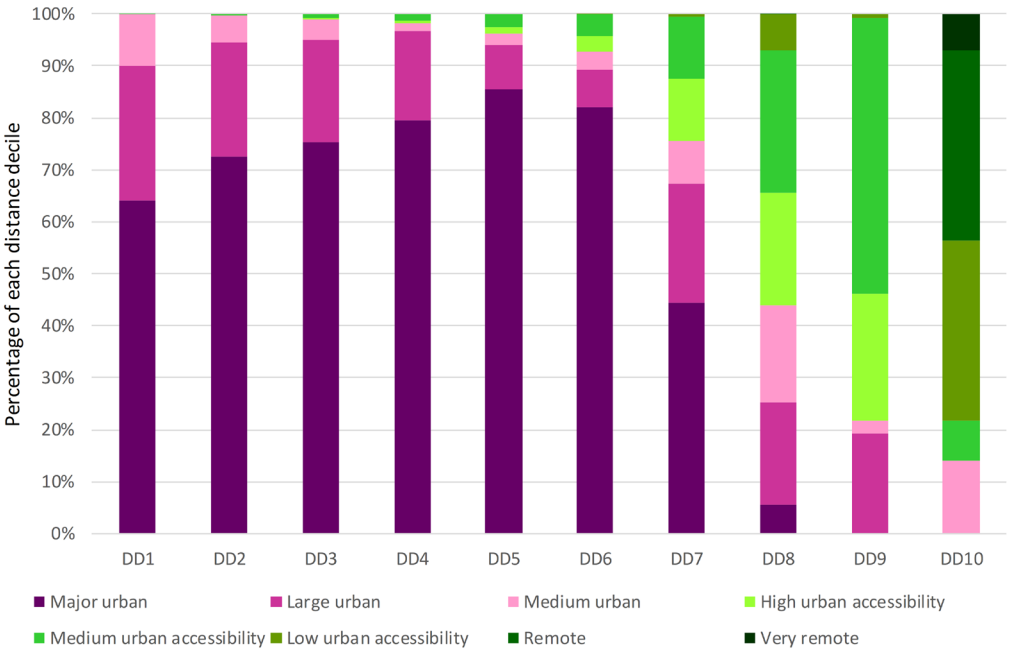


Figure 3: Estimated percentage of validated PHO enrollees at March 2020 in Stats NZ's urban accessibility categories in each distance decile (30%/70% weighting)



of areas with high or medium urban accessibility, as well as some large urban areas—these will be urban areas without secondary or tertiary hospitals and at a considerable distance from the nearest secondary/tertiary hospital. Most of distance decile 10 (78%) consists of remote or very remote areas or areas with low urban accessibility. However, distance decile 10 also includes some medium urban areas that are a long way from secondary/tertiary hospitals (eg, Queenstown and Taupō). In the urban accessibility classification, by definition such medium urban areas cannot be remote, because remoteness is based on distance from medium or larger urban areas.

In terms of distance deciles, all of the remote and very remote areas in the urban accessibility classification fall into distance decile 10, as do 82% of the low urban accessibility areas, whereas 50% of the medium urban accessibility areas and 41% of the high urban accessibility areas are in distance decile 9.

The two classifications show considerable agreement in terms of representing rurality and remoteness. A key difference is that the distance decile classification allows for the possibility that medium and large urban areas can be remote from secondary/tertiary hospitals.

Distance deciles in the North and South islands

The distance deciles are defined for the whole country: by definition, 10% of all validated PHO enrollees fall into each decile. However, the distribution of enrollees by distance decile is quite different in the two islands, as shown in Figure 4.

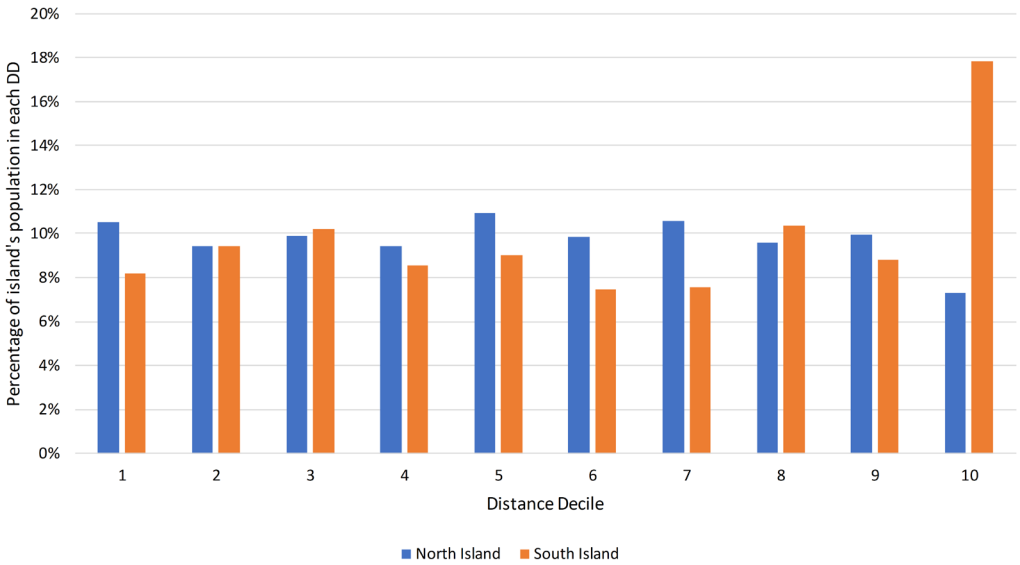
The outstanding difference is the proportion of enrollees in distance decile 10: 18% in the South Island and 7% in the North Island.

Distribution of health-related factors

Rurality and remoteness are not solely matters of distance: other factors can combine with distance in complex ways that need to be taken into account when providing health services and analysing health outcomes.

This section examines the spatial distribution in the analysis dataset of a number of factors known to be related to health outcomes: age, ethnicity and socioeconomic deprivation.[16] These factors vary according to distance decile, and the patterns of variation are quite different in the North and South islands. Accordingly, the patterns for each island are analysed separately and compared.

Figure 4: Distribution of validated PHO enrollees by distance decile in the North and South islands (March 2020).



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Age

Older age is associated with greater demand for health services. In the North Island, the proportion of enrollees aged 60 and over is clearly higher in distance deciles 9 (26%) and 10 (28%) than in deciles 1 to 8 (19% to 23%), whereas in the South Island the highest proportion is in decile 9 (29%), though the pattern is somewhat more variable. For most distance deciles, the 60+ proportion is higher in the South Island than the North Island. These patterns can be seen in Figure 5.

Ethnicity

Māori and Pacific Peoples tend to be less well served by the health system and tend to have poorer health outcomes and greater health needs.[1,16–19] The geographical distributions of the two groups are quite different. Figure 6 shows the percentage of validated PHO enrollees who are Māori in each distance decile for the two islands.

In the South Island, the Māori percentage trends slightly downward from distance decile 1 (11%) to 10 (8%). The Māori percentages are generally higher in the North Island and are particularly high in deciles 9 (22%) and 10 (32%).

Figure 7 shows the corresponding percentages for Pacific Peoples. The percentage of Pacific Peoples in each decile in the South Island shows a downward trend from decile 1 to 10, which is similar to the trend for Māori in the South Island. In the North Island, the highest percentages of Pacific Peoples (over 10%) are in distance deciles 1 to 6, which correspond to larger urban areas.

Deprivation

The socioeconomic deprivation of small areas or neighbourhoods can be measured using the New Zealand Index of Deprivation based on the 2013 census (NZDep2013).[20] Figure 8 shows the percentage of validated PHO enrollees in each distance decile who live in the most deprived areas (NZDep2013 deciles 9 and 10 or, equivalently, quintile 5).

In the South Island, the percentage in greatest deprivation is highest in distance deciles 1 to 4 (15% or higher), and very low in deciles 6 to 10 (5% or less). In contrast, in the North Island the percentage in greatest deprivation peaks in deciles 1 to 2 (30%) and decile 10 (33%).

Given the strong associations between distance decile and other factors known to be associated with variation in health outcomes, it should not be assumed that variation in health outcomes according to distance decile is due to distance in itself. Rather, the patient-centred spatial accessibility index provides a tool for distinguishing the effects of distance from the effects of other factors.

Figure 5: Percentage of validated PHO enrollees aged 60+ in each distance decile (March 2020).

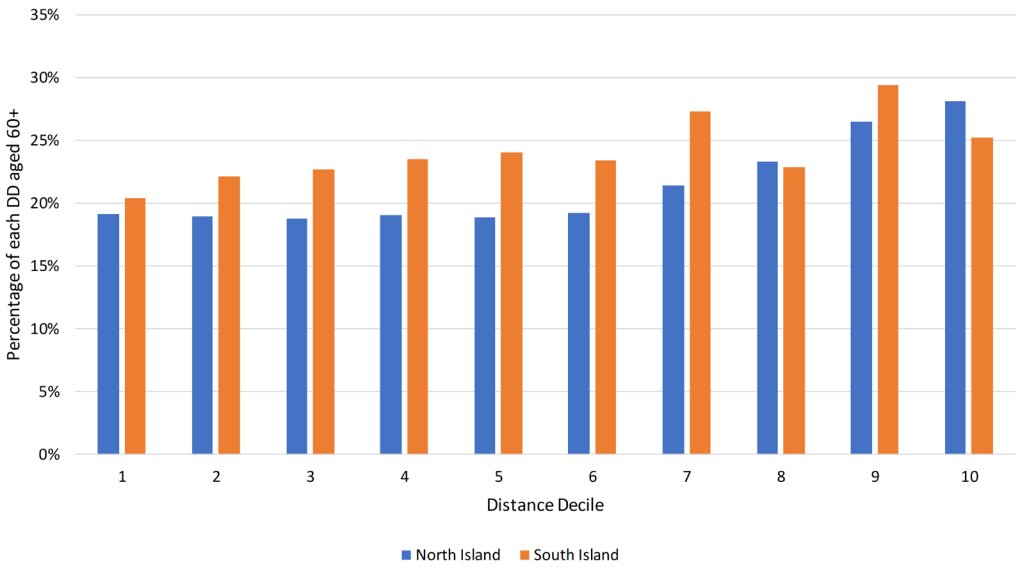

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Figure 6: Māori percentage of validated PHO enrollees in each distance decile (March 2020).

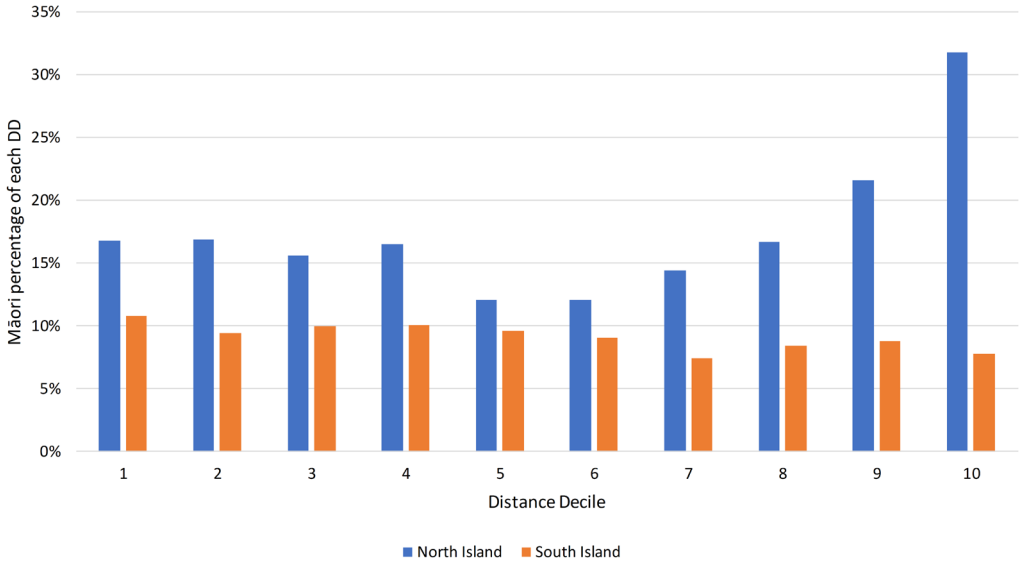
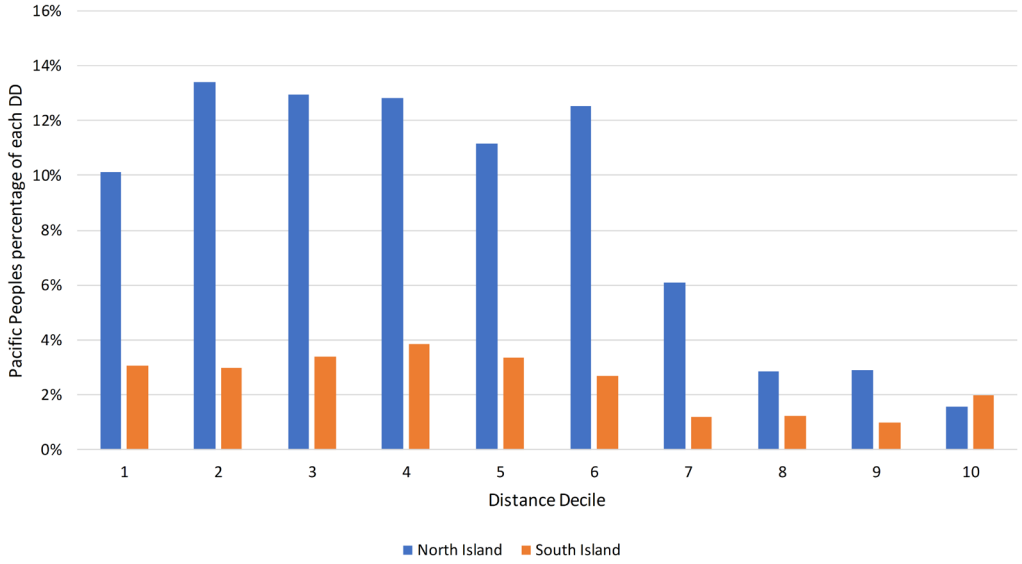


Figure 7: Pacific Peoples as percentage of validated PHO enrollees in each distance decile (March 2020).



Discussion

Limitations

One of the major limitations of the patient-centred health services spatial accessibility index (PCHSSAI) is the use of straight-line distance as an indicator of relative distance, rather than actual road distances or travel times. Another limitation is that the analysis applies to validated PHO enrollees rather than the total population: 6% of New Zealand residents are not enrolled with a PHO. Non-enrollees are more likely than enrollees to be aged 15 to 24, to live in the Auckland District Health Board area, to be Māori and to live in areas of higher deprivation.[21] It is not clear how these disparities might affect the overall distribution of distance scores if non-enrollees were to be included in the analysis. Furthermore, the analysis reported here is based on a single snapshot in time: we have not investigated seasonal or other temporal variation in enrollees' locations.

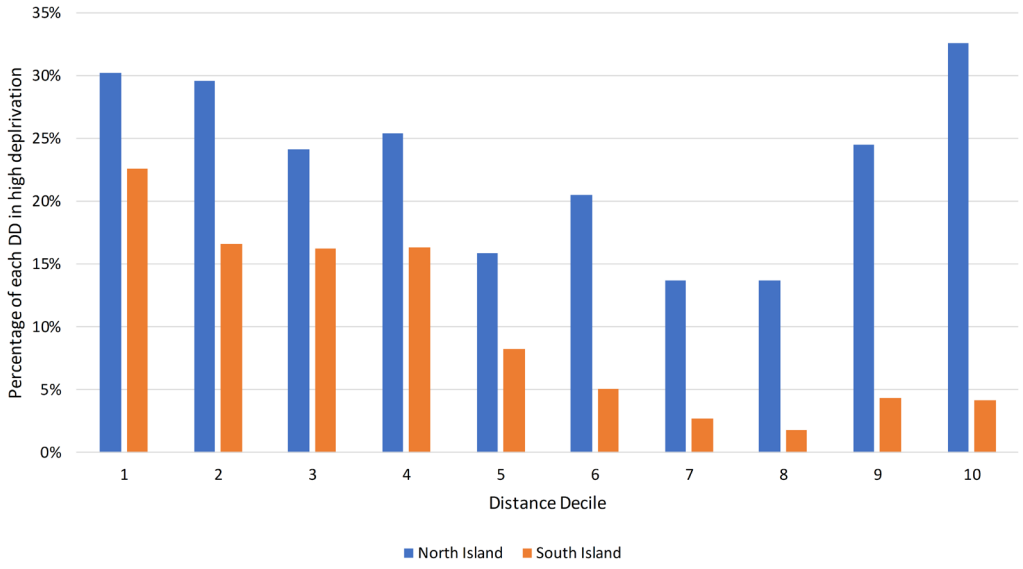
Comparison of approaches to urban, rural and remote health

The PCHSSAI is by design a narrowly focused measure of just one aspect of health care accessibility, namely patients' spatial distances from healthcare facilities. In this respect it resembles the revised Accessibility/Remoteness Index of Australia (ARIA+),[22–24] which is based on road distances to urban areas where various services, including health services, are located. Like ARIA+, the PCHSSAI is neither tied to any particular geographical classification nor complicated by considerations of population density but on the other hand, locations with the same score can have quite different characteristics: in the case of the PCHSSAI, locations with large distance scores (distance decile 10) can be in uninhabited wilderness or in bustling urban areas.

Like ARIA+ and the Index of Relative Rurality (IRR) developed in the United States,[25] the PCHSSAI provides a continuous numerical scale, which is an advantage from the point of view of statistical analysis and modelling. In addition, the PCHSSAI provides distance scores that can be matched to demographics and health outcomes at the individual patient level, which affords precision and flexibility in analysis and modelling.

The new Geographic Classification for Health (GCH)[7,26] is a modified version of Stats NZ's urban accessibility classification (UA). There are a number of differences

Figure 8: Percentage of validated PHO enrollees in greatest deprivation (NZDep 2013 deciles 9 and 10) in each distance decile (March 2020).



in methodology between the UA and the PCHSSAI approach. The UA is based on distances between areas, namely a SA1 (Statistical Area 1, a small geographical area with 100–200 residents,[27] measured from a central point) and a boundary of a larger urban area, whereas the PCHSSAI is based on the point-to-point distance between each enrollee's location and the locations of health facilities. On the other hand, the UA uses driving times which provide a more realistic measure than the straight-line distances used to calculate the PCHSSAI, and the PCHSSAI is not directly translatable into driving times. The UA is based on five-yearly census data, although it could be updated on the basis of population projections for SA1s (reflecting urban growth), which will start to be available from late 2021. The PCHSSAI has so far been updated on an annual basis but, in theory, could be constructed at any time, so that it could be updated six-monthly or quarterly. Unlike the UA, the PCHSSAI is health-specific: for example, if a hospital is upgraded to secondary status, then the PCHSSAI can be updated to take account of the changed healthcare environment.

The basic PCHSSAI methodology can also be adapted to measure accessibility to different types of health service: we have constructed another version based on distances to hospital emergency facilities (as well as primary care facilities) to analyse emergency presentations. The methodology could be adapted to include other types of health service, such as pharmacies and oral health services, as in Hobbs, Tomintz and Kingham's geographic analysis of child ambulatory sensitive hospitalisation (ASH) rates.[28]

Spatial accessibility and health outcomes

The PCHSSAI is not an end in itself. Rather, it is a tool for analysing health provision and health outcomes. We have analysed ASH rates for children aged 0–4 and found that these rates decline steadily from distance decile 1 to distance decile 10, in line with Hobbs, Tomintz and Kingham's[28] findings. Both sets of findings raise a question for further research as to whether this pattern is due at least in part to distance presenting a barrier to hospitalisation, or whether rural and remote primary practices provide more effective care of such children, or both.

The PCHSSAI is the basis of graphs published by the Rural General Practice Network[29] that compare mortality rates stratified by age in urban (distance deciles 1–8) and rural/remote areas (distance deciles 9–10) and highlighted higher age-specific mortality rates in rural/remote areas compared with urban areas. However, further analysis (at the individual patient level) has indicated that the overall difference between these urban and rural/remote rates can be largely accounted for by an overall difference in mortality rates between Māori and non-Māori and the greater proportion of Māori in some rural/remote areas, as noted above. This may indicate a need for more effective health services in those rural/remote areas which have relatively high Māori populations.

Conclusion

Distance score and distance decile provide an approach to rurality and remoteness that is based on where patients are rather than just where healthcare facilities are. They directly measure patients' relative spatial access to key healthcare facilities, namely secondary/tertiary hospitals and primary care practices.

With respect to Stats NZ's standard population-based urban-rural indicator (IUR 2020), the distance decile analysis indicates that the areas that Stats NZ labels "small urban areas" largely show the same low level of access to health services as the areas labelled "rural settlements" and "rural other."

Stats NZ's urban accessibility classification groups small urban areas with rural and remote areas as its starting point and then classifies these areas on the basis of distance to larger urban areas. It is thus conceptually similar to the patient-centred health services spatial accessibility index approach, and in practice there is a considerable amount of agreement between the two. This agreement provides an initial validation of our patient-centred health services spatial accessibility index as a tool for investigating rurality and remoteness in health services and health outcomes.

Distance deciles 9 and 10 correspond to the most rural and remote areas (including some remote urban areas) and are asso-

ciated with different health-related factors in the South and North islands. In the South Island, there is a particularly high proportion of PHO enrollees aged 60 and over in these distance deciles, whereas in the North Island, distance deciles 9 and 10 are characterised by high percentages of enrollees aged 60 and over, of Māori and of enrollees living in highly deprived areas, in line with the disadvantaged groups identified in a previous study of geographical access to emergency care.[5] Thus in both islands in distance deciles 9 and 10 there are factors indicating high healthcare needs that are likely to be exacerbated by difficulties of spatial access to healthcare facilities, especially secondary or tertiary hospitals.

Author contributions

The original concept and design of the index was formulated by EJ, coding and data matching was conducted by KM, summary and analysis was conducted by CL, writing the original manuscript was shared by EJ, CL and FX, and all co-authors contributed to revising the manuscript.

Appendix

Appendix Figure 1: Secondary/tertiary hospitals.

District health board	Hospital
Northland	Whangārei Hospital
Waitematā	North Shore Hospital Waitākere Hospital
Auckland	Auckland City Hospital
Counties Manukau	Middlemore Hospital
Waikato	Waikato Hospital
Lakes	Rotorua Hospital
Bay of Plenty	Tauranga Hospital Whakatāne Hospital
Hauora Tairāwhiti	Gisborne Hospital
Hawke's Bay	Hawke's Bay Hospital
Taranaki	Taranaki Base Hospital
MidCentral	Palmerston North Hospital
Whanganui	Whanganui Hospital
Capital and Coast	Wellington Hospital
Hutt Valley	Hutt Hospital
Wairarapa	Wairarapa Hospital
Nelson Marlborough	Nelson Hospital Wairau Hospital
West Coast	Greymouth Base Hospital
Canterbury	Christchurch Hospital
South Canterbury	Timaru Hospital
Southern	Dunedin Hospital Southland Hospital

Competing interests:
Nil.
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REFERENCES

1. Health and Disability System Review. Health and Disability System Review - Final Report - Pūrongo Whakamutunga. Wellington: HDSR [Internet]. 2020 [cited 2020 Nov 11]. Available from: www.systemreview.health.govt.nz/final-report
2. Nixon G, Samaranayaka A, de Graaf B, et al. Geographic disparities in the utilisation of computed tomography scanning services in southern New Zealand. Health Policy. 2014;118:222-8. https://doi.org/10.1016/j.healthpol.2014.05.002
3. Nixon G, Samaranayaka A, de Graaf B, et al. The impact of a rural scanner in overcoming urban versus rural disparities in the utilisation of computed tomography. Aust J Rural Health. 2015;23(3):150-4. https://doi.org/10.1111/ajr.12125
4. Fearnley D, Kerse N, Nixon G. The price of 'free'. Quantifying the costs incurred by rural residents attending publically [sic] funded outpatient clinics in rural and base hospitals. J Prim Health Care. 2016;8(3): 204-9. https://doi.org/10.1071/HC16014
5. Lilley R, de Graaf B, Kool B et al. Geographical and population disparities in timely access to prehospital and advanced level emergency care in New Zealand: a cross-sectional study. BMJ Open. 2019;9:e026026. https://doi.org/10.1136/bmjopen-2018-026026
6. McGrail M, Humphreys J. Spatial access disparities to primary health care in rural and remote Australia. Geospat Health. 2015;10:138-43. https://doi.org/10.4081/gh.2015.358
7. University of Otago. Rural-urban classification for NZ health research and policy [Internet] 2021. [cited 2021 May 26]. Available from: https://blogs.otago.ac.nz/rural-urbannz
8. Stats NZ. New Zealand: An Urban/Rural Profile [Internet]. 2004 [cited 2020 Nov 11]. Available from: http://infoshare.stats.govt.nz/browse_for_stats/Maps_and_geography/Geographic-areas/urban-rural-profile.aspx
9. Fearnley D, Lawrenson R, Nixon G. 'Poorly defined': unknown unknowns in New Zealand Rural Health. N Z Med J. 2016;129:77-81.
10. Stats NZ. Urban accessibility – methodology and classification [Internet]. 2020 [cited 2020 Nov 11]. Available from: https://www.stats.govt.nz/methods/

urban-accessibility-methodology-and-classification

11. Ministry of Health. The 2005 Rural Health Workforce Survey [Internet]. 2006 [cited 2021 May 26]. Available from: https://www.health.govt.nz/publication/2005-rural-health-workforce-survey
12. Privacy Commissioner. Health Information Privacy Code 1994 [Internet]. 2017 [cited 2021 Jun 16]. Available from: https://privacy.org.nz/assets/Codes-of-Practice-2020/REVOKED-CODES/Consolidated-HIPC-current-as-of-28-Sept-17.pdf
13. Privacy Commissioner. Health Information Privacy Code 2020 [Internet]. 2020 [cited 2021 Jun 16]. Available from: https://privacy.org.nz/privacy-act-2020/codes-of-practice/hipc2020/
14. Health and Disability Ethics Committees, Ministry of Health. Letter to Emmanuel Jo, 31 August 2020.
15. Ministry of Health. National Enrolment Service [Internet]. 2018 [cited 2020 Nov 11]. Available from: https://www.health.govt.nz/our-work/primary-health-care/primary-health-care-subsidies-and-services/national-enrolment-service
16. Ministry of Health. Health and Independence Report: The Director-General of Health's Annual Report on the State of Public Health [Internet]. 2020 [cited 2021 May 26]. Available from: https://www.health.govt.nz/system/files/documents/publications/health-and-independence-report-2019-25feb2021.pdf
17. Cram F, Te Huia B, Te Huia T, et al. Oranga and Māori health inequalities, 1769-1992 [Internet]. 2019 [cited 2021 May 26]. Available from: https://forms.justice.govt.nz/search/Documents/WT/wt_DOC_152096130/Wai%202575%2C%20B025.pdf
18. Health Quality and Safety Commission. Equity Explorer [Internet]. 2021 [cited 2021 May 26]. Available from: https://www.hqsc.govt.nz/our-programmes/health-quality-evaluation/projects/atlas-of-healthcare-variation/equity-explorer/
19. Selak V, Rahiri J, Jackson R, Harwood M. Acknowledging and acting on racism in the health sector in Aotearoa New Zealand. N Z Med J. 2020;133:7-13.
20. University of Otago Department of Public Health. Socioeconomic deprivation indexes: NZDep and NZiDep [Internet]. 2021 [cited 2021 May 27]. Available from: https://www.otago.ac.nz/wellington/departments/publichealth/research/hirp/otago020194.html
21. Irurzun-Lopez M, Jeffreys M, Cumming J. The enrolment gap: who is not enrolling with primary health organizations in Aotearoa New Zealand and what are the implications? An exploration of 2015-2019 administrative data. Int J Equity Health. 2021;20:93. https://doi.org/10.1186/s12939-021-01423-4
22. Hugo Centre for Population and Migration Studies, University of Adelaide. Accessibility/Remoteness Index for Australia (ARIA) [Internet]. 2020 [cited 2021 May 27]. Available from: https://arts.adelaide.edu.au/hugo-centre/services/aria
23. Glover J, Tennant S. Remote areas statistical geography in Australia: Notes on the Accessibility/Remoteness Index for Australia (ARIA+ version). Working Paper Series No. 9, Public Health Information Development Unit, University of Adelaide. 2003. Available from: http://hdl.handle.net/2440/45471
24. McGrail M, Humphreys J. Geographical classifications to guide rural health policy in Australia. Aust New Zealand Health Policy. 2009;6(28). https://doi.org/10.1186/1743-8462-6-28
25. Waldorf B, Kim A. Defining and measuring rurality in the US: From typologies to continuous indices [Internet]. 2015 [cited 2021 May 27]. Available from: https://sites.nationalacademies.org/cs/groups/dbassesite/documents/webpage/dbasse_167036.pdf
26. Otago Medical School. Geographic Classification for Health (GCH): Developing a new rural-urban classification for NZ health research and policy [Internet]. 2020 [cited 2021 May 27]. Available from: https://www.otago.ac.nz/oms/education/postgraduate-rural-health/research/otago637911.html
27. Stats NZ. Geographic hierarchy [Internet]. 2019 [cited 2021 May 27]. Available from: https://www.stats.govt.nz/methods/geographic-hierarchy
28. Hobbs M, Tomintz M, Kingham S. Investigating the rates and spatial distribution of childhood ambulatory sensitive hospitalisations in New Zealand. GeoHealth Laboratory, Geospatial Research Institute, University of Canterbury [Internet]. 2019 [cited 2020 Nov 9]. Available from: https://ir.canterbury.ac.nz/handle/10092/16898
29. Rural Health Networks. Briefing to the incoming Minister of Health, December 2020 [Internet]. 2020 [cited 2021 May 27]. Available from: https://rgpn.org.nz/wp-content/uploads/2020/12/BIM2020-E-version.pdf

Quality of life after oesophageal stenting in patients with palliative oesophageal cancer

Cameron Schauer, Anurag Sekra, Ibrahim Hassan, Yi-Ting Wu, Michael TM Wang, Henry Wei, David McGouran, Ming Han Lim, Dinesh Lal, Ravinder Ogra

ABSTRACT

BACKGROUND AND AIM: Patients with incurable oesophageal cancer have poor outcomes, with disabling symptoms and a poor quality of life (QOL), which may be improved by oesophageal stenting. We aimed to measure change in symptoms related specifically to oesophageal cancer and overall QOL before and 30 days after stent insertion, to measure adverse effects and to define any patient factors that may be significant in predicting patients who may benefit most.

METHODS: We prospectively enrolled patients in an observational study at Middlemore Hospital, New Zealand, and administered validated QOL- and symptomatology-based questionnaires before and 30 days after stent insertion. Additional patient-related demographics, procedural characteristics, adverse events and outcomes were collected.

RESULTS: Between 31 March 2014 and 3 July 2020, 57 patients were initially recruited. Four patients withdrew from the study, and 13 patients died before 30 days. Forty patients (29 males; mean±SD age, 72±12 years) completed the study. A significant improvement was noted at one-month post stent insertion in the overall global QOL score (mean 35 to 46, p=0.01). The most significant score improvements were seen in dysphagia, trouble eating, trouble swallowing saliva and dry mouth (p<0.001). Physical, emotional, cognitive and social functioning did not change. Post-procedural adverse events occurred in 17 patients (43%). A poorer initial level of functioning was associated with reduced improvement in global QOL (p≤0.04). Patients followed-up died a mean of 2.8 months after insertion.

CONCLUSION: In patients surviving longer than 30 days, there is significant improvement of overall QOL and dysphagia one-month post oesophageal stent insertion for malignant, palliative dysphagia. Multiple psychosocial facets were unchanged with this intervention. Stent-related adverse events were common.

Oesophageal carcinoma remains a leading cause of cancer death worldwide, with over 500,000 cases diagnosed in 2018.[1] It is increasing in incidence, with reports of an annual increase of 4.2% per year in Australia.[2–4] In New Zealand in 1950, the age-standardised registration rate was 2.2/100,000 with 46 cases diagnosed, which increased to 4.3/100,000 with 364 cases diagnosed by 2000.[5] Despite advances in diagnosis and screening being available in some countries, over 50% of patients have either unresectable lesions or metastasis at diagnosis.[6] Outcomes are poor for these patients, with an overall five-year survival of less than 5%.[7] In addition, there is a disproportionate incidence in ethnic minorities with poorer global outcomes.[8,9] Averaged over time, excess mortality is 68% greater for Māori oesophageal cancer patients, and patients in the lowest income quintile experience 10% greater excess mortality compared to patients in the highest income quintile.[10]

Quality of life in these patients may be poor. Pain, malnutrition and significant dysphagia are thought to be the most debilitating symptoms.[11] Various endoluminal palliative treatments for dysphagia have been trialled, including dilatation,

photodynamic therapy, laser therapy and brachytherapy.[12] However, oesophageal self-expanding metal stent (SEMS) insertion has become the most widely accepted treatment and is thought to improve quality of palliation.[11,13–17] Nonetheless, there are conflicting data, with some trials utilising specific comprehensive disease-specific questionnaires, wherein stenting is shown to even worsen overall quality of life with inferior outcomes compared to brachytherapy or thermal tumour ablation.[18,19] No studies have been conducted to corroborate findings in Australasia, where health systems may differ not only in delivery of supportive care, but also in personal financial cost. This publicly funded healthcare may reduce financial distress, which is known to lead to maladaptive coping and poor subsequent health and non-health outcomes in palliative cohorts.[20] In addition, the additive effect of palliative care involvement has not been measured.

SEMS insertion also has a known significant adverse event rate, including complication during insertion, requirement for admission post endoscopic procedure, bleeding, pain, reflux, migration, perforation and stent failure.[21] Given the alternative options, possible adverse events, limited life-expectancy and cost, further analysis of demographic or tumour-related factors that may assist in patient selection to help decide which patients may benefit most is currently limited.

The primary aim of our study was to assess change in symptoms related specifically to oesophageal cancer and overall quality of life both before and 30 days after stent insertion. We wanted to secondarily assess procedural adverse effects and perform an analysis to define any factors which may be significant in improving symptoms.

Materials and methods

We completed a prospective, observational study at Middlemore Hospital, Auckland, New Zealand, from 31 March 2014 to 3 July 2020. This is a tertiary centre servicing a population of 550,000.

Patients were included if they had a confirmed diagnosis of oesophageal cancer and were deemed to be for palliative care due to either metastatic extension or co-morbid conditions by a local multidisciplinary team. Patients complaining of dysphagia to liquids (grade 3) or complete dysphagia (grade 4)[22] were considered for stenting. Patients were excluded if they did not consent to enter the study; if they changed their mind and did not wish to complete the final questionnaire; or if they had passed away within 30 days of stent insertion. Demographic and disease details were abstracted from clinical notes, and if the details were unclear, they confirmed at time of initial interview. Additional palliative care services were offered to all patients. Its uptake and length of involvement was also included.

The study received institutional ethics approval by the Counties Manukau District Health Board research review committee, with all patients enrolled with written informed consent. All authors had access to the study data and reviewed and approved the final manuscript.

Questionnaire

Patients were assessed with two sets of questionnaires before the procedure in a one-on-one interview and then via phone call 30 days post procedure.[23] We administered the European Organisation for Research and Treatment of Cancer (EORTC) questionnaire for patients with oesophageal cancer (OES-18) consisting of 18 disease specific questions [24] and the 30-item overall quality of life (EORTC QLQ-C30) questionnaire. The scoring was completed using the EORTC QLQ-C30 scoring manual (third edition).[25] These validated questionnaires include measurement of emotional and social performance indices in addition to physical performance.

Endoscopic procedure

Patients referred by a clinician as either inpatients or outpatients were considered for stenting by three main gastroenterologists (AS, DL, RO) experienced in performing endoluminal stents. All procedures were performed under conscious sedation with xylocaine throat spray and intravenous midazolam and fentanyl. Three main types of stents were used in this study: Niti-S fully covered single layer, Niti-S double-layered stent[26] (Taewoong Medical, Seoul, Korea) and EndoMAXX (Merit Medical). Technique

of insertion and type of stent insertion was left to the discretion of the user. Following insertion, all patients were provided with a detailed post-stent dietary and pain management guide.

Statistical analysis

Sample size calculations were conducted using NCSS PASS 12 (Utah, USA), with dysphagia score as the designated outcome, and showed that a minimum of 36 participants was required to detect a change in 15 points before and after stent insertion with 80% power (β=0.2) and a two-sided statistical significance level of 5% (α=0.05). The standard deviation of normal values was estimated to be approximately 20 to 25 points.

Statistical analysis was performed using IBM SPSS Statistics version 26.0 (New York, USA) and GraphPad Prism version 8.2.0 (California, USA). Data are presented as mean±SD, median (IQR) or number of participants (% of participants), unless otherwise stated. All tests were two-tailed, and $p<0.05$ was considered statistically significant. Comparisons between baseline and post-treatment symptomology scores were performed using the paired t-test. Preliminary univariate linear regression analysis was used to identify potential predictors for the change in symptomology scores. Multivariable linear regression analysis was then conducted incorporating relevant variables with a univariate association threshold of $p<0.15$.

Results

Between 31 March 2014 and 3 July 2020, 57 patients were initially recruited. Four patients withdrew from the study, and 13 patients died before 30 days. Therefore, a total of 40 patients (29 males, 11 females; mean±SD age, 72±12 years) completed the study. Twenty-three patients (58%) had co-existing hypertension and 23% had coronary artery disease and diabetes mellitus. Histological subtypes included 27 (68%) with adenocarcinoma, 11 (28%) with squamous cell carcinoma and 2 (5.0%) patients with other subtypes (Table 1). The mean stricture length was 5cm, with 63% of lesions located in the lower third of the oesophagus. Six patients (15%) received additional chemotherapy, and 15 (38%) received additional radiotherapy. Most patients (80%) accepted and received palliative care input, and 20 of these patients had their initial consultation while in hospital. Their average length of involvement was 2.4 months.

A significant improvement was noted at one-month post stent insertion in the overall global quality of life (QOL) score (mean 35 to 46, $p=0.01$). The most significant score improvements were seen in dysphagia, trouble eating, trouble swallowing saliva and dry mouth ($p<0.001$) (Table 2, Figure 1). Furthermore, there were significant reductions in nausea and vomiting, appetite loss, oesophageal pain and choking (all $p\leq0.03$). Other measured parameters did not significantly alter, such as physical, emotional, cognitive or social functioning. Stenting did not improve fatigue, insomnia or constipation, which remained substantial issues.

Post-procedural adverse events occurred in 17 patients (43%), including pain in seven (18%), reflux in four (10%), bleeding in two (5.0%) and stent migration in four (10%). A total of 16 patients (40%) required further gastroscopy following stent insertion.

Unadjusted univariate and multivariable-adjusted linear regression analysis of predictors of change in global QOL and dysphagia scores are presented in Appendix Table 1. Multivariable regression analysis demonstrated that poorer ASA (American Society of Anaesthesiologists) physical status classification grading[27] and coronary artery disease were associated with reduced improvement in global QOL scores (both $p\leq0.04$), and additional chemotherapy treatment was associated with greater reduction in dysphagia scores ($p=0.02$).

Stents were inserted a mean of 1.5 months after initial diagnosis of cancer, and patients followed-up died a mean of 2.8 months after its insertion (Figure 2).

Discussion

This research demonstrates stenting of advanced, incurable oesophageal cancer results in a substantial 30-day improvement of dysphagia and overall quality of life in patients surviving to this time. However, there is little effect on individual psychosocial outcomes. Secondarily, many patients reported adverse events requiring

Table 1: Baseline and procedural characteristics of patients. Data are presented as mean±SD, median (IQR) or number of participants (% of participants).

Parameter	Value
Demographics	
Age (years)	71.6±12.1
Male sex	29 (72.5%)
Ethnicity	
New Zealand European	22 (55.0%)
Māori	9 (22.5%)
Other ethnicity	9 (22.5%)
Co-morbidities	
American Society of Anaesthesiologists (ASA) physical status classification	
ASA II	21 (52.5%)
ASA III	15 (37.5%)
ASA IV	4 (10.0%)
Body mass index (kg/m^2)	24.6±5.8
Coronary artery disease	9 (22.5%)
Chronic obstructive respiratory disease	5 (12.5%)
Diabetes mellitus	9 (22.5%)
Hypertension	23 (57.5%)
Current smoker	8 (20.0%)
Clinical characteristics	
Previous gastroscopy prior to diagnosis	6 (15.0%)
Anti-reflux medication dose	
None	9 (22.5%)
20mg	1 (2.5%)
40mg	14 (35.0%)
60mg	2 (5.0%)
80mg	14 (35.0%)
Histology	
Adenocarcinoma	27 (67.5%)
Sqamous cell carcinoma	11 (27.5%)
Other histology type	2 (5.0%)
Additional treatments	
Chemotherapy	6 (15.0%)
Radiotherapy	15 (37.5%)
Length of palliative care involvement (months)	2.4 (0.8–6.2)

Table 1: Baseline and procedural characteristics of patients. Data are presented as mean±SD, median (IQR) or number of participants (% of participants) (continued).

Parameter	Value
Procedural characteristics	
Conscious sedation	40 (100.0%)
Image intensifier use	24 (60.0%)
Stent crossing gastro-oesophageal junction	22 (55.0%)
Tumour location	
Middle third	15 (37.5%)
Lower third	25 (62.5%)
Stricture length (cm)	5.4±2.2
Stent type	
EndoMAXX	22 (55.0%)
Niti-S covered	18 (45.0%)
Stent length	
100mm	17 (42.5%)
120mm	16 (40.0%)
150mm	7 (17.5%)
Stent diameter	
18mm	31 (77.5%)
24mm	9 (22.5%)
Outcome	
Length of hospital admission following stent insertion (days)	1 (0–2)
Complications	17 (42.5%)
Pain	7 (17.5%)
Reflux	4 (10.0%)
Bleeding	2 (5.0%)
Stent migration	4 (10.0%)
Further gastroscopy performed following stent insertion	16 (40.0%)
Time from diagnosis to stent insertion (months)	1.5 (0.5–7.6)
Time from diagnosis to death (months)	7.8 (3.3–13.3)
Time from stent insertion to death (months)	2.8 (1.5–6.3)

Table 2: Baseline and one-month post-treatment symptomology and quality of life (QOL) scores. Data are presented as mean±SD.

Parameter	Baseline	Post-treatment	Change	*P* value
EORTC QLQ-C30				
Global health status				
Quality of life	34.6±22.6	45.5±26.9	+10.9±27.4	0.01
Functional scales				
Physical functioning	56.8±28.9	55.8±29.9	-1.0±28.9	0.83
Role functioning	49.2±35.8	49.2±34.8	+0.0±31.4	>0.99
Emotional functioning	64.8±26.0	66.9±29.9	+2.1±28.4	0.51
Cognitive functioning	64.2±32.8	66.3±29.6	+2.1±26.7	0.63
Social functioning	50.4±35.7	54.6±36.8	+4.2±40.3	0.51
Symptom scales and items				
Fatigue	66.7±27.3	61.4±31.7	-5.3±19.5	0.09
Nausea and vomiting	42.5±28.0	29.2±31.3	-13.3±31.8	0.01
Pain	37.9±32.5	37.1±33.0	-0.8±28.2	0.85
Dyspnoea	30.8±33.2	32.5±32.0	+1.6±35.0	0.64
Insomnia	47.5±36.9	40.8±38.1	-6.7±36.4	0.24
Appetite loss	72.5±34.5	56.7±40.1	-15.8±44.6	0.03
Constipation	47.0±35.6	40.4±38.9	-6.7±37.4	0.31
Diarrhoea	12.5±25.8	6.8±19.0	-5.7±30.1	0.20
Financial difficulties	32.5±35.8	26.5±32.6	-6.0±32.2	0.34
EORTC QLQ-OES 18				
Symptom scales and items				
Dysphagia	65.8±27.6	31.1±18.5	-34.7±34.8	<0.001
Trouble eating	68.3±23.8	39.5±25.9	-28.8±27.5	<0.001
Reflux	36.3±37.0	34.6±27.6	-1.7±32.2	0.70
Oesophageal pain	33.1±30.1	24.2±20.4	-8.9±25.6	0.03
Trouble swallowing saliva	47.0±36.4	19.2±31.9	-27.8±48.5	<0.001
Choking	34.2±37.1	12.8±22.4	-21.4±37.5	<0.001
Dry mouth	50.4±38.9	25.6±28.1	-24.8±37.7	<0.001
Altered taste	35.8±38.8	32.5±35.4	-3.4±40.8	0.76
Cough	35.8±37.3	28.2±32.0	-7.6±41.2	0.19
Trouble talking	21.7±31.6	13.7±22.6	-8.0±38.3	0.16

Figure 1: Baseline and one-month post-treatment global quality of life and dysphagia scores. Each point represents the score of an individual patient. Bars represent the mean score, and error bars represent the standard deviation.

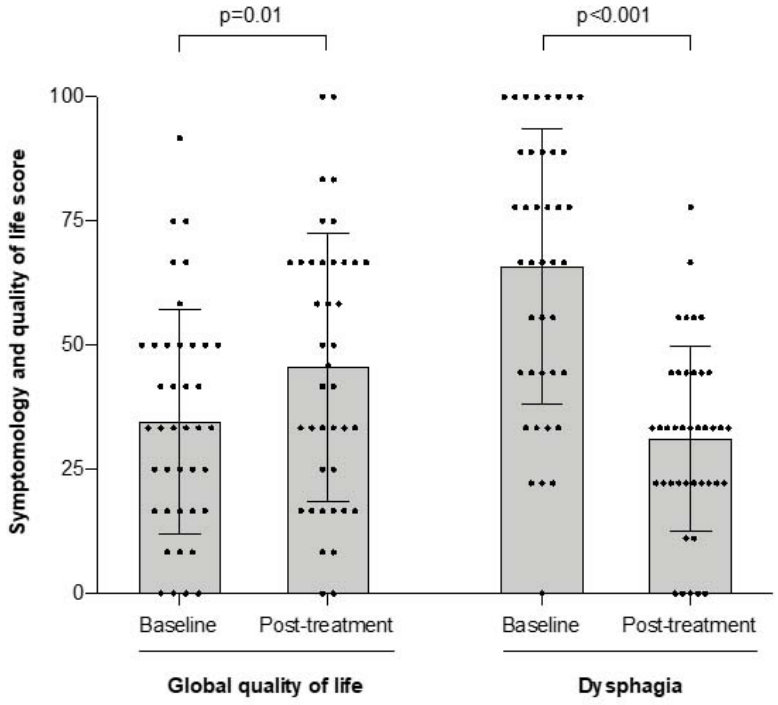
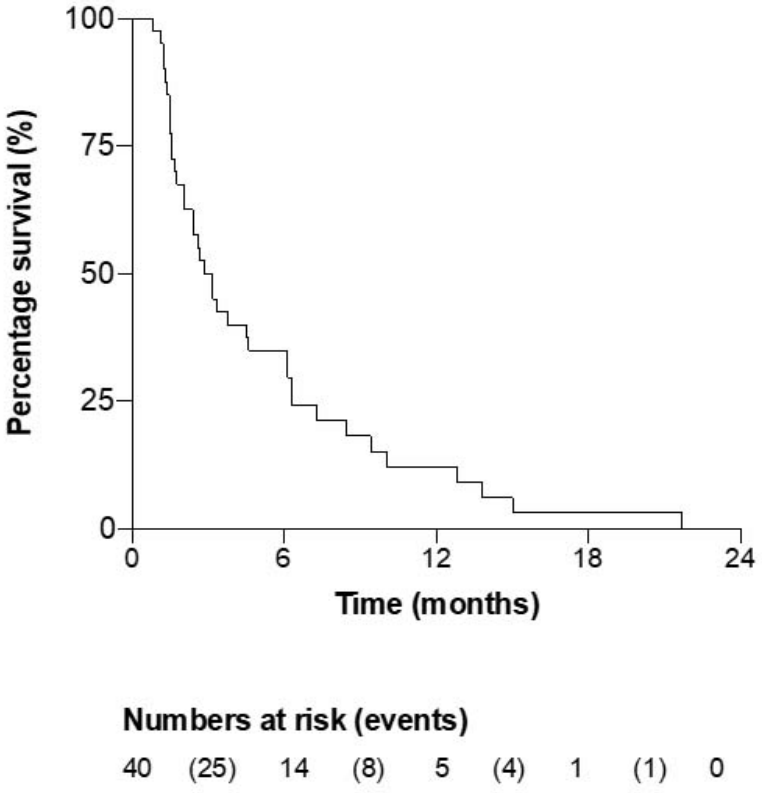


Figure 2: Kaplan–Meier survival curve following initial diagnosis of oesophageal cancer (excludes death prior to 30 days).



further medicalisation. Other than initial poorer overall physical status, there are no predictive features to indicate which patients may benefit the most from stenting.

A similar paper from an Indian cohort using a different brand of SEMS noted similar findings, but the paper also recorded significant improvements in fatigue, insomnia, constipation and financial strain[15] The latter may be in part explained by the New Zealand medical system, whereby patients are covered by fully subsidised national healthcare and are therefore not financially impacted by having to pay for endoscopy, stenting and supplementary medical care. Of note, stenting is thought to be cost effective.[17]

Another prospective study in malignant but not palliative dysphagia from America that only included patients requiring stenting of the distal third of the oesophagus or the gastroesophageal junction (GOJ) also noted improvements in dysphagia and overall quality of life.[28] They noted significant reflux in the first two weeks and improvements thereafter, which was also our experience in the 55% of patients in our cohort in whom the stent crossed the GOJ. Four patients in our study had very severe reflux and had a repeat endoscopy for this reason. In the American cohort, patients had neoadjuvant chemotherapy, with a subsequent 63% stent migration rate, which corresponded to a pathological response in 85% of these patients.[28] Two out of the four cases of stent migration in our cohort also occurred in patients receiving chemotherapy or radiotherapy, highlighting the likelihood of this occurrence in these clinical situations.

Similar rates of adverse events were also noted in other studies, including a 21–39% reintervention rate for stent blockage, overgrowth or migration.[15,17,29] A cohort from the Netherlands using through-the-scope (TTS) placement noted adverse events in 63%.[30] Although we did note a similarly high rate of adverse events, there were no instances of aspiration, haemorrhage or perforation, as noted in 6/32 patients (19%) in the Dutch study. Unlike in our study, many of these studies performed pre-stent dilation,[15,18] which, in a malignant stricture, poses large risks in itself.[31] This study included use of stents containing nitinol, known for improved conformability and a smaller profile compared to earlier woven stainless steel stents described in some of the previous studies.[13,29] Without appropriately designed research, we cannot draw conclusions about whether this may have improved safety with less serious adverse events. Of the 13 deaths prior to one month, one patient died suddenly after 14 days of haematemesis, but it was not clear that this was stent related, and no post-mortem was undertaken; the other 12 were not thought to be stent related. Our overall adverse event rate of 43% is in keeping with other series[32–34] and should be used to both educate and consent patients to help manage expectations for this procedure.

This study illustrates the importance of patency of swallow on overall quality of life. Dysphagia is known to be an incredibly disabling symptom, and improvement of dysphagia (>50% improvement on EORTC QLQ-OES 18 scale) led to an overall improvement in quality of life, despite limited improvement in other important parameters. Interestingly, although there was no improvement in overall pain, there was a small and statistically significant improvement in oesophageal-specific pain (-9 points, p=0.03). Madhusudhan and colleagues noted initial worsening of pain post stent, with a gradual reduction to baseline levels, but similarly no overall improvement in scores.[15] This should remind clinicians of the limits of our endoscopic intervention, with the incredible multifactorial burden and stress of this diagnosis seen in these patients with ongoing high levels of not only physical pain, but also emotional, cognitive and social distress, which we must aim to address with additional supportive care measures.

The mean survival of only 2.8 months after stent insertion shown in this study suggests that any additional treatment needs to be given without delay. Waiting the estimated 4–6 weeks required for improvement in dysphagia with primary palliative radiotherapy[35] is wholly unsatisfactory. This poor prognosis is in keeping with other large series.[18,29,36] With a meaningful and rapid improvement in quality of life and short estimated life expectancy, it could be appropriate to argued for prompter referrals for palliative stenting. We were able to place all

the stents under conscious sedation, with 16 patients (40%) discharged as day-cases, suggesting expeditious referrals could feasibly be performed quickly. Furthermore, this study was the first to measure the additive palliative care involvement, which was accepted by 80% of patients for an average of 2.4 months. There was no significant impact on any quality-of-life factors with regard to its uptake or length of involvement.

Poorer overall ASA physical status classification, and coronary artery disease specifically, were associated with reduced quality of life scores, reflecting a poorer outcome in a cohort that (as could be expected) are co-morbid, physically frail and diminished. Standard palliative intent platinum-based chemotherapy may prolong overall survival by less than one month, with some additional improvement in quality of life, including dysphagia. These changes in quality of life may take some time to come into effect, and patients may opt to forgo this option given the known higher treatment-related toxicity.[37] In our study, only additional chemotherapy treatment was associated with reduction in dysphagia scores, whereas concomitant radiotherapy was not, confirming that the routine additive effect of radiation is minimal once a stent is sited.[38] We feel that very frail and co-morbid patients with a high ASA score in particular should be carefully discussed, informed and consented of the likelihood of adverse events that may also require repeat endoscopy, in the context of possible very short life expectancy and a lesser improvement of overall quality of life.

Strengths of this paper include use of detailed validated questionnaires including the disease-specific oesophageal cancer (OES-18) score. The prospective nature allowed for complete and accurate data collection.

The results of this paper must be interpreted in the context of some important limitations. Final analysis of these data excludes 13 patients who died prior to 30-day follow-up, which may lead to possible bias.

Most notably, potential factors that may confound emotional and psychosocial outcomes, such as social support networks, health literacy, access to healthcare and financial reserves, were not collected. Additional therapies, such as brachytherapy, are not widely available in our centre and therefore additive effects of these interventions that may be beneficial were not able to be assessed.[18,39] It was difficult to discern causality with some of the adverse events noted, which may have been related to disease progression as opposed to the stent intervention.

In conclusion, despite a considerable proportion of patients developing stent-related adverse events, there is significant improvement of overall quality of life and dysphagia in patients who survive to one-month post oesophageal stent insertion for malignant, palliative dysphagia. Multiple psychosocial facets are not improved with this intervention.

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Appendix

Appendix Table 1: Linear regression analysis of predictors of change in global quality of life and dysphagia scores.

	Univariate linear regression		Multiple linear regression	
	Standardised coefficient	***P* value**	**Standardised coefficient**	***P* value**
Change in global quality of life score				
Age (years)	-0.131	0.42	-	-
Male sex	-0.079	0.63	-	-
Ethnicity				
New Zealand European	-0.014	0.93	-	-
Māori	-0.107	0.51	-	-
Other ethnicity	0.124	0.45	-	-
ASA physical status classification grade	-0.320	0.04	-0.381	0.002
Body mass index (kg/m^2)	0.180	0.27	-	-
Coronary artery disease	-0.247	0.12	-0.311	0.04
Chronic obstructive respiratory disease	-0.153	0.35	-	-
Diabetes mellitus	-0.015	0.93	-	-
Hypertension	-0.143	0.38	-	-
Current smoker	-0.067	0.68	-	-
Previous gastroscopy prior to diagnosis	-0.084	0.61	-	-
Anti-reflux medication dose (mg)	-0.201	0.22	-	-
Adenocarcinoma versus squamous cell carcinoma histology type	0.128	0.44	-	-
Additional chemotherapy	0.048	0.77	-	-
Additional radiotherapy	-0.146	0.37	-	-
Middle versus lower third tumour location	0.005	0.24	-	-
Stricture length (cm)	-0.030	0.88	-	-
EndoMAXX versus Niti-S covered stent type	-0.052	0.75	-	-
Length of palliative care involvement (months)	-0.136	0.42	-	-

Appendix Table 1: Linear regression analysis of predictors of change in global quality of life and dysphagia scores (continued).

	Univariate linear regression		Multiple linear regression	
	Standardised coefficient	***P* value**	**Standardised coefficient**	***P* value**
Change in dysphagia score				
Age (years)	0.095	0.56	-	-
Male sex	0.120	0.46	-	-
Ethnicity				
New Zealand European	0.078	0.63	-	-
Māori	0.094	0.56	-	-
Other ethnicity	-0.188	0.25	-	-
ASA physical status classification grade	0.267	0.10	0.199	0.18
Body mass index (kg/m^2)	-0.140	0.39	-	-
Coronary artery disease	0.039	0.81	-	-
Chronic obstructive respiratory disease	-0.140	0.39	-	-
Diabetes mellitus	0.057	0.73	-	-
Hypertension	0.174	0.28	-	-
Current smoker	-0.032	0.85	-	-
Previous gastroscopy prior to diagnosis	-0.027	0.87	-	-
Anti-reflux medication dose (mg)	-0.125	0.44	-	-
Adenocarcinoma versus squamous cell carcinoma histology type	-0.234	0.16	-	-
Additional chemotherapy	-0.429	0.006	-0.368	0.02
Additional radiotherapy	0.125	0.44	-	-
Middle versus lower third tumour location	0.251	0.14	0.121	0.43
Stricture length (cm)	0.236	0.15	-	-
EndoMAXX versus Niti-S covered stent type	0.109	0.52	-	-
Length of palliative care involvement (months)	-0.0234	0.89	-	-

Competing interests:
Nil.
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REFERENCES

1. Ferlay J, Colombet M, Soerjomataram I, Mathers C, Parkin DM, Piñeros M, et al. Estimating the global cancer incidence and mortality in 2018: GLOBOCAN sources and methods. Vol. 144, International Journal of Cancer. Wiley-Liss Inc.; 2019. p. 1941–53.
2. Lepage C, Rachet B, Jooste V, Faivre J, Coleman MP. Continuing rapid increase in esophageal adenocarcinoma in England and Wales. Am J Gastroenterol [Internet]. 2008 Nov [cited 2020 Sep 10];103(11):2694-9. Available from: https://pubmed.ncbi.nlm.nih.gov/18853967/
3. Pennathur A, Gibson MK, Jobe BA, Luketich JD. Oesophageal carcinoma. In: The Lancet. Lancet Publishing Group; 2013. p. 400–12.
4. Stavrou EP, McElroy HJ, Baker DF, Smith G, Bishop JF. Adenocarcinoma of the oesophagus: incidence and survival rates in New South Wales, 1972–2005. Med J Aust [Internet]. 2009 Sep 21 [cited 2020 Sep 10];191(6):310–4. Available from: https://onlinelibrary.wiley.com/doi/abs/10.5694/j.1326-5377.2009.tb02813.x
5. Cancer: Historical summary 1948–2017 | Ministry of Health NZ [Internet]. [cited 2021 May 15]. Available from: https://www.health.govt.nz/publication/cancer-historical-summary-1948-2017
6. Enzinger PC, Mayer RJ. Esophageal Cancer [Internet]. Vol. 349, New England Journal of Medicine. Massachusetts Medical Society ; 2003 [cited 2020 Sep 10]. p. 2241–52. Available from: http://www.nejm.org/doi/abs/10.1056/NEJMra035010
7. Tanaka T, Fujita H, Matono S, Nagano T, Nishimura K, Murata K, et al. Outcomes of multimodality therapy for stage IVB esophageal cancer with distant organ metastasis (M1-Org). Dis Esophagus [Internet]. 2010 Nov 1 [cited 2020 Sep 10];23(8):646-51. Available from: https://

academic.oup.com/dote/article-lookup/doi/10.1111/j.1442-2050.2010.01069.x

8. Nassri A, Zhu H, Muftah M, Ramzan Z. Epidemiology and Survival of Esophageal Cancer Patients in an American Cohort. Cureus [Internet]. 2018 Apr 19 [cited 2020 Sep 10];10(4). Available from: /pmc/articles/PMC6007500/?report=abstract
9. Revels SL, Morris AM, Reddy RM, Akateh C, Wong SL. Racial disparities in esophageal cancer outcomes. In: Annals of Surgical Oncology [Internet]. Springer; 2013 [cited 2020 Sep 10]. p. 1136–41. Available from: https://link.springer.com/article/10.1245/s10434-012-2807-3
10. Soeberg M, Blakely T, Sarfati D, Tobias M, Costilla R, Carter K, Atkinson J. 2012. Cancer Trends: Trends in cancer survival by ethnic and socioeconomic group, New Zealand 1991–2004. Wellington: University of Otago and Ministry of Health.
11. Diamantis G, Scarpa M, Bocus P, Realdon S, Castoro C, Ancona E, et al. Quality of life in patients with esophageal stenting for the palliation of malignant dysphagia. World J Gastroenterol [Internet]. 2011 Jan 14 [cited 2020 Sep 10];17(2):144-50.
12. Christie NA, Patel AN, Landreneau RJ. Esophageal palliation - Photodynamic therapy/stents/brachytherapy [Internet]. Vol. 85, Surgical Clinics of North America. Elsevier; 2005 [cited 2020 Sep 10]. p. 569–82. Available from: http://www.surgical.theclinics.com/article/S0039610905000265/fulltext
13. Yakoub D, Fahmy R, Athanasiou T, Alijani A, Rao C, Darzi A, et al. Evidence-based choice of esophageal stent for the palliative management of malignant dysphagia. World J Surg [Internet]. 2008 Sep 3 [cited 2020 Sep 10];32(9):1996-2009. Available from: https://link.springer.com/article/10.1007/s00268-008-9654-1
14. Abdelshafy M, Omar MA, Abdel Bary M, Wahaman MM, Bakheet RA elaal. Self-expandable metal stent for palliation of malignant dysphagia & quality of life improvement in advanced cancer esophagus: Upper Egypt experience. J Egypt Soc Cardio-Thoracic Surg. 2017 Sep 1;25(3):262-9.
15. Madhusudhan C, Saluja SS, Pal S, Ahuja V, Saran P, Dash NR, et al. Palliative stenting for relief of dysphagia in patients with inoperable esophageal cancer: impact on quality of life. Dis Esophagus [Internet]. 2009 Jun 1 [cited 2020 Sep 10];22(4):331-6. Available from: https://academic.oup.com/dote/article-lookup/doi/10.1111/j.1442-2050.2008.00906.x
16. Kishore Maroju N, Kate V, Ananthakrishnan N. Improvement in dysphagia and quality of life with self-expanding metallic stents in malignant esophageal strictures. 2006.
17. Xinopoulos D, Dimitroulopoulos D, Moschandrea I, Skordilis P, Bazinis A, Kontis M, et al. Natural course of inoperable esophageal cancer treated with metallic expandable stents: Quality of life and cost-effectiveness analysis. J Gastroenterol Hepatol [Internet]. 2004 [cited 2020 Nov 8];19(12):1397-402. Available from: https://pubmed.ncbi.nlm.nih.gov/15610314/
18. Homs MYV, Steyerberg EW, Eijkenboom WMH, Tilanus HW, Stalpers LJA, Bartelsman JFWM, et al. Single-dose brachytherapy versus metal stent placement for the palliation of dysphagia from oesophageal cancer: Multicentre randomised trial. Lancet. 2004;364(9444).
19. Dallal HJ, Smith GD, Grieve DC, Ghosh S, Penman ID, Palmer KR. A randomized trial of thermal ablative therapy versus expandable metal stents in the palliative treatment of patients with esophageal carcinoma. Gastrointest Endosc. 2001;54(5).
20. Carrera PM, Kantarjian HM, Blinder VS. The financial burden and distress of patients with cancer: Understanding and stepping-up action on the financial toxicity of cancer treatment. CA Cancer J Clin. 2018;68(2).
21. Medeiros VS, Martins BC, Lenz L, Ribeiro MSI, de Paulo GA, Lima MS, et al. Adverse events of self-expandable esophageal metallic stents in patients with long-term survival from advanced malignant disease. Gastrointest Endosc [Internet]. 2017 Aug 1 [cited 2020 Sep 10];86(2):299-306. Available from: https://pubmed.ncbi.nlm.nih.gov/28024985/
22. Knyrim K, Wagner HJ, Bethge N, Keymling M, Vakil N. A Controlled Trial of an Expansile Metal Stent for Palliation of Esophageal Obstruction Due to Inoperable Cancer. N Engl J Med [Internet]. 1993 Oct 28 [cited 2020 Sep 10];329(18):1302-7. Available from: https://pubmed.ncbi.nlm.nih.gov/7692297/
23. Lin SY, Kerse N, McLean C, Moyes SA. Validation of quality of life and functional measures for older people for telephone administration. J Prim Health Care [Internet]. 2010 [cited 2021 May 17];2(1):35-42. Avail-

able from: https://pubmed.ncbi.nlm.nih.gov/20690401/

24. Blazeby JM, Conroy T, Hammerlid E, Fayers P, Sezer O, Koller M, et al. Clinical and psychometric validation of an EORTC questionnaire module, the EORTC QLQ-OES18, to assess quality of life in patients with oesophageal cancer. Eur J Cancer [Internet]. 2003 [cited 2020 Nov 4];39(10):1384-94. Available from: https://pubmed.ncbi.nlm.nih.gov/12826041/
25. Fayers P, Aaronson NK, Bjordal K, Groenvold M, Curran D, Bottomley A. EORTC QLQ-C30 Scoring Manual [Internet]. European Organisation for Research and Treatment of Cancer; 2001 [cited 2020 Sep 10]. Available from: https://abdn.pure.elsevier.com/en/publications/eortc-qlq-c30-scoring-manual-3rd-edition
26. Hussain Z, Diamantopoulos A, Krokidis M, Katsanos K. Double-layered covered stent for the treatment of malignant oesophageal obstructions: Systematic review and meta-analysis. World J Gastroenterol [Internet]. 2016 Sep 14 [cited 2020 Sep 10];22(34):7841-50. Available from: /pmc/articles/PMC5016384/?report=abstract
27. Doyle DJ, Garmon EH. American Society of Anesthesiologists Classification (ASA Class) [Internet]. StatPearls. StatPearls Publishing; 2018 [cited 2020 Nov 9]. Available from: http://www.ncbi.nlm.nih.gov/pubmed/28722969
28. Philips P, North DA, Scoggins C, Schlegel M, Martin RCG. Gastric-esophageal stenting for malignant dysphagia: Results of prospective clinical trial evaluation of long-term gastroesophageal reflux and quality of life-related symptoms. J Am Coll Surg [Internet]. 2015 Jul 1 [cited 2020 Nov 5];221(1):165-73. Available from: https://pubmed.ncbi.nlm.nih.gov/26095567/
29. Battersby NJ, Bonney GK, Subar D, Talbot L, Decadt B, Lynch N. Outcomes following oesophageal stent insertion for palliation of malignant strictures: A large single centre series. J Surg Oncol. 2012;105(1).
30. Vermeulen BD, Reijm AN, van der Bogt RD, van Hooft JE, Spaander MCW, Siersema PD. Through-the-scope placement of a fully covered metal stent for palliation of malignant dysphagia: a prospective cohort study (with video). Gastrointest Endosc [Internet]. 2019 Dec 1 [cited 2020 Nov 9];90(6):972-9. Available from: https://pubmed.ncbi.nlm.nih.gov/31265819/
31. Quine MA, Bell GD, McCloy RF, Matthews HR. Prospective audit of perforation rates following upper gastrointestinal endoscopy in two regions of England. Br J Surg. 1995;82(4).
32. Walter D, Van Den Berg MW, Van Hooft JE, Boot H, Scheffer RCH, Vleggaar FP, et al. A new fully covered metal stent with anti-migration features for the treatment of malignant dysphagia. Endoscopy [Internet]. 2014 Aug 6 [cited 2020 Nov 9];46(12):1101-5. Available from: https://pubmed.ncbi.nlm.nih.gov/25268307/
33. Van Heel NCM, Haringsma J, Boot H, Cats A, Vanhoutvin SALW, Kuipers EJ. Comparison of 2 expandable stents for malignant esophageal disease: A randomized controlled trial. Gastrointest Endosc [Internet]. 2012 Jul [cited 2020 Nov 9];76(1):52-8. Available from: https://pubmed.ncbi.nlm.nih.gov/22726466/
34. Didden P, Reijm AN, Erler NS, Wolters LMM, Tang TJ, Ter Borg PCJ, et al. Fully vs. partially covered selfexpandable metal stent for palliation of malignant esophageal strictures: A randomized trial (the COPAC study). Endoscopy [Internet]. 2018 [cited 2020 Nov 9];50(10):961-71. Available from: https://pubmed.ncbi.nlm.nih.gov/29895072/
35. Shin JH, Song HY, Kim JH, Kim SB, Lee GH, Park S Il, et al. Comparison of temporary and permanent stent placement with concurrent radiation therapy in patients with esophageal carcinoma. J Vasc Interv Radiol. 2005;16(1).
36. Burstow M, Kelly T, Panchani S, Khan IM, Meek D, Memon B, et al. Outcome of palliative esophageal stenting for malignant dysphagia: A retrospective analysis. Dis Esophagus. 2009;22(6).
37. Janmaat VT, Steyerberg EW, van der Gaast A, Mathijssen RHJ, Bruno MJ, Peppelenbosch MP, et al. Palliative chemotherapy and targeted therapies for esophageal and gastroesophageal junction cancer [Internet]. Vol. 2017, Cochrane Database of Systematic Reviews. John Wiley and Sons Ltd; 2017 [cited 2021 May 15].
38. Adamson D, Byrne A, Porter C, Blazeby J, Griffiths G, Nelson A, et al. Palliative radiotherapy after oesophageal cancer stenting (ROCS): a multicentre, open-label, phase 3 randomised controlled trial. Lancet Gastroenterol Hepatol [Internet]. 2021 Apr 1 [cited 2021 May 15];6(4):292–303.
39. Amdal CD, Jacobsen AB, Sandstad B, Warloe T, Bjordal K. Palliative brachytherapy with or without primary stent placement in patients with oesophageal cancer, a randomised phase III trial. Radiother Oncol. 2013;107(3).

Testing for dihydropyrimidine dehydrogenase deficiency in New Zealand to improve the safe use of 5-fluorouracil and capecitabine in cancer patients

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ABSTRACT

Dihydropyrimidine dehydrogenase deficiency is a rare inherited disorder. Approximately 3% of people of European ancestry are likely to have a partial deficiency in this enzyme. These individuals are typically asymptomatic until exposed to 5-fluorouracil (5-FU) or capecitabine (which forms 5-FU) for treatment of gastrointestinal or breast cancer. These individuals are then at considerably increased risk of severe to life-threatening adverse events. There are four well established risk variants within the *DPYD* gene that encodes dihydropyrimidine dehydrogenase. Although consensus guidelines for genotype-guided dosing of 5-FU and capecitabine have existed for a number of years, the implementation of this type of personalised medicine has not been widely adopted. This viewpoint covers the current state of knowledge about both genotype and phenotype testing, as well as the reported cost-savings and clinical effectiveness of pre-screening patients followed by dose-adjustment. Recent recommendations by agencies and professional societies, both in Europe and the USA, highlight the need for New Zealand oncologists to begin an informed discussion about whether it is now an appropriate time to advocate for routine access to testing for this enzyme deficiency in New Zealand cancer patients.

Intravenous 5-fluorouracil (5-FU) and oral capecitabine (which forms 5-FU) are commonly used in New Zealand to treat a range of solid tumour types, particularly gastrointestinal and breast cancers. Routine use of these agents carries a risk of treatment-limiting toxicities, including diarrhoea, mucositis, myelosuppression, Hand-Foot syndrome and sometimes cardiotoxicity. Overall, severe (Common Terminology Criteria for Adverse Events grade 3 or greater) toxicities are observed in up to one third of individuals and are fatal for approximately 1% of patients.[1–4]

5-FU is extensively (>80%) eliminated from the body by the enzyme dihydropyrimidine dehydrogenase (DPD), and decreased activity of this enzyme can result in severe to life-threatening toxicity. Inherited differences in DPD activity are well characterised as a cause of hereditary thymine-uracilemia.[5] This autosomal codominant inherited disorder is rare, with around 0.2% of people having complete deficiency (homozygotes) and about 3% of people of European ancestry have a partial deficiency (heterozygotes). These individuals are typically asymptomatic until challenged with 5-FU or capecitabine.

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DPYD genotyping

It is well established that loss of function (LoF) polymorphisms in the *DPYD* gene that encodes the DPD enzyme have high sensitivity for prediction of risk of 5-FU/capecitabine-induced severe to life-threatening toxicity.[3,6–14] These LoF variants (Table 1) have high specificity (~80–100%) for prediction of severe toxicity risk. However, due to scarcity of these variants (~3% of a population), variant testing has poor sensitivity (<25%) for severe toxicity. This poor sensitivity may be due to either the presence of other rare (private) mutations in *DPYD* or low expression of the enzyme due to epigenetic mechanisms. This low sensitivity has led to some reluctance from clinicians to incorporate routine pre-screening of patients prior to use of 5-FU/capecitabine-containing regimens.

Evidence based *DPYD* genotype-based dosage adjustment guidelines have been extensively disseminated within the pharmacogenomics community (Table 1).[15–17]

Severe toxicity due to this enzyme deficiency often occurs in the first cycle of treatment. It is now clear from large prospective clinical trials that pre-screening patients for these *DPYD*^{LoF} variants, combined with recommended dose adjustments prior to first dose, improves the therapeutic index of 5-FU/capecitabine.[3] Indeed that multicentre study of 1,103 evaluable patients found that genotype-guided dosing (compared to an historical cohort) decreased the relative risk (RR) of severe fluoropyrimidine-related toxicity. Patients who were *DPYD*13* carriers and given a 50% dose decrease experienced no toxicity compared with RR of 4.30 (95% CI 2.10–8.80) in the historical cohort. In *DPYD*2A* carriers who received 50% dose decrease, there was significant decrease in RR from 2.87 (2.14–3.86) to 1.31 (0.63–2.73). Of note, the genotype-guided dose decrease was increased at subsequent cycles in 13% of the *DPYD* variant carriers, and this was not tolerated in most of these individuals. Other studies have also demonstrated that *DPYD*2A* carriers given a 50% dose reduction had a significant decrease in grade ≥3 toxicity from 73% (95% CI 58% to 85%) in historical controls to 28% (10% to 53%).[19] Similar decreases in toxicity risk in *DPYD*2A* carriers from 77% to 18% following genotype-guided dose adjustment have also been reported.[20]

Importantly genotype-guided dose adjustment produces similar plasma concentrations of 5-FU as observed in wildtype individuals receiving a standard dosage.[3,19] Therefore, genotype-guided dosage adjustment is not expected to alter clinical effectiveness. This has been formally tested in one study,[20] which found similar median overall and progression-free survival between genotype-guided dosing in *DPYD*2A* carriers and wild-type (matched pairs). There was no difference in hazard ratio (HR) for overall survival (HR 0.82, 95%CI 0.47–1.43; p=0.47) or progression free-survival (HR 0.83, 95%CI 0.47-1.5, p=0.83), confirming that genotype-guided dosing is unlikely to alter clinical effectiveness.

Cost effectiveness

The cost effectiveness of *DPYD* genotyping to prevent severe 5-FU/capecitabine toxicity is also well established.[10] A recent study (n=571, Italian patients) showed that the cost of management of the adverse effects of 5-FU/capecitabine is substantially higher in patients positive for any of the four *DPYD*^{LoF} variant alleles compared with those wildtype for these variants (€3,712 vs €1,010).[21] Moreover, these *DPYD*^{LoF} patients also had worse survival, and this results in decreased quality-adjusted life years (QALY) (3.62±0.70 years vs 4.18±0.61 years). Substantial evidence has also reported that a genotype-guided dosage approach is cost effective because it decreases the costs of prolonged hospitalisation of toxicity cases. Pre-screening patients (n=2,038) for a single *DPYD* variant (**2A*), followed by 50% dose reduction for carriers of this variant, decreased treatment costs from €2,817 to €2,772.[19] A similar pre-emptive genotype-guided dose reduction study in 2,617 Canadian patients also indicated that this approach is suitable, based on the assumption that *DPYD*2A* carriers have an average hospitalisation of 15 days.[22] Of note, we recently reported in a smaller study that the median length of stay for New Zealand patients with severe 5-FU/capecitabine induced toxicity was seven days (range 2–17 days).[23] Finally, a prospective study that included all four *DPYD*^{LoF} variants in the genetic screen prior to dosage adjustment

Table 1: The key loss of function *DPYD* gene variants that should be assessed in patients prior to treatment.

Common name	Nucleotide variant, amino acid change, ID number		Enzyme activity (relative to normal)	[b]Minor allele frequency (global)	Recommended dosage adjustment for heterozygote carriers (partial deficiency[c])
***2A**	c.1905+1G>A **exon 14 skipping** rs3918290	**Non-functional** protein missing aa residues 581-635.	None	0.0043	50%
***13**	c.1679T>G **I560S** rs55886062	Missense mutation affects the cofactor binding and **substantially decreases activity.**	None	0.0006	50%
***9B**	c.2846 A>T **D949V** rs67376798	SNP affects the electron transfer mechanism, which is key for activity. **Low function protein.**	Decreased	0.0052	>25%
Hap-B3[a]	c.1129-5923C>G **Intronic** rs75017182	Intronic variant which affects pre-mRNA splicing. Truncated **non-functional protein.**	Decreased	0.0048	>25%

[a]The haplotype includes c.1236G>A & c.483+18G>A (rs56038477 & rs56276561, with MAF=0.0181 & 0.0153 respectively). [b]Little is known about the minor allele frequency of these variants in people of Māori or Pacific Island ancestry. Individuals of East Asian ancestry have very low prevalence of HapB3 (MAF>0.0000) and *2A (MAF=0.0000) compared with Europeans or South Asians (MAF=0.000 and 0.0034, respectively). There is an additional loss of function variant observed in people of African ancestry (rs115232898, Y186C, with MAF=0.0183). [c]Dosages should not be increased to standard dosage at subsequent cycles based on treatment tolerance. 5-FU and capecitabine use is *contraindicated* in individuals who are homozygous loss of function variant for these alleles (complete deficiency). However, recent studies have demonstrated that extremely low doses (<1% of a standard dose) achieve suitable therapeutic 5-FU plasma concentrations and are safe.[18] Individuals who are compound heterozygote (carrier of more than one of these variant alleles) should be considered as having a complete enzyme deficiency.

demonstrated a net healthcare cost-saving of €51, confirming previous simulation studies of cost–benefit for prevention of a single adverse event (neutropenia).[24,25]

Phenotyping for dihydropyrimidine dehydrogenase enzyme deficiency

Although *DPYD*^{LoF} genotyping clearly is of considerable value, the poor sensitivity of this test means that the risk of severe 5-FU/capecitabine toxicity in most patients is still poorly predicted.[26] Screening for enzyme activity has been proposed as an additional method of detecting at-risk individuals. Phenotypic assays have been developed to assess the degradation rate of 5-FU in leucocytes, plasma uracil concentrations, or challenge dosing with uracil or thymine.[23,27–29] A prospective study of a thymine challenge dose for detecting patients at risk of severe toxicity is currently underway across New Zealand (ACTRN12617001109392). Preliminary data suggest that this approach may be more sensitive than endogenous uracil levels.[27] However, there is currently a lack of prospective validation confirming that dose adjustments based upon endogenous uracil levels lead to a decreased incidence of severe toxicity and maintain effectiveness, although a study to investigate this has started (NCT04194957).

Pharmacokinetically guided dose-individualisation

Data from thirteen clinical studies have shown that therapeutic drug monitoring (TDM) of infusional 5-FU improves both safety and clinical effectiveness (reviewed in Beumer et al[30]). The International Association of Therapeutic Drug Monitoring and Clinical Toxicology recommend that the therapeutic exposure range for a 46 h infusion schedule of 5-FU is an area under the curve (AUC) between 20–30 mg.h/L.[30] This approach has highlighted that, although approximately 20% of patients have elevated AUC (indicative of DPD enzyme deficiency), many patients receiving standard dosages do not achieve target AUC and may be underdosed.[31,32] One concern with the TDM-based approach is that patients are initially exposed to a full dose (prior to dosage adjustment), and because severe fluoropyrimidine-related toxicity will occur rapidly in DPD-deficient patients, pharmacokinetically guided dose-individualisation cannot prevent this risk. Notably, TDM of the 5-FU concentrations achieved after oral capecitabine dosing has not been established. Moreover, the precision of pharmacokinetically guided dosage adjustment for capecitabine may be limited by the available tablet sizes (150 mg and 500 mg).[33] Both the European Medicines Agency (EMA) and the Medicines and Healthcare products Regulatory Agency (MHRA) recommend TDM for infusional 5-FU.

Renal impairment

Whilst inherited variation can account for some of the variability in plasma concentrations of 5-FU and risk of excessive toxicity other factors, such as co-medications (eg, sorivudine) and renal impairment, also play a role. Although urinary excretion is a minor pathway for 5-FU elimination, a number of studies have reported a significant association between creatinine clearance and 5-FU related toxicity.[23,34–37] Following dosing with either infusional 5-FU or oral capecitabine, the incidence of severe to life-threatening toxicity is higher in patients with moderate renal impairment (30–50 mL/min creatinine clearance) than patients with normal function (>80 mL/min).[35] The mechanism by which renal impairment increases risk of toxicity is unclear since this does not substantially impact the pharmacokinetics of capecitabine and its metabolites, including 5-FU.[38] The relationship between poor renal function and infusional 5-FU pharmacokinetics is not well studied, but there is little effect on 5-FU plasma AUC.[39] For patients with moderate renal impairment (30–50 mL/min), capecitabine dosage adjustment is recommended, and it is contraindicated in patients with poor renal function (<30 mL/min).[35,40] In contrast, no dosage adjustments are recommended in patients with moderate renal impairment treated with infusional 5-FU, even though they have the same increased risk of toxicity as those treated with capecitabine.

Other risk factors

Older age, female sex and worse performance status have been reported as possible risk factors. To some extent, age and performance status may be covariates of low renal function. Importantly, males have 26% higher total body clearance of 5-FU.[41] This could explain the significantly higher AUC

observed in females compared to males and hence the increased risk of supratherapeutic concentrations following standard dosages.[41]

Regulatory agency and oncology society recommendations

Despite the ~25% sensitivity of *DPYD* testing for prediction of which patients are at risk of severe toxicity (due in part to other risk factors or rare *DPYD* variants), pre-screening patients prior to fluoropyrimidine treatment for four *DPYD*^{LoF} variants (**2A*, **13*, **9B* and *HapB3*) has recently been recommended by the EMA.[42] The UK MHRA have followed the same recommendations.[43] The UK Chemotherapy Board have also published guidelines on their website.[44] French, German and Belgian jurisdictions have provided consensus documents regarding testing,[45–47] and the province of Quebec in Canada has implemented this practice.[22] Most recently, the American Society of Clinical Oncologists has provided information regarding targeted *DPYD* testing.[48] Although the Cancer Institute of New South Wales eviQ resource[49] provides information about testing for *DPYD*, this test is not reimbursed in Australia.

In addition, the EMA recommend endogenous plasma uracil testing prior to initiating a 5-FU-containing treatment regimen.[42] In the Netherlands, when it is not possible to undertake genotyping, DPD enzyme activity testing in leucocytes has been adopted into clinical practice.[17]

Of note, uridine triacetate has FDA approval for treatment of unintentional overdose of 5-FU/capecitabine. But this antidote must be administered within 96 h of overdose, and the effectiveness in patients with early onset severe-adverse reactions is less clear.[50]

New Zealand perspective

As part of the ongoing clinical trial (ACTRN12617001109392), genotyping for the four key *DPYD*^{LoF} variants is currently being undertaken in New Zealand by an accredited facility (Grafton Clinical Genomics). The laboratory-based costs for this genotyping are relatively low and the turnaround time within the Auckland region for a clinical test is expected to be short (<1–2 days). In addition, a validated liquid chromatography tandem mass spectrometry (LCMS/MS)-based assay, which can be used to measure both plasma 5-FU levels for pharmacokinetically guided dose adjustment, as well endogenous uracil levels, is currently available at Canterbury Health Laboratories, Christchurch, New Zealand.[51]

To date, most of the studies regarding *DPYD*^{LoF} have focused on populations of primarily European ancestry. The minor allele frequencies of these alleles are much lower in individuals of East Asian ancestry compared with Europeans (Table 1), and a different prevalence of these genetic risk factors has also been reported for people of South Asian ancestry.[52] An additional LoF variant that associates with toxicity has been identified in people of African ancestry.[53] However, the prevalence of novel LoF variants in people of Māori or Pacific Island ancestry, and possible associations with toxicity risk, are not known.

The antidote (uridine triacetate) is a high-cost medicine and is not registered in New Zealand.

Summary

In New Zealand, there is currently no regulatory obligation to screen for dihydropyrimidine dehydrogenase deficiency prior to treatment with 5-FU or capecitabine. However, there is now substantial evidence that targeted genotyping for *DPYD*^{LoF} variants (**2A*, **13*, **9B* and *HapB3*) followed by dose adjustment is a cost-effective way to decrease severe toxicity whilst maintaining clinical effectiveness. We suggest that it is now an appropriate time for New Zealand oncologists to advocate for routine access to *DPYD* genotyping within their district health boards. Furthermore, for patients receiving continuous infusional 5-FU, access to TDM should also become part of routine clinical practice. We also highlight that moderate renal function appears to be an under-appreciated non-genetic risk factor. Finally, although some overseas jurisdictions have recommended using endogenous uracil levels for phenotyping for DPD deficiency, the prospective validation of this is currently lacking. Determination of whether prospective phenotyping with a challenge dose of thymine is an improvement on genotyping alone will be reported following the conclusion of our current clinical trial (ACTRN12617001109392).

Competing interests:
Nil.

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REFERENCES

1. Chionh F, Lau D, Yeung Y, et al. Oral versus intravenous fluoropyrimidines for colorectal cancer. Cochrane Database Syst Rev. 2017;7:CD008398.
2. Van Cutsem E, Twelves C, Cassidy J, et al. Oral capecitabine compared with intravenous fluorouracil plus leucovorin in patients with metastatic colorectal cancer: results of a large phase III study. Journal of Clinical Oncology. 2001;19:4097-106.
3. Henricks LM, Lunenburg C, de Man FM, et al. DPYD genotype-guided dose individualisation of fluoropyrimidine therapy in patients with cancer: a prospective safety analysis. Lancet Oncology. 2018;19:1459-67.
4. Hoff PM, Ansari R, Batist G, et al. Comparison of oral capecitabine versus intravenous fluorouracil plus leucovorin as first-line treatment in 605 patients with metastatic colorectal cancer: results of a randomized phase III study. Journal of Clinical Oncology. 2001;19:2282-92.
5. Tuchman M, Stoeckeler JS, Kiang DT, et al. Familial pyrimidinemia and pyrimidinuria associated with severe fluorouracil toxicity. New England Journal of Medicine. 1985;313:245-9.
6. Etienne-Grimaldi M-C, Boyer J-C, Beroud C, et al. New advances in DPYD genotype and risk of severe toxicity under capecitabine. PLOS ONE. 2017;12:e0175998.
7. Froehlich TK, Amstutz U, Aebi S, et al. Clinical importance of risk variants in the dihydropyrimidine dehydrogenase gene for the prediction of early-onset fluoropyrimidine toxicity. International journal of cancer. 2015;136:730-9.
8. Lee AM, Shi Q, Pavey E, et al. DPYD variants as predictors of 5-fluorouracil toxicity in adjuvant colon cancer treatment (NCCTG N0147). JNCI: Journal of the National Cancer Institute. 2014;106.
9. Loganayagam A, Arenas Hernandez M, Corrigan A, et al. Pharmacogenetic variants in the DPYD, TYMS, CDA and MTHFR genes are clinically significant predictors of fluoropyrimidine toxicity. British Journal of Cancer. 2013;108:2505-15.
10. Lunenburg C, Henricks LM, Guchelaar HJ, et al. Prospective DPYD genotyping to reduce the risk of fluoropyrimidine-induced severe toxicity: Ready for prime time. European Journal of Cancer. 2016;54:40-8.
11. Meulendijks D, Henricks LM, Sonke GS, et al. Clinical relevance of DPYD variants c. 1679T> G, c. 1236G> A/HapB3, and c. 1601G> A as predictors of severe fluoropyrimidine-associated toxicity: a systematic review and meta-analysis of individual patient data. The Lancet Oncology. 2015;16:1639-50.
12. Rosmarin D, Palles C, Church D, et al. Genetic markers of toxicity from

capecitabine and other fluorouracil-based regimens: investigation in the QUASAR2 study, systematic review, and meta-analysis. Journal of Clinical Oncology. 2014;32:1031-9.

13. Terrazzino S, Cargnin S, Del Re M, et al. DPYD IVS14+ 1G> A and 2846A> T genotyping for the prediction of severe fluoropyrimidine-related toxicity: a meta-analysis. Pharmacogenomics. 2013;14:1255-72.
14. Toffoli G, Giodini L, Buonadonna A, et al. Clinical validity of a DPYD-based pharmacogenetic test to predict severe toxicity to fluoropyrimidines. International Journal of Cancer. 2015;137:2971-80.
15. Amstutz U, Henricks LM, Offer SM, et al. Clinical Pharmacogenetics Implementation Consortium (CPIC) Guideline for Dihydropyrimidine Dehydrogenase Genotype and Fluoropyrimidine Dosing: 2017 Update. Clinical Pharmacology & Therapeutics. 2018;103:210-6.
16. Caudle KE, Thorn CF, Klein TE, et al. Clinical Pharmacogenetics Implementation Consortium guidelines for dihydropyrimidine dehydrogenase genotype and fluoropyrimidine dosing. Clinical Pharmacology & Therapeutics. 2013;94:640-5.
17. Lunenburg CATC, Van Der Wouden CH, Nijenhuis M, et al. Dutch Pharmacogenetics Working Group (DPWG) guideline for the gene–drug interaction of DPYD and fluoropyrimidines. European Journal of Human Genetics. 2020;28:508-17.
18. Henricks LM, Kienhuis E, De Man FM, et al. Treatment Algorithm for Homozygous or Compound Heterozygous DPYD Variant Allele Carriers With Low-Dose Capecitabine. JCO Precision Oncology. 2017:1-10.
19. Deenen MJ, Meulendijks D, Cats A, et al. Upfront Genotyping of DPYD*2A to Individualize Fluoropyrimidine Therapy: A Safety and Cost Analysis. Journal of Clinical Oncology. 2016;34:227-34.
20. Henricks LM, Van Merendonk LN, Meulendijks D, et al. Effectiveness and safety of reduced-dose fluoropyrimidine therapy in patients carrying the DPYD *2A variant: A matched pair analysis. International Journal of Cancer. 2019;144:2347-54.
21. Fragoulakis V, Roncato R, Fratte CD, et al. Estimating the Effectiveness of DPYD Genotyping in Italian Individuals Suffering from Cancer Based on the Cost of Chemotherapy-Induced Toxicity. The American Journal of Human Genetics. 2019;104:1158-68.
22. Jolivet C, Nassabein R, Soulières D, et al. Implementing DPYD * 2A Genotyping in Clinical Practice: The Quebec, Canada, Experience. The Oncologist. 2020.
23. Helsby NA, Duley J, Burns KE, et al. A case-control study to assess the ability of the thymine challenge test to predict patients with severe to life threatening fluoropyrimidine-induced gastrointestinal toxicity. British Journal of Clinical Pharmacology. 2020;86:155-64.
24. Henricks LM, Lunenburg CATC, De Man FM, et al. A cost analysis of upfront DPYD genotype–guided dose individualisation in fluoropyrimidine-based anticancer therapy. European Journal of Cancer. 2019;107:60-7.
25. Cortejoso L, García-González X, García MI, et al. Cost–effectiveness of screening for DPYD polymorphisms to prevent neutropenia in cancer patients treated with fluoropyrimidines. Pharmacogenomics. 2016;17:979-84.
26. Wigle TJ, Povitz BL, Medwid S, et al. Impact of pretreatment dihydropyrimidine dehydrogenase genotype-guided fluoropyrimidine dosing on chemotherapy associated adverse events. Clinical and Translational Science. 2021.
27. Burns KE, Chavani O, Jeong SH, et al. Comparison of a thymine challenge test and endogenous uracil-dihydrouracil levels for assessment of fluoropyrimidine toxicity risk. Cancer Chemotherapy and Pharmacology. accepted.
28. Meulendijks D, Henricks LM, Jacobs BAW, et al. Pretreatment serum uracil concentration as a predictor of severe and fatal fluoropyrimidine-associated toxicity. British Journal of Cancer. 2017;116:1415-24.
29. Pallet N, Hamdane S, Garinet S, et al. A comprehensive population-based study comparing the phenotype and genotype in a pretherapeutic screen of dihydropyrimidine dehydrogenase deficiency. British Journal of Cancer. 2020;123:811-8.
30. Beumer JH, Chu E, Allegra C, et al. Therapeutic Drug Monitoring in Oncology: International Association of Therapeutic Drug Monitoring and Clinical Toxicology Recommendations for 5-Fluorouracil Therapy. Clinical Pharmacology & Therapeutics. 2018;105:598-613.
31. Dolat M, Macaire P, Goirand

F, et al. Association of 5-FU Therapeutic Drug Monitoring to DPD Phenotype Assessment May Reduce 5-FU Under-Exposure. Pharmaceuticals. 2020;13:416.

32. Mindt S, Aida S, Merx K, et al. Therapeutic drug monitoring (TDM) of 5-fluorouracil (5-FU): new preanalytic aspects. Clinical Chemistry and Laboratory Medicine (CCLM). 2019;57:1012-6.
33. Ratain MJ. Dear Doctor: We Really Are Not Sure What Dose of Capecitabine You Should Prescribe for Your Patient. Journal of Clinical Oncology. 2002;20:1434-5.
34. Meulendijks D, van Hasselt JGC, Huitema ADR, et al. Renal function, body surface area, and age are associated with risk of early-onset fluoropyrimidine-associated toxicity in patients treated with capecitabine-based anticancer regimens in daily clinical care. European Journal of Cancer. 2016;54:120-30.
35. Cassidy J, Twelves C, Van Cutsem E, et al. First-line oral capecitabine therapy in metastatic colorectal cancer: a favorable safety profile compared with intravenous 5-fluorouracil/leucovorin. Annals of Oncology. 2002;13:566-75.
36. Makihara K, Mishima H, Azuma S, et al. Plasma concentrations of 5-FU and creatinine clearance as predictive markers for severe toxicities of capecitabine in patients with colorectal cancer. Journal of Clinical Oncology. 2013;31:428.
37. Meulendijks D, Cats A, Beijnen JH, Schellens JH. Improving safety of fluoropyrimidine chemotherapy by individualizing treatment based on dihydropyrimidine dehydrogenase activity–ready for clinical practice? Cancer treatment reviews. 2016;50:23-34.
38. Poole C, Gardiner J, Twelves C, et al. Effect of renal impairment on the pharmacokinetics and tolerability of capecitabine (Xeloda) in cancer patients. Cancer Chemotherapy and Pharmacology. 2002;49:225-34.
39. Fleming G, Schilsky R, Schumm L, et al. Phase I and pharmacokinetic study of 24-hour infusion 5-fluorouracil and leucovorin in patients with organ dysfunction. Annals of Oncology. 2003;14:1142-7.
40. European Medicines Agency. Xeloda : EPAR - Product Information. 03/07/2020 Xeloda - EMEA/H/C/000316 - A31/0085 Edition [cited 2021 Jan 14]. Available from: https://www.ema.europa.eu/en/documents/product-information/xeloda-epar-product-information_en.pdf
41. Müller F, Büchel B, Köberle D, et al. Gender-specific elimination of continuous-infusional 5-fluorouracil in patients with gastrointestinal malignancies: results from a prospective population pharmacokinetic study. Cancer chemotherapy and pharmacology. 2013;71:361-70.
42. European Medicines Agency. EMA recommendations on DPD testing prior to treatment with fluorouracil, capecitabine, tegafur and flucytosine. 30 April 2020 EMA/229267/2020 Edition [cited 2021 Jan 14]. Available from: https://www.ema.europa.eu/en/documents/press-release/ema-recommendations-dpd-testing-prior-treatment-fluorouracil-capecitabine-tegafur-flucytosine_en.pdf
43. Medicines and Healthcare Products Regulatory Agency. 5-fluorouracil (intravenous), capecitabine, tegafur: DPD testing recommended before initiation to identify patients at increased risk of severe and fatal toxicity. Drug Safety Update. 2020;14.
44. UK Chemotherapy Board. Personalised Medicine Approach For Fluoropyrimidine-based Therapies. July 2020 Edition [cited 2021 May 24]. Available from: https://4bd2316d-e45d-4e90-96b5-431f1c12dd3e.filesusr.com/ugd/638ee8_852a3c89120242118e76d8cc303b2fef.pdf
45. Casneuf V, Borbath I, Van Den Eynde M, et al. Joint Belgian recommendation on screening for DPD-deficiency in patients treated with 5-FU, capecitabine (and tegafur). Acta Clinica Belgica. 2021:1-7.
46. Loriot M-A, Ciccolini J, Thomas F, et al. Dépistage du déficit en dihydropyrimidine déshydrogénase (DPD) et sécurisation des chimiothérapies à base de fluoropyrimidines : mise au point et recommandations nationales du GPCO-Unicancer et du RNPGx. Bulletin du Cancer. 2018;105:397-407.
47. Wörmann B, Bokemeyer C, Burmeister T, et al. Dihydropyrimidine Dehydrogenase Testing prior to Treatment with 5-Fluorouracil, Capecitabine, and Tegafur: A Consensus Paper. Oncology Research and Treatment. 2020;43:628-36.
48. Di Paolo A, Cremolini C, Bocci G. Universal Pretreatment DPYD Genotyping in Fluoropyrimidine Candidates: Still Controversial

but With Clear Instructions for Practitioners, at Last! JCO Oncology Practice. 2020;16:801-2.

49. Cancer Institute NSW. Clinical Resource 1744: Dihydropyrimidine dehydrogenase (DPD) enzyme deficiency v.5. eviQ Cancer Treatments Online [cited 2021 May 24]. Available from: https://www.eviq.org.au/clinical-resources/side-effect-and-toxicity-management/prophylaxis-and-treatment/1744-dihydropyrimidine-dehydrogenase-dpd-enzyme
50. Ison G, Beaver JA, McGuinn WD, et al. FDA approval: uridine triacetate for the treatment of patients following fluorouracil or capecitabine overdose or exhibiting early-onset severe toxicities following administration of these drugs. Clinical Cancer Research. 2016;22:4545-9.
51. Chavani O, Jensen BP, Strother RM, et al. Development, validation and application of a novel liquid chromatography tandem mass spectrometry assay measuring uracil, 5,6-dihydrouracil, 5-fluorouracil, 5,6-dihydro-5-fluorouracil, α-fluoro-β-ureidopropionic acid and α-fluoro-β-alanine in human plasma. Journal of Pharmaceutical and Biomedical Analysis. 2017;142:125-35.
52. Hariprakash JM, Vellarikkal SK, Keechilat P, et al. Pharmacogenetic landscape of DPYD variants in south Asian populations by integration of genome-scale data. Pharmacogenomics. 2018;19:227-41.
53. Saif MW, Lee AM, Offer SM, et al. A DPYD Variant (Y186C) Specific to Individuals of African Descent in a Patient With Life-Threatening 5-FU Toxic Effects: Potential for an Individualized Medicine Approach. Mayo Clinic Proceedings. 2014;89:131-6.

Pheochromocytoma in pregnancy: a case report

Jignal Bhagvandas, Sylvia Lin, Richard Foon

ABSTRACT

A case of large 11cm phaeochromocytoma at 35 weeks with preceding diagnoses of pre-eclampsia and gestational diabetes (GDM), which confounded initial management.

Phaeochromocytoma in pregnancy is rare, with an incidence of 0.007%,[1] but carries high mortality of 40–50% if untreated.[2] Our case highlights the diagnostic challenges and complexity of management.

A 24-year-old primigravida presented at 33+2 weeks with symptoms of anxiety, nausea and vomiting. Her blood pressure was 206/90mmHg. She had persistent sinus tachycardia but an otherwise normal examination. The bloods were unremarkable, but proteinuria was evident (protein creatinine ratio 134.9mg/g). A large for gestation fetus was identified (>95th percentile, estimated fetal weight 3082g). OGTT at 34 weeks confirmed gestational diabetes (GDM). Pre-eclampsia was diagnosed and oral labetalol commenced. Blood pressure on the ward was labile and her sinus tachycardia persisted. Once her symptoms and hypertension settled, she was discharged on oral labetalol.

At 35 weeks she re-presented with intermittent headaches, ongoing anxiety, a systolic pressure of 210mmHg (the diastolic was not recorded) and ongoing maternal tachycardia, which prompted further investigation. IV hydralazine and magnesium sulphate were commenced for acute hypertensive control and eclampsia prevention. She was found to have paroxysmal hypertension and no excessive weight gain despite diagnosis of GDM and pre-eclampsia on assessment by the endocrinologist.

On investigation, plasma normetanephrines were raised (58,153pg/mL) and she had newly deranged liver function tests but no other evidence of end organ damage. Ultrasound revealed a 9x8x11cm right suprarenal mass.

Upon suspecting phaeochromocytoma, phentolamine and magnesium infusion was commenced and the patient was admitted to ICU. Initially, the plan was made for phentolamine for seven days prior to surgery. However, the next day, following a multi-disciplinary team (MDT) discussion including anaesthetics, obstetrics, endocrinology and obstetric medicine, a lower segment caesarean was performed under general anaesthesia at 36+6 weeks with ongoing IV phentolamine infusion and magnesium. The indication was suboptimal control of blood pressure in pregnancy and risk of severe morbidity and mortality to both mother and fetus. Efforts were made to minimise pressure exerted on the tumour at delivery. There were no episodes of labile blood pressure intraoperatively, and a well male infant of 3,395gm was delivered by forceps via hysterotomy without fundal pressure.

Post-partum MRI revealed imaging consistent with a phaeochromocytoma. The patient underwent successful transperitoneal laparoscopic excision of adrenal tumour two months later and T2Nx phaeochromocytoma was confirmed. Family history and genetic testing for common susceptibility genes were negative and she is receiving ongoing endocrinology follow-up.

Diagnosis of phaeochromocytoma can be difficult in pregnancy. More common causes of hypertension, such as pre-existing hypertension and pregnancy-related hypertension, are difficult to differentiate from rare causes such as phaeochromocytoma. Labile, paroxysmal, difficult-to-control blood pressure associated with additional features, including palpitation/tachycardia, flushing, sweating and light-headedness, should

prompt further investigation.[3] Fifty percent experience sustained hypertension, 35–45% paroxysmal hypertension and up to 50% are found to have orthostatic hypotension.[5] Presence of proteinuria does *not* exclude the diagnosis and is not uncommon,[4] as an altered renal function can be attributed to catecholamine-mediated renovascular changes found to reverse after tumour removal.[4] GDM is also common and reported in a third of cases. This may be explained by altered glucose metabolism by inhibition of insulin secretion or induced insulin resistance.[3,4]

Twenty-four-hour catecholamine urine collection is recommended, as pregnancy does not elevate urinary catecholamine levels within the diagnostic range for phaeochromocytoma. Plasma metanephrines can be considered, but specificity is low (85–89%). False positives are reported with concurrent use of antihypertensives or incorrect collection method. MRI is advised over USS as the gravid uterus can make visualisation difficult.[3]

The primary goal is to prevent complication from hypertensive crisis. Although catecholamines do not cross the placenta into the fetal circulation, the paroxysmal hypertension can lead to placental abruption as rebound hypotension causes severe hypoxia and fetal demise.[3] Medical treatment with alpha-blockade should be started as soon as diagnosis is made. Caution should be given before prescribing beta-blockade; if administered alone, it may cause precipitous blood pressure rise due to unopposed alpha-adrenergic effects, as observed in our case.[3] Other commonly used medications, such as oxytocin, methyldopa and anaesthetic agents, should also be avoided.[5] Surgery is the definitive treatment. Successful adrenalectomy has been reported in the second trimester.[3] In cases of later gestation diagnosis, the general consensus is for adrenalectomy after an elective caesarean section (CS). Vaginal delivery is associated with a higher mortality (31%) compared with CS (19%).[3] Vaginal delivery is considered in multiparous mothers who have had rapid, safe deliveries.[5] The evidence for timing of delivery, adrenalectomy and mode of delivery is based on case reports and remains an area of ongoing research.

Our case demonstrates the importance of considering the diagnosis of phaeochromocytoma in the context of resistant hypertension or pre-eclampsia in the third trimester. A careful, individualised approach with MDT collaboration is required.

Competing interests:
Nil.

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REFERENCES

1. Harrington J, Farley D, Van Heerden J, Ramin K. 1999. Adrenal Tumors and Pregnancy. Journal of Urology. 162(3 Part 1): 959-60.
2. Huddle K, Nagar A. 1999. Phaeochromocytoma in Pregnancy. The Australian and New Zealand Journal of Obstetrics and Gynaecology. 39(2): 203-6.
3. Oliva R, Angelos P, Kaplan E, Bakris G. 2010. Pheochromocytoma in Pregnancy. Hypertension. 55(3): 600-6.
4. Van der Weerd K, van Noord C, Loeve M, Knapen M, Visser W, de Herder W, Franssen G, van der Marel C, and Feelders R. 2017. ENDOCRINOLOGY IN PREGNANCY: Pheochromocytoma in pregnancy: case series and review of literature. European Journal of Endocrinology. 177(2):R49-R58.
5. Prete A, Paragliola R, Salvatori R, Corsello S. 2016. MANAGEMENT OF CATECHOLAMINE-SECRETING TUMORS IN PREGNANCY: A REVIEW. Endocrine Practice: 22(3):357-70.

Michael King: prolific researcher and one of the first doctors to "come out"

1950–2021

MD, PhD, FRCGP, FRCP, FRCP

Renowned as brilliant, kind, and humorous, Michael King helped to transform University College London's division of psychiatry into an international centre of excellence. A gay man, he was among the first doctors to "come out." In characteristic forthright and courageous fashion, he attacked medicine for perceiving homosexuality as a diagnosis to treat. Speaking on a podcast for the University of Melbourne in 2017, he said: "I think it's been one of the most stigmatising prejudicial things to have happened."

The popular perception may be that society is increasingly more accepting of diversity, but King questioned how much deep-rooted prejudice had been exorcised, fearing that Russia and some east European countries had gone backwards because of their homophobic leaders.

He said: "Homophobia from childhood onwards has severe and long-lasting effects, making people vulnerable to suicide, even people who seem to be in stable relationships. Parental attitudes and support is one of the strongest predictors of trouble in youth or in your 20s as a gay person. An accepting parent can reduce your risk of suicide attempts by 50–70%."

Gentle ferocity

As a debater King was known for disarming his opponents by the gentle ferocity of his curiosity. His friend and fellow psychiatrist Helen Killaspy, also of UCL, recalls a House of Lords debate when King underlined the dangers of reparative therapy—attempts to change a person's sexual orientation from homosexuality or bisexuality to heterosexuality.

She said: “We never had a chance of winning the debate. The numbers were stacked against us, but the opposing speakers could not but warm to questions from Michael such as: ‘But why do you think like this?’ He was so calm and non-defensive.

“He had an insatiable interest in people and brought this to his work, combining his natural curiosity and humour with methodological rigour.”

King was far more than a gay crusader. A prolific researcher, with 796 peer reviewed publications, and more due posthumously, he supervised 30 doctoral students and was influential in attracting and supporting the development of junior clinical and non-clinical academics in psychiatry. Speaking French, German, and Spanish, he started numerous longstanding international collaborations in Australasia, Europe, India, and South America.

Life and career

The son of a New Zealand farmer, Bruce King, and his wife, Patricia, young Michael studied zoology at Canterbury University, Christchurch, before qualifying in medicine in Auckland and training there as a physician. He moved to the UK in 1976 to study general practice.

He trained in psychiatric epidemiology at the GP research unit at the Institute of Psychiatry, London, and gained an MD (University of Auckland, 1986) and a doctorate (University of London, 1989) before he became a senior lecturer in the department of academic psychiatry at the Royal Free Hospital School of Medicine. He took over as head of department in 1996.

His numerous contributions to psychiatry encompassed risk prediction for mental disorders, evaluation of talking therapies and other complex interventions, end-of-life care for cancer patients, and religious and spiritual beliefs in mental wellbeing.

An excellent clinician, he founded the psychosexual service at Camden and Islington NHS Foundation Trust, where he was consultant psychiatrist for 30 years.

In the 1990s he was instrumental in changing how the cause of death was recorded for patients with HIV/AIDS to mitigate the associated stigma without compromising the collection of accurate statistics.

He and Gillian Mezey, now professor of forensic psychiatry at St George’s Hospital, London, co-wrote *Male Victims of Sexual Assault*, and contributed towards changes in the legal definition of male rape. King and Mezey were among the first to examine the impact of male sexual assault on mental health.

Appearing frequently in custody cases with lesbian and gay parents, King also helped to change the popular perception that children with gay parents were at risk. He also gave expert evidence to the Church of England Synod on same-sex marriage and the ordination of LGBT ministers. Although he was not a theologian, he quoted elegantly from the Bible—a reflection, friends say, of an exceptionally widely read man.

In 2001, King co-founded the Royal College of Psychiatrists’ special interest group on LGBT mental health, remaining an active member until a few weeks before his death.

He met his life partner, Irwin Nazareth, in 1984 at the Gay Medical Association. Nazareth is professor of primary care and population sciences at UCL. Having celebrated their civil partnership in 2006 they married in 2017. King leaves Nazareth, two nieces, and a nephew.

In 2019 King contracted a non-tuberculous mycobacterium (NTM) infection, later found to be linked to an extremely rare lung condition, pleuroparenchymal fibroelastosis (PPFE). Until 2017 only 100 cases of PPFE were thought to have been identified, leaving patients feeling isolated. Highlighting his positive approach to life, King founded the first NTM patient support group, NTM Patient Care UK (www.ntmpatientcare.uk).

Michael King (b 1950; q Auckland, New Zealand, 1975; MD, PhD, FRCGP, FRCP, FRCP), died from pleuroparenchymal fibroelastosis on 20 September 2021.

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Case of Foreign Body in the Right Lower Lobe Bronchus

1921

By T. A. MacGibbon, M.D., F.R.C.S.E.

Dr. F. V. Bevan-Brown sent Miss L. A. B., aged 30, with the following notes: "Miss B. was undergoing treatment for dyspepsia. She had a septic lower molar tooth, which was extracted, under gas anæsthesia, by a competent exodontist. The tooth was a mere shell with a large amalgam filling. The extraction was very difficult, the tooth breaking in the process. The dentist was not certain that he had recovered every piece. He X-rayed the upper half of the chest, but found no evidence of any foreign body in the main air passages. The following day the patient developed a troublesome dry cough, and a sense of irritation in the throat. There was some pharyngitis secondary to the pus from the septic stump, and this was considered sufficient to account for the cough, since careful examination of the chest revealed no abnormal signs. The patient did not report herself for nine days, during which she had coughed incessantly, and had become rather exhausted. There were still no physical signs in the chest, but a sign of considerable omen had by now developed, namely, fœtor of the breath. The cough was mostly dry, with, occasionally, a little muco-pus. An X-ray examination of the whole chest was now made, and a foreign body was clearly visible lying low down in the right lung, one inch and a-half above the dome of the diaphragm. It was the size of a pea, and so opaque that it was considered to be a piece of amalgam, and not a portion of the tooth."

During the evening of the day, after I had examined the photograph, the patient was taken into the theatre of the Christchurch Hospital, and an attempt was made to locate the foreign body by means of Chevalier-Jackson's instruments. The patient was placed in the supine position, and the pharynx and hypo-pharynx painted with 10 per cent solution of cocaine. Dr. Hamilton Gould then took charge of the head which was brought over the end of the table. Jackson's laryngoscope, with distal illumination, was passed down to the entrance of the larynx, the bronchoscope, also with distal illumination, passed down inside the laryngoscope and through between the cords into the trachea. The slide of the laryngoscope was withdrawn, and the laryngoscope removed. The bronchoscope was slowly pushed down until the carina was encountered. Dr. Gould then inclined the head and neck to the left, and the tip of the instrument slipped easily into the right bronchus and down the mainstem bronchus to the lower lobe bronchus. Here pus was found, and removed after Jackson's simple but ingenious method. The body as not found, and it was decided to wait.

Two evenings later a second attempt was made to remove the piece of amalgam. The instrument was introduced as before, quite easily, but this time the patient was laid across the X-ray couch. More muco-pus was pumped out, and the small bronchus, in which the body was lying, was recognised by the pus oozing from it. The tip of the tube was now found lying over the amalgam, but this could not be felt or seen with forceps. This effort was also abandoned. The following night the same procedure was gone through. Now a right angled probe was passed over the cartilagenous lip of the bronchus and the foreign body tilted into the lumen. Jackson's forceps were passed, and the foreign body grasped and removed.

The patient bore the operation well, and said there was no pain experienced after the discomfort of passing the tube through the glottis. No anæsthetic, beyond the concainising of the hypopharynx, was used.

The patient was taken back to bed and placed in a steam tent. Dr. Bevan-Brown's subsequent notes:

"Hoarseness and soreness on swallowing were present for two or three days after the removal of the foreign body, but the

patient's general condition was satisfactory. The temperature remained normal, the cough grew less severe, and there was very little expectoration. The fœtor gradually improved. She was very thin and weak, however, due chiefly to her chronic dyspepsia and exhaustion following a fortnight of incessant coughing. An X-ray examination of the chest, a week after the bronchoscopy, shewed everything clear. The infiltration previously seen round the foreign body had dispersed. A few days later, however, pain began to develop in the right chest, and there was evening pyrexia ranging from 90 degrees F., to 100 degrees F. for four or five days. This and the pain both eventually subsided without giving rise to any abnormal physical signs. The patient is now—six weeks from the operation—definitely better in every way."

This is the first time I have removed a foreign body from the lung of a living subject. This foreign body was difficult to remove because of its weight and smallness, and because it lay out of sight in a branch bronchus. The operation confirmed my opinion that distal illumination was better than proximal. With the proximal light one's instruments and fingers constantly interfered with one's vision, and the carrier interfered with the insertion of forceps and probes. Further, Jackson's instruments are so made that trauma is almost exceptional, while Brüning's instruments, unless in the hands of much practised manipulators, seemed to invite damage.

My thanks are due to Dr. Hamilton Gould for ably assisting me. Jackson used to say: "It's team-work, gentlemen."

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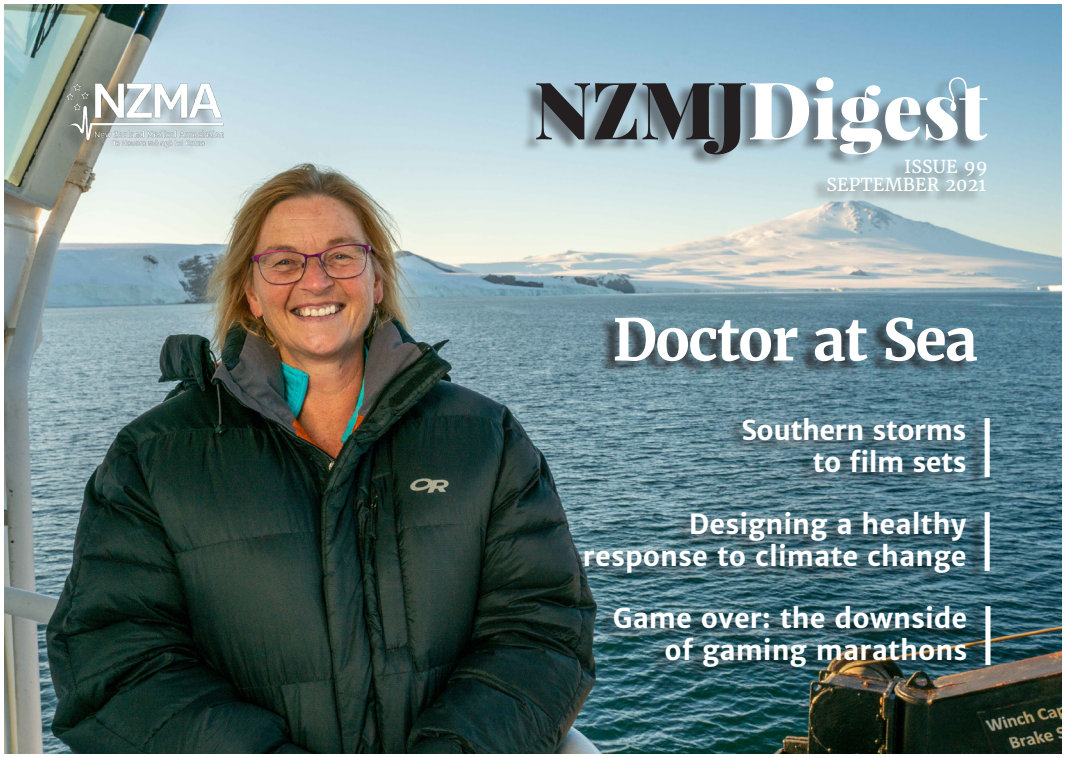

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