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The interaction between pre-operative anaemia and peri-operative blood transfusion on patient outcomes following general surgical procedure: a retrospective review

Leesa J Morton, Katy L Konrad, Teresa (Jibin) Xu, Nicholas J Lightfoot

Anaemia is common in patients undergoing surgery. In this study we found that patients who are anaemic when they have their operation need to stay in hospital longer and are more likely to have infectious complications. Anaemic patients are also more likely to need blood transfusions, which further increases these risks. This highlights the importance of diagnosing and if possible treating anaemia before surgery.

Urinary and faecal incontinence: psychological factors and management recommendations

Kenley LJ Kuoch, Geoffrey S Hebbard, Helen E O'Connell, David W Austin, Simon R Knowles

Urinary and faecal incontinence substantially impacts upon physical health and is associated with significant psychological distress and reduced quality of life. Due to stigma and embarrassment, many patients do not see their general practitioner (GP) for management of incontinence. This article aims to summarise the forms and causes of incontinence, highlight the psychological mechanisms associated with incontinence, and provide management recommendations for GPs.

Patient-reported quality of life for cataract surgery: prospective validation of the 'Impact on Life' and Catquest-9SF questionnaires in New Zealand

Sunny S Li, Stuti L Misra, Henry B Wallace, Lyn Hunt, James McKelvie

With limited resources for publicly funded surgery, prioritising patients for cataract surgery is essential to enable equal access to surgery for all New Zealand residents and ensure those who are most likely to benefit from surgery are prioritised highest. Currently, the prioritisation system incorporates use of the Impact on Life questionnaire (IoL), which we have found to not accurately assess vision-related quality of life (VRQoL) for patients that require cataract surgery in New Zealand. On the other hand, the Catquest-9SF questionnaire has been shown to be a domain-specific assessment tool that can accurately measure VRQoL in New Zealand, and has also been validated internationally.

Infectious pulmonary tuberculosis in a New Zealand cancer centre

James Chancellor, Julianna Lees, Kate Grimwade, Neil de Wet, Lynnette Borissenko

This report details the investigation of cancer patients, as well as cancer centre staff, friends and family who were exposed to a cancer patient with reactivated tuberculosis (TB) in a New Zealand cancer centre. A total of 67 patients, staff members, family and friends were identified as being exposed to the case of TB. These people were screened for TB infection by the use of a symptom questionnaire, a blood test and a chest x-ray. Of the people tested no one was found to have acquired TB, but surveillance for signs and symptoms of TB disease in those with significant risk is ongoing. In this article we discuss the public health response to TB in a cancer centre and potential preventative strategies for the future.

The projected burden of knee osteoarthritis in New Zealand: healthcare expenditure and total joint replacement provision

Ross Wilson, J Haxby Abbott

Treatment of knee osteoarthritis cost the New Zealand healthcare system $200 million in 2013, an amount projected to increase to $370 million by 2038. If current standards of treatment remain unchanged, an additional 4,000 knee replacement surgeries per year will be needed by 2038. Public health measures to address the growing obesity epidemic and better use of effective, low-cost, early interventions for knee osteoarthritis, such as exercise therapy, are required to alleviate the rising burden of osteoarthritis.

Mate wareware: Understanding 'dementia' from a Māori perspective

Margaret Dudley, Oliver Menzies, Hinemoa Elder, Lisa Nathan, Nick Garrett, Denise Wilson

This paper explains an understanding of *mate wareware* (dementia) as obtained from interviews with over 200 elderly Māori and whānau from across Aotearoa New Zealand. The issues of wairua (spirituality) and whānau (family) were central to the findings thereby indicating a need for culturally appropriate services for Māori who live with this disease. It was found that the burden of caregiving may be greater for Māori whānau and must be factored in when providing services for Māori. Generally, there was found to be a lack of easily accessible knowledge available to Māori regarding *mate wareware*.

Availability of automated external defibrillators in Hamilton, New Zealand

Peter A O'Callaghan, Janice Swampillai, Martin K Stiles

The aim of this study was to visit 50 publicly listed defibrillators in Hamilton, New Zealand, to assess their true availability and visibility to the public in the event of an out-of-hospital cardiac arrest (OHCA). During office hours there is a reasonable number of accessible defibrillators, however access is limited outside office hours, with only 7% available 24 hours seven days a week, and few available after 6pm and on weekends. There are no outdoor automated external defibrillators (AEDs) available, with none of the AEDs listed clearly visible from the outside. Combined with the lack of signposting, there would be an inevitable delay in obtaining an AED in an OHCA.

Tailoring a rapid autopsy protocol to explore cancer evolution: a patient collaboration

Cherie Blenkiron, Tamsin Robb, Kate Parker, Nicole Kramer, Simon Stables, Rexson Tse, Lucy Modahl, Esther Coats, Cris Print, Ben Lawrence

The donation of a patient's body, upon their natural death, for research purposes is an invaluable gift. In our study we have shown the value of that donation to further our understanding of how a tumour can change and develop in order to spread around the body. In the paper we have highlighted the scientific value of the gift but also carefully considered the ongoing engagement with the family and the significant efforts needed to coordinate the process.

Pelvic mesh in colorectal pelvic floor surgery—implications of recent developments

Rowan J Collinson, Andrew R Moot

The use of prosthetic mesh products in pelvic prolapse surgery is under significant scrutiny, because of widely reported adverse outcomes. However, the reasons why patients are recommended this type of surgery, and the surgical techniques used, vary between different surgical specialty groups. In the bowel surgery subspeciality ('colorectal surgery'), a mesh repair is sometimes recommended for bowel prolapse problems, which can cause functional problems such as loss of bowel control. The emergence of bowel mesh procedures has provided an extra treatment option, in some cases where a satisfactory treatment did not exist before. The available evidence suggests that bowel prolapse surgery using the mesh technique is much safer than that of the gynaecological approach and should not necessarily be dismissed without due consideration. However, there are recommendations relating to improved reporting, training and patient education around this procedure.

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Medicinal Cannabis Scheme in New Zealand: lessons from international experience and our own recent drug policy reform setbacks

Marta Rychert, Chris Wilkins, Geoff Noller

The Ministry of Health (MOH) recently released a consultation document outlining proposals for the New Zealand Medicinal Cannabis Scheme (NZMCS) and completed a series of public consultations seeking feedback from industry, patients and medical professionals on a number of complex regulatory issues.[1] With less than three months left to finalise the new scheme, pressure is mounting to balance the sometimes conflicting expectations of the various stakeholders. Medical professionals overseas and in New Zealand have long expressed concerns about the quality of evidence concerning the medical benefits of cannabis (ie, specifically the limited number of double-blind placebo-controlled trials).[2,3] As a consequence, engaging medical professionals in similar regimes overseas has proved a key challenge.[4]

Broadly, the MOH consultation document proposes a pharmaceutical access model where products will be available via prescription from pharmacies. The discussion document asked whether an additional recommendation from a specialist doctor should also be required. This level of oversight would be higher than for most other medicines, including opioids—an irony that has not escaped some commentators.[5] The suggestion that the New Zealand scheme will require specialist sign-off has attracted negative feedback from patients and the industry, and a mixed response from medical professionals concerned there will not be enough specialists and with the additional pressure placed on the resources of the health system.[6]

In Australia, the requirement for specialist sign-off led to the opening of private 'cannabis clinics' with specialist teams on site, adding to the cost of such consultations and related inequities. However, recent modifications of the Australian regime have addressed these issues, with monthly prescribing figures subsequently increasing 10-fold, from 229 in August 2018 to 2,206 in July 2019.[7] The modifications include the streamlining of the GP application process using an online portal, thus avoiding the paperwork previously involved, and most states now allowing specialist GPs to prescribe without having to be endorsed by condition specialists (eg, pain specialists).[8]

Further key issues put forward for discussion include what medical cannabis products will be available and the related manufacture standards. Smoking and edible products have already been ruled out due to the health risks of smoking and variability in metabolism of edibles respectively, but vaping will most likely be permitted. In terms of manufacture, the Ministry has suggested one scenario in which all products will need to comply with Good Manufacturing Practice (GMP) requirements, the gold standard for pharmaceutical products. An alternative approach is to allow some products to be manufactured to a lower Good Production Practice (GPP) standard. The proposed GPP standard is based on the Canadian approach to *non-prescription*

health products containing cannabis. These products do not undergo any pre-market review for safety.[1] Given this NZMCS proposal is strongly based in the pharmaceutical paradigm, it is unclear whether GPs would be comfortable prescribing products manufactured to any standard lower than GMP. Many countries have already adopted GMP for medicinal cannabis and some fledgling New Zealand medicinal companies have expressed interest in this international export market.

We are left wondering if the GPP standard has been proposed in anticipation of a more liberal approach to cannabinoids in the future. The New Zealand Medical Cannabis Council, the cannabis industry group, is currently lobbying to reschedule cannabis-derived cannabidiol (CBD) products from 'prescription' to 'pharmacy-only' medicines. We have previously argued that CBD products could be classified as dietary supplements due to the absence of the psychoactive ingredient THC.[9] CBD is marketed in this way in some countries, but legal uncertainties remain.[10] For example, French authorities recently released a new interpretation of the law that allows traces of THC (0.2%) to be present in the plant, but *not* in the finished CBD products, leading to the closure of numerous 'CBD cafes'.[11] Meanwhile, an American CBD producer received a license to sell CBD foods and supplements in Bulgaria, the first European Union country to officially regulate CBD as a food (potentially at odds with EU law requiring prior market authorisation by the European Food Safety Authority).[12] The current review of CBD by the US Food and Drug Administration will likely influence the global industry and regulations in other countries,[13] including New Zealand.

The speed at which the NZMCS is now being finalised raises concerns that the new framework may have deficiencies and unintended impacts. While the Misuse of Drugs (Medicinal Cannabis) Amendment Bill was introduced into the house in late January 2018 (as part of the Government's 100 day plan), it took 11 more months to pass into law, and the legislation states the regulations must be finalised by 18 December 2019. This leaves an extremely tight timeframe to resolve some complex issues. As previously seen with the attempt to regulate "legal highs" via the Psychoactive Substances Act, a rushed policy process can have fatal consequences for implementation.[14–16]

On social media, medicinal cannabis patients have expressed their frustration at the MOH scheduling of July NZMCS consultation sessions for patients in the evening when their symptoms worsen, and this appears to have contributed to low turnouts.[17] In contrast, the morning consultation sessions for the industry were very well attended. This raises the question of who will be the central focus of the regime. The composition of the Medicinal Cannabis Advisory Group includes two representatives from the industry: a cannabis growing company and a private consultancy specialising in commercialisation of biomedical and pharmaceutical products. Some commentators have argued that keeping the industry at arm's length during the development phase would have been preferable.[18] The decision to recover the cost of the new regime from industry licensing fees also appears to establish a dangerous dependency on the commercial success of the new sector. Proposed high licensing fees also create barriers for small-scale, artisan producers who are less focused on commercial success.

The nascent domestic New Zealand medicinal cannabis industry may face considerable competition from already well-established firms from the US, Canada and Israel, raising questions about the extent to which the Government is interested in nurturing a domestic industry. In Thailand, which legalised medicinal cannabis earlier in 2019, foreign investment and imports will be prohibited for five years to allow the domestic medical cannabis industry to become established.[19] Under the Jamaican medicinal cannabis scheme (established in 2015), licensed companies must have 'substantial' Jamaican ownership control.[20] A domestic medicinal cannabis sector may provide opportunities for enhanced regulatory control and local economic development and employment.

There are also questions about the equity of the new regime with regard to addressing the previous disproportionately high Māori arrest rate for minor cannabis offences and

the need to promote Māori economic development. The New Zealand Health Survey found that 10.2% of Māori compared to 4.4% of Pakeha self-reported using cannabis medicinally.[21,22] The recent legalisation of cannabis in Illinois included expungement of previous cannabis convictions (involving around 770,000 cannabis-related records), and support for people from communities that had been disproportionately impacted by cannabis law enforcement to obtain cannabis business licenses. The Jamaican government is currently implementing an Alternative Development Programme to support local farmers to grow cannabis in a regulated medicinal scheme environment.[23]

Finally, throughout the NZMCS consultation process there has been little mention of how the medicinal scheme will fit with a possible framework for recreational cannabis use if next year's referendum is positive. With "grow your own" as an option under the recently released Government framework,[24] patients may opt to utilise this means of supply as an alternative to a strictly regulated and likely more expensive NZMCS. Alternatively, if the referendum does not endorse legal recreational cannabis access, disaffected patients may continue to access the potentially cheaper cannabis black market. In Canada, following legalisation of recreational use, the Canadian Medical Association has called for abandonment of medical access scheme, stating it is "no longer necessary".[25] The danger with this outcome is those wishing to use cannabis for medicinal reasons may not have access to safer, medical grade cannabis products and may be less likely to seek professional medical advice.[26]

Experience from overseas shows medicinal cannabis schemes can be too strictly regulated with overly bureaucratic systems leading to higher healthcare costs, barriers to access and overburdening of the health system. Yet if cannabis is to be treated as a medicine, patient safety and treatment efficacy must remain central principles. There are clear reasons to keep the medicinal cannabis industry at arm's length from regulatory design decisions. Experience from overseas also suggests that schemes often need to be adjusted over the years to achieve their original objectives, and this underlines the need for regulatory design flexibility and, importantly, ongoing evaluation of outcomes. A central lesson from previous drug policy reform in New Zealand is the need for investment of time and resources in implementation planning, regulatory agency capacity, and ongoing engagement with health stakeholders and the public.

Competing interests:
Conflict of interests: MR and CW are currently conducting a study of medicinal cannabis use funded by the Health Research Council (19/647) and Massey University Research Fund. GN is conducting a study of medicinal cannabis use funded by Medical Cannabis Awareness New Zealand (MCANZ), a medical cannabis patient advocacy organisation.

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The interaction between pre-operative anaemia and peri-operative blood transfusion on patient outcomes following general surgical procedure: a retrospective review

Leesa J Morton, Katy L Konrad, Teresa (Jibin) Xu, Nicholas J Lightfoot

ABSTRACT

AIM: To assess the incidence of pre-operative anaemia in patients presenting for general surgery and determine the relationship between pre-operative anaemia, transfusion and post-operative metrics including length of stay (LOS) and infectious complications.

METHOD: A retrospective cohort of 1,186 patients. Stratification into two groups with and without pre-operative anaemia through propensity score matching. Logistic regression was used to determine the relationship between pre-operative anaemia, blood transfusion and infectious complications.

RESULTS: The incidence of pre-operative anaemia was 17.4%. Red blood cell (RBC) transfusion was greater in those with PA than those without, 13.1% versus 0.7% (OR 21.7 (2.9–166.7, p<0.001)). In the propensity matched cohort, pre-operative anaemia was associated with an increase in LOS from 2.1 to 3.0 days (p=0.006) and increased infectious complications from 6.4% to 18.4%, (OR 3.3 (1.4–7.7), p=0.004). The risk of infectious complications was amplified in the patients receiving RBC transfusion. After adjustment for transfusion, in patients with pre-operative anaemia the OR for infectious complications became 2.3 (0.95–5.7, p=0.06) for those not transfused and 5.5 (2.0–15.3, p=0.001) for those transfused.

CONCLUSION: Pre-operative anaemia is associated with an increase in hospital LOS and infectious complications. When adjusted for transfusion the effect of pre-operative anaemia alone on hospital LOS and infectious complications is not statistically significant. Expeditious investigation and treatment of PA could reduce complications and save resources.

Pre-operative anaemia is common before major surgery. Anaemia is often multifactorial, particularly in those with cancer, in elderly or malnourished patients and in those with auto-immune and pro-inflammatory conditions.[1] The World Health Organization (WHO) defines anaemia as insufficient red cell mass to meet the body's physiological needs, with a haemoglobin (Hb) threshold of <130g/L in men and <120g/L in non-pregnant women.[2]

Anaemia in patients undergoing major surgery has been recognised as a problem which needs to be addressed. The 30-day morbidity and mortality in anaemic patients is greater than in those with normal haemoglobin levels pre-operatively.[3] The presence of pre-operative anaemia independently predicts the need for blood transfusion and increases the risk of post-operative infectious complications. Anaemia may also increase the costs associated with

healthcare through prolongation of length of stay, and the expenses associated with increased need for blood transfusion or blood procurement.[3] Furthermore, blood transfusion itself also increases post-operative mortality and morbidity including wound infection, pneumonia and sepsis through modulation of the immune system or inducing a procoagulant state.[1]

Pre-operative anaemia is an important modifiable risk factor. The Australian National Blood Authority recommends that healthcare providers establish programmes to optimise pre-operative haemoglobin, coagulation status and minimise blood loss.[1] These evidence-based initiatives aim to avoid exposing patients to potential harm from both anaemia and exposure to blood transfusion. Patients at increased risk of anaemia should have pre-operative haemoglobin and iron studies performed and receive timely treatment with iron or erythropoietin, if appropriate.[1,4] In patients with pre-operative anaemia undergoing colorectal surgery, pre-operative treatment with iron increases haemoglobin level and is associated with reduced need for blood transfusion.[5,6]

The purpose of this study is to delineate the prevalence of anaemia in a patient population presenting for general surgical procedures at Counties Manukau Health (CMH) and to determine the interaction between pre-operative anaemia, blood transfusion and post-operative metrics including length of stay (LOS) and infectious complications. This information will help to plan future initiatives to reduce the burden of pre-operative anaemia and rationalise blood produce use in the peri-operative period.

Method

Ethics

An exemption from formal Health and Disability Ethics Committee (HDEC) review was obtained as the project was out of scope. Institutional approval from the CMH Research Review Committee (number 164) was granted prospectively.

Aims

The aims were to determine the relationship between pre-operative anaemia and blood transfusion in patients undergoing either elective or emergency general surgical procedures at CMH. Specific outcomes include hospital LOS and peri-operative infectious complications defined through ICD-10 discharge coding (see Appendix 1).

Study design and population

This is a retrospective cohort study of both elective and emergency patients presenting for general surgical procedures at CMH between 1 January and 31 December 2015. A one-year period was chosen for convenience. We considered our sample to be large enough to include a representative spectrum of our population and practice. Patients over the age of 16 years presenting for either elective or emergency general surgical procedures during the study period were eligible for inclusion. Patients were excluded if they were having surgery under local anaesthesia (LA) alone, or if pre-operative haemoglobin was not measured within the 30 days before surgery. Patients meeting the above criteria were identified using their National Health Index (NHI) number through the Patient Information Management System (PiMS).

Data collection

Demographic data was collected from the hospital electronic data warehouse managed by the HealthAlliance including age, sex, American Association of Anesthesiology (ASA) score, ethnicity, ICD-10 comorbidity and ICD-10 complication codes, surgical venue, procedure name and duration, hospital length of stay, readmission to hospital at 30- and 90-days post-discharge and mortality.

Blood test results including Hb and creatinine were electronically extracted from the hospital DELPHIC and ÉCLAIR systems. We identified pre-operative haemoglobin and creatinine recordings within 30 days prior to surgery. The value closest to the date and time of surgery served as the surrogate for the pre-operative value for the purpose of statistical analyses as outlined below. Pre-operative measurement of haemoglobin is guided by local guidelines, with oversight from the Choosing Wisely campaign, which aim to rationalise blood testing. The administration of blood products was determined from the DELPHIC system. Blood products were defined as packed red blood cells (RBC), fresh frozen plasma (FFP), platelets, cryoprecipitate and human albumin.

Analysis and statistics

Data was stored in a Microsoft Excel spreadsheet. All statistical analyses were performed using SPSS statistics software (IBM Corp. Released 2017. IBM SPSS Statistics for Windows, Version 25.0. Armonk, NY: IBM Corp). Results are presented as number (percent), median (interquartile range) and odds ratios (OR) (95th percent confidence interval) as appropriate. Propensity score matching by age, sex, ethnicity, ASA score, surgical duration and pre-operative creatinine was performed to obtain two balanced cohorts with and without pre-operative anaemia. These factors were chosen as potential confounders of risk factors for anaemia and threshold for transfusion. Pre-operative anaemia was defined as Hb <120g/L in females and <130g/L in males as per the most recent WHO criteria.[2] Haemoglobin levels of 110–119, 80–109 or <80g/L are used to categorise severity of anaemia in non-pregnant women as mild, moderate or severe respectively. In men, haemoglobin levels of 110–129, 80–109 or <80 g/L are used. Logistic regression was used to determine the relationship between pre-operative anaemia, blood transfusion and infectious complications. Comparisons were made with the Fisher Exact test and the Mann-Whitney U-test for categorical and continuous variables respectively. A two-tailed p-value of $p<0.05$ defined statistical significance.

Results

During the study period, 2,537 patients underwent general surgical procedures. Of these, 1,186 were excluded leaving 1,351 patients. Reasons for exclusion were; 164 patients having surgery under LA alone and 1,022 patients without a pre-operative Hb recording. In those where a pre-operative haemoglobin measurement available, 236/1,351 (17.5%) were anaemic by the standard WHO definition (see Figure 1). The overall mortality rate at 30 days was 0.12% (3/2,537) and 1.58% (40/2,537) at one year.

Propensity score matching to account for age, sex, ethnicity, ASA score, surgical duration and pre-operative creatinine was possible for 61.4% of patients using a match tolerance of 0.001. This produced two balanced cohorts with and without pre-operative anaemia, each with 145 patients (see Table 1).

Incidence and severity of pre-operative anaemia

The distribution of severity of anaemia is seen in Table 2. Severity of anaemia was classified as per the most recent WHO definitions appropriate to patient sex.[7]

Pre-operative anaemia and length of stay

In the propensity matched patients, pre-operative anaemia was associated with increase in median hospital LOS from 2.1 days (IQR 1.2–3.2) to 3.0 days (1.2–6.3)

Figure 1: Patient flow.

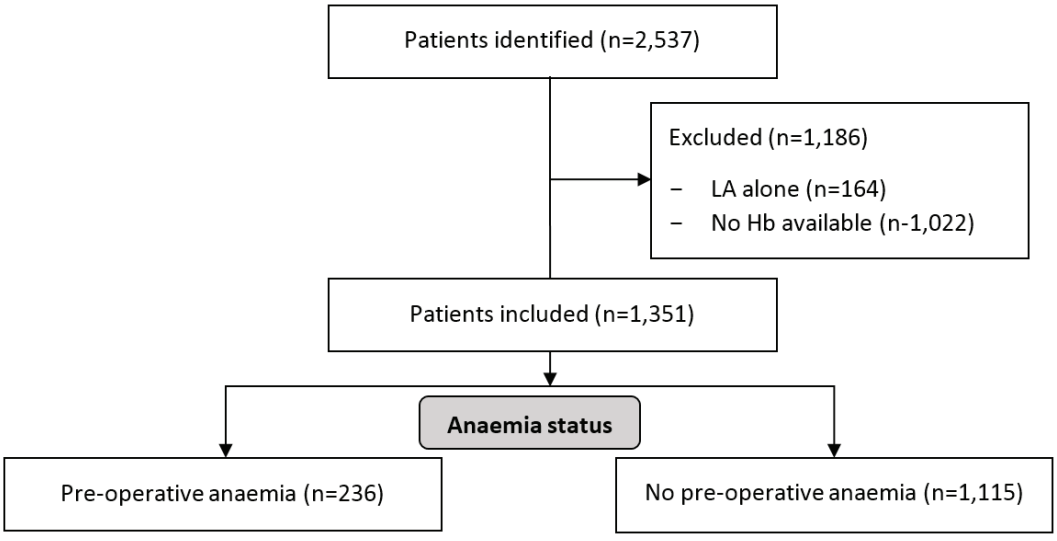

Table 1: Results of propensity score matching.

		Anaemia (n=145)	**No anaemia** (n=145)	**p-value**
Sex N (%)	Female	78 (53.8)	91 (62.8)	0.12
	Male	67 (46.2)	54 (37.2)	
Ethnicity N (%)	Asian	15 (10.3)	8 (5.5)	0.41
	European	65 (44.8)	79 (54.5)	
	Indian	6 (4.1)	7 (4.8)	
	Māori	17 (11.7)	19 (13.1)	
	Pacific Island	33 (22.8)	25 (17.2)	
	Other	9 (6.2)	7 (4.8)	
ASA Score N (%)	1	16 (11.0)	28 (19.3)	0.29
	2	71 (49.0)	71 (49.0)	
	3	53 (36.6)	43 (29.7)	
	4	4 (2.8)	2 (1.4)	
	Not recorded	1 (0.7)	1 (0.7)	
Surgical time Minutes	Median	114	119	0.63
	IQR	79–179	82–265	
Closest creatinine Mmol/L	Median	74	72	0.79
	IQR	65–91	65–86	
Age Years	Median	60	57	0.31
	IQR	47–71	42–67	

(p=0.006). The LOS in patients with mild pre-operative anaemia was similar to those with no evidence of pre-operative anaemia (p=1.00), whereas in those with moderate (p<0.001) and severe pre-operative anaemia (p=0.04) the LOS was significantly prolonged compared with those without pre-operative anaemia.

Pre-operative anaemia and infectious complications

Information on infectious complications was available for 125 patients from each of the propensity matched groups. Pre-operative anaemia was associated with an increase in overall infectious complications from 6.4% to 18.4% (OR 3.3 (1.4–7.7)

Table 2: Severity of anaemia in the propensity matched patients.

Mild		**Moderate**		**Severe**	
N =	%	N =	%	N =	%
87	60.0%	55	37.9%	3	2.1%

Table 3: Infectious complications by anaemia status in the propensity matched groups.

	Anaemia (n=125)		**No anaemia** (n=125)		
	N=	%	N=	%	p-value
Infectious complications	23	18.4	8	6.4	0.004
Wound infections	6	4.8	0	0.0	0.013
Sepsis	10	8.0	2	1.6	0.018

p=0.004). There was an increase in sepsis in the group with pre-operative anaemia from 1.6% to 8.0% (OR 5.4 (1.2–25.0) p=0.018). There was also an increase in wound infections in those with pre-operative anaemia compared to those without, 4.8% versus 0% (p=0.013). See Table 3.

Rate of transfusion

In the overall cohort the rate of RBC transfusion was 19.1% (45/236) in those with pre-operative anaemia, and 0.6% (7/1,115) in those without (p<0.001). The OR for RBC transfusion in the presence of pre-operative anaemia was 37.0 (16.7–83.3, p<0.001). The use of individual blood products (namely FFP and cryoprecipitate) was significantly increased in those with pre-operative anaemia. Likewise, for a composite measure encompassing the use all blood products, the rate of transfusion was again increased in those with pre-operative anaemia 22.5% (53/236) compared to those without 1.3% (14/1,115) (p<0.001).

RBC transfusion in the propensity matched cohort was greater in the group with pre-operative anaemia 13.1% versus 0.7%, OR 21.7 (2.9–166.7, p<0.001) (see Table 4). Exposure to all blood products was greater in the group with pre-operative anaemia. When blood product use was analysed separately, this difference was driven by RBC use between the groups.

RBC transfusion and infectious complications

Using logistic regression, the effect of RBC use on infectious complications was examined. After adjustment for both RBC transfusion and pre-operative anaemia the OR for overall infectious complications in those with pre-operative anaemia became 2.3 (0.95–5.7, p=0.06), while OR for infectious complications in those transfused RBC was 5.5 (2.0–15.3, p=0.001).

Discussion

We have shown that pre-operative anaemia is common and leads to an increased hospital length of stay of approximately 20 hours in a population of patients undergoing elective and emergency general surgical procedures at a tertiary New Zealand Hospital. Patients with pre-operative anaemia had an increased risk of infectious complications with a concurrent increased exposure to red blood cell transfusion. However, when these results were adjusted for the effect of red blood cell transfusion, this factor had greater significance than anaemia alone. These results have obvious implications for the provision of peri-operative care, especially in those undergoing procedures associated with significant blood loss and transfusion exposure.

Table 4: Transfusion in the propensity matched groups.

	Anaemia		**No anaemia**		
	N=	%	N=	%	p-value
Any blood product transfused	22	15.2	4	2.8	<0.001
RBC transfusion	19	13.1	1	0.7	<0.001

Table 5: Infectious complications by transfusion in the propensity matched groups.

	No RBC transfusion		RBC transfusion		
	N=	%	N=	%	p-value
Infectious complications	22	9.6	9	45.0	<0.001
Wound infections	4	1.7	2	10.0	0.075
Sepsis	7	3.0	5	25.0	0.001

Pre-operative anaemia is a highly prevalent condition with the rate varying by age, ethnicity, the type of surgery, whether surgery is elective or emergent and by patient comorbidities. A 2011 analysis of the American College of Surgeons' National Surgical Quality Improvement Program (ACS-NSQIP) database reported that pre-operative anaemia was seen in 28.9% of general surgical patients.[3] Larger cohorts looking at patients undergoing all forms of non-cardiac surgery have found the prevalence of anaemia to be approximately 30%.[8,9] These studies have also demonstrated a relationship between pre-operative anaemia and adverse perioperative outcomes, particularly infectious complications, which was echoed in this study. The slightly lower incidence of pre-operative anaemia of 17.5% identified in our study is possibly attributable to differences in the patients included. Our cohort was younger and included a higher proportion of patients with lower ASA scores than the aforementioned studies. However, our figure is in line with the prevalence of pre-operative anaemia across all surgical specialties of 14–20% quoted in Western Australia.[10]

The fact that blood transfusion is associated with increased morbidity and mortality is now well recognised and widely reported.[11] Furthermore, the increase in adverse outcomes with blood transfusion is dose dependent, the exact mechanism for these findings has not been fully elucidated.[12] This may be related to modulation of the immune system or the activation of an inflammatory response which presents a paradox given desired effect of RBC transfusion is to increase the blood haemoglobin level to reverse the anaemia and to increase arterial blood oxygen. There is evidence from randomised controlled trials linking blood transfusion and infectious complications.[11] Given the strong link between pre-operative anaemia, RBC transfusion and the similar complication profiles induced by both conditions, further investigation is required to determine the risks attributable to each and potential strategies to alleviate these risks. Others have shown that anaemia alone is associated with increases in infectious complications, whereas in the current study it appears that transfusion rather than anaemia is a greater driver.[3,8]

Pre-operative anaemia is a strong predictor of the need for blood transfusion. We found that in patients presenting for general surgery, after adjusting for potential confounders, that RBC transfusion was more frequent in those with pre-operative anaemia. Both pre-operative anaemia and transfusion can contribute to poor outcomes due to the links between these parameters. Given this information the financial implications of both anaemia and transfusion should be investigated further.

The WHO defines anaemia as a haemoglobin below 130g/L in males and 120g/L in females. These definitions were first disseminated in 1968 and have since been refined to include specific thresholds for neonates, children of different ages and for the parturient. This definition now also includes mild, moderate and severe sub-classifications. The key effect of anaemia on human physiology is the reduction in oxygen transport and delivery to the tissues, which can lead to anaerobic metabolism in circulations with fragile or impaired blood supplies. This can lead to impaired wound healing and wound infections. The objective of an allogeneic blood transfusion is to increase the circulating red cell mass with a concurrent increase in the haemoglobin level to improve cellular oxygen delivery.

There is now evidence to suggest that the transfusion of allogeneic blood does not achieve these goals in the short-term. This may be related to decreased red cell deformability in capillary beds and to the changes in the oxygen-haemoglobin dissociation curve induced by the storage of blood. Lysis of transfused red cells and the resultant release of free haemoglobin may also serve as a trigger for the induction of inflammatory responses, which may contribute to the observed morbidity and mortality seen following red blood cell transfusion.[13]

Following propensity score matching we found an increase in hospital length of stay of approximately 20 hours in patients with pre-operative anaemia. Although this figure by itself is not especially impressive, when combined with the cost associated with red blood cell transfusion and the increase in infectious complications seen with both anaemia and blood transfusion scaled to the total number of discharges each year following general surgical procedures across all public hospitals in New Zealand (of which there were 44,502 in 2018),[14] the costs associated with anaemia could become considerable. A secondary analysis of the European Surgical Outcomes Study (EuSOS) found a similar increase in length of hospitalisation and number of intensive care unit (ICU) admissions in patients with pre-operative anaemia undergoing non-cardiac surgery.[8] Furthermore, hospital length of stay and ICU admission rates increased with increasing severity of pre-operative anaemia.[8] The increased hospital expenditure generated by these additional bed days and higher level of care may provide financial incentives to introduce robust pre-operative anaemia screening and management clinics.[9,15]

At the core of a patient blood management (PBM) programme is the prevention of allogeneic blood transfusion. PBM programmes adopt an evidence-based approach to the expeditious investigation and treatment of pre-operative anaemia prior to planned surgical procedures as a multidisciplinary effort.[9] The National Blood Authority guidelines recommended healthcare services implement multidisciplinary, multimodal peri-operative patient blood management programmes.[1] These are the most commonly referred to guidelines in Australasia and are in line with other international recommendations.[16] They emphasise the need to improve pre-operative management of anaemic patients—in an ideal setting this assessment would take place more than two weeks before surgery to allow for any latency of treatment with agents such as iron or erythropoietin.[9,17] There is evidence to suggest that early intervention against anaemia is more cost-effective than treating the condition at the time of surgery with a red blood cell transfusion.[18,19] A recent study provided data on the implementation of PBM programmes in four Australian tertiary hospitals. They found that five years after the implementation of PBM programmes, the prevalence of pre-operative anaemia decreased from 20.8% to 14.4%, RBC transfusions decreased by 41% and there were savings of approximately one million dollars over the course of the programme.[10] Despite strong evidence, these initiatives remain uncommon in New Zealand, likely due to resource constraints.

Despite the obvious links between pre-operative iron deficiency anaemia and increased rates of perioperative red blood cell transfusion and impaired perioperative outcomes, there is minimal evidence to suggest that the treatment of iron deficiency anaemia with oral or intravenous iron can lead to improved post-operative outcomes.[17] This may relate to an insufficient treatment window before surgery or the provision of iron in oral form, which is poorly tolerated and not readily absorbed.[17] The lack of outcome data, combined with both the financial and time investment required to establish a robust, multidisciplinary patient blood management programme has meant that uptake has been slow.[9] In 2019 several large prospective studies are scheduled to report their results, which may provide some direction as to whether the identification and treatment of iron deficiency anaemia is a sound use of resources in an era of fiscal constraint.

Our study has several limitations. The retrospective nature reduced the ability to collect some forms of data, meaning that our ability to control for all potential confounding factors was reduced. We were reliant on the accuracy of the routinely collected data from PiMS, laboratory testing and blood transfusion databases. The

data authenticity was reviewed to remove truly spurious values (eg, incorrect year of surgery) however on an individual patient level there was minimal capacity to review paper records to ensure that ICU admissions or additional complications were not missed. This is a single-centre study conducted over a period of 12 months which provides a snapshot of our service provision and patient outcomes, which may not be applicable to other centres due to differences in patient demographics such as ethnicity or patient age.

Patients were only included where a pre-operative haemoglobin recording was available within 30 days before surgery. This may have led to the exclusion of younger and more healthy patients who did not meet criteria for preoperative laboratory testing, meaning our results are skewed towards an older and more comorbid cohort. A report from the ACS-NSQIP database found a haemoglobin recording in more than 90% of patients four weeks before surgery, whereas in the current series only 60% of patients possessed a haemoglobin value in the same time window. This may reflect differing thresholds for investigation prior to surgery between countries. Our data does not differentiate between the numerous causes of anaemia. There are numerous acute and chronic disease processes where iron use may be contraindicated. The WHO definitions of anaemia used in this study have been subject to recent debate around the validity of the chosen thresholds and whether sex-specific differences should continue to exist.[9,20] We chose to use the existing WHO definitions of anaemia to be consistent with other literature in this area.

The use of propensity score matching has given us additional control over potential confounders. We chose to match patient pairs by age, sex, ethnicity, renal function, surgical duration and ASA score to produce two matched cohorts which were stratified by the presence or absence of anaemia. We chose to use surgical duration as a surrogate for operative severity due to frequent errors in coding. Other studies have identified surgical duration as a predictor of infectious complications and increased hospital LOS.[21,22] This was included in the propensity match to reduce confounding. Each of these factors are important predictors of surgical outcomes and in some cases may be linked to the rate of anaemia (eg, those with severe renal dysfunction). By balancing these factors our ability to detect differences in outcomes in relation to the presence or absence of anaemia is enhanced. The use of a precise match tolerance limited the size of the propensity score matched groups. This reduces the power of the analysis. By only selecting one surgical speciality we were able to somewhat reduce the number of potential procedures which were included, making our results more applicable to this patient group.

Conclusion

We have identified a significant burden of anaemia in a patient population undergoing general surgical procedures at a tertiary New Zealand hospital. Anaemia is strongly associated with red blood cell use, which in turn is a significant predictor of adverse post-operative outcomes. Importantly, we found that the effect of blood transfusion was of greater significance to infectious complications than anaemia itself.

This study adds to the body of literature supporting the establishment of pre-operative programmes designed to diagnose, investigate and optimise anaemia prior to surgery. The expeditious management of anaemia without resorting to blood transfusion could prevent complications and save resources. We plan to investigate these findings across other surgical specialities to further refine the risks associated with pre-operative anaemia.

Appendix 1: ICD-10 Infectious Complication Codes

A047	Enterocolitis due to Clostridium difficile
A099	Gastroenteritis and colitis of unspecified origin
A402	Sepsis due to streptococcus, group D
A408	Other streptococcal sepsis
A410	Sepsis due to Staphylococcus aureus
A411	Sepsis due to other specified staphylococcus
A414	Sepsis due to anaerobes
A4151	Sepsis due to Escherichia coli [E. Coli]
A4152	Sepsis due to Pseudomonas
A4158	Sepsis due to other Gram-negative organisms
A418	Other specified sepsis
A419	Sepsis, unspecified
A428	Other forms of actinomycosis
A4901	Staphylococcus aureus infection, unspecified site
A491	Streptococcal infection, unspecified site
A498	Other bacterial infections of unspecified site
B948	Sequelae of other specified infectious and parasitic diseases
B950	Streptococcus, group A, as the cause of diseases classified to other chapters
B951	Streptococcus, group B, as the cause of diseases classified to other chapters
B952	Streptococcus, group D, as the cause of diseases classified to other chapters
B9541	Streptococcus, group C, as the cause of diseases classified to other chapters
B9548	Streptococcus, other specified group, as the cause of diseases classified to other chap-ters
B956	Staphylococcus aureus as the cause of diseases classified to other chapters
B957	Other staphylococcus as the cause of diseases classified to other chapters
B961	Klebsiella pneumoniae [K. pneumoniae] as the cause of diseases classified to other chapters
B962	Escherichia coli [E. coli] as the cause of diseases classified to other chapters
B9639	Haemophilus influenzae [H. influenzae] type not specified, as the cause of diseases classified to other chapters
B964	Proteus (mirabilis)(morganii) as the cause of diseases classified to other chapters
B965	Pseudomonas (aeruginosa) as the cause of diseases classified to other chapters
B966	Bacillus fragilis [B. fragilis] as the cause of diseases classified to other chapters
B9688	Other and unspecified bacterial agents as the cause of diseases classified to other chap-ters
B977	Papillomavirus as the cause of diseases classified to other chapters
B978	Other viral agents as the cause of diseases classified to other chapters

B99	Other and unspecified infectious diseases
J13	Pneumonia due to Streptococcus pneumoniae
J14	Pneumonia due to Haemophilus influenzae
J150	Pneumonia due to Klebsiella pneumoniae
J151	Pneumonia due to Pseudomonas
J155	Pneumonia due to Escherichia coli
J156	Pneumonia due to other (aerobic) Gram-negative bacteria
J180	Bronchopneumonia, unspecified
J181	Lobar pneumonia, unspecified
J189	Pneumonia, unspecified
J22	Unspecified acute lower respiratory infection
L0302	Cellulitis of toe
L0310	Cellulitis of upper limb
L0311	Cellulitis of lower limb
L032	Cellulitis of face
L033	Cellulitis of trunk
L038	Cellulitis of other sites
L020	Cutaneous abscess, furuncle and carbuncle of face
L022	Cutaneous abscess, furuncle and carbuncle of trunk
L023	Cutaneous abscess, furuncle and carbuncle of buttock
L024	Cutaneous abscess, furuncle and carbuncle of limb
L028	Cutaneous abscess, furuncle and carbuncle of other sites
L088	Other specified local infections of skin and subcutaneous tissue
L089	Local infection of skin and subcutaneous tissue, unspecified
M8696	Unspecified osteomyelitis, lower leg
M8697	Unspecified osteomyelitis, ankle and foot
N300	Acute cystitis
N308	Other cystitis
N309	Cystitis, unspecified
R650	Systemic inflammatory response syndrome [SIRS] of infectious origin without acute organ failure
R651	Systemic inflammatory response syndrome [SIRS] of infectious origin with acute organ failure
R652	Systemic inflammatory response syndrome [SIRS] of noninfectious origin without acute organ failure
R653	Systemic inflammatory response syndrome [SIRS] of noninfectious origin with acute organ failure
T845	Infection and inflammatory reaction due to internal joint prosthesis

T846	Infection and inflammatory reaction due to internal fixation device [any site]
T847	Infection and inflammatory reaction due to other internal orthopaedic prosthetic devices, implants and grafts
T8578	Infection and inflammatory reaction due to other internal prosthetic devices, implants and grafts
T8141	Wound infection following a procedure
T8142	Sepsis following a procedure
T835	Infection and inflammatory reaction due to prosthetic device, implant and graft in urinary system
T836	Infection and inflammatory reaction due to prosthetic device, implant and graft in genital tract

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Urinary and faecal incontinence: psychological factors and management recommendations

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ABSTRACT

BACKGROUND: Urinary and faecal incontinence substantially impacts upon physical health and is associated with significant psychological distress and reduced quality of life. Due to stigma and embarrassment, many patients do not present for management of their incontinence.

AIM: The objective of this article is to summarise the forms and causes of urinary and faecal incontinence, highlight the psychological mechanisms and psychopathology associated with incontinence, and provide management recommendations.

CONCLUSION: Urinary and faecal incontinence can have a significant impact on an individual's psychological wellbeing and quality of life. Psychological factors may either contribute to or arise from incontinence and should be addressed as part of the overall management plan.

Urinary incontinence (UI) is defined by The International Continence Society as "the complaint of any involuntary loss of urine".[1] The prevalence of UI has been suggested to be around 3.0% to 60.0% of the population.[2] Faecal incontinence (FI) refers to "the involuntary loss of liquid or solid stool that is a social or hygienic problem".[1,3] The reported prevalence of FI in the general population ranges between 2.2% to 20.7%.[4] Risk factors for incontinence include patient characteristics (eg, obesity), existing urological or gastrointestinal (GI) conditions, obstetric injury/other injuries to pelvic floor, sequelae from surgical procedures and/or radiotherapy, and neurological disease.[3] Treatment-resistant incontinence refer to conditions where symptoms continue despite treatment being provided.[5] While treatment-resistant incontinence poses challenges regarding treatment of symptoms, success has been noted for surgical intervention of stress UI (median cure rate of 82.3%), and pharmacological intervention of urgency UI (median cure rates of 49%).[6] Despite relatively high prevalence, many patients do not present for management of treatable incontinence, which may need to be specifically enquired about in consultation.[7] This may be due to the stigma and embarrassing nature of,[4] or the perception that UI is a normal part of aging.[7,8] Incontinence negatively impacts many aspects of a sufferer's life, including physical health, psychological wellbeing and economic, social and functional domains.[7,9,10] General practitioners (GPs) are ideally positioned to diagnose, treat and support patients with suspected urinary and faecal incontinence, but must be proactive in assessing for the condition.

Forms and causes of incontinence

There are five forms of incontinence (see Table 1), with all forms sharing the common feature of loss of bladder or bowel control. Clinicians should be mindful of the risk factors which can lead to incontinence and have a low threshold for enquiring about the presence of incontinence. Providing a normalising experience and working on strategies to identify and address incontinence symptoms is essential.

Table 1: Types of urinary and faecal incontinence.

Type of incontinence	Urinary[7,11]	Faecal[12]
Urgency incontinence	The sudden, compelling need to pass urine which is difficult to defer.	Faecal incontinence despite attempts to hold on to bowel contents. This may be due to weak/damaged anal sphincter/pelvic floor, to loose stool or to rapid colonic transit.
Overflow incontinence	Urinary incontinence due to sudden increase in intra-abdominal or bladder (detrusor overactivity) pressure in over-distention of bladder.	Presence of stool-stained mucus or constant leakage of loose stool due to severe constipation.
Functional incontinence	Patients who have intact urinary storage functions, but are physically unable to reach bathroom in time to pass urine (eg, due to arthritis)	Faecal incontinence due to inability to manage bowel function or access bathroom in time (eg, due to vision impairment).
Stress urinary incontinence	Urinary incontinence during physical exertion (eg, exercise), or due to coughing or sneezing.	-
Mixed urinary incontinence	Urinary incontinence that is associated with or preceded by urgency urinary incontinence, in addition to physical exertion, coughing or sneezing.	-

Urinary incontinence

Causes of urinary incontinence include pregnancy, labour, vaginal delivery, hysterectomy, and menopause, in addition to diabetes, lower urinary tract symptoms (LUTS) and infections (UTI), advancing age, prostatectomy, and neurological disorders and cognitive dysfunction (eg, dementia, Parkinson's disease, multiple sclerosis, traumatic spinal and/or brain injuries, and cerebrovascular accidents).[13] Urethral obstruction is also a cause of overactive bladder, which may occur secondary to sling and pelvic organ prolapse surgery, as well as prostatic or bladder neck obstruction.[14,15]

Initial assessment of UI symptoms include collection of a medical history, physical examination, laboratory testing and radiographic examination.[16] Specific procedures may involve urinalysis and urine cytology, post-void residual measurement, along with urodynamic testing and pelvic ultrasonography.[16]

Faecal incontinence

Causes of faecal incontinence include sphincter damage, diarrhoea and rapid colonic transit. Overflow incontinence should be considered (hence the importance of the rectal examination with or without abdominal film) as this condition requires specific management (ie, disimpaction). If the stool is watery, the cause of that should be sought, including inflammation, infection, surgery (including cholecystectomy or procedures that shorten the bowel or predispose to bacterial overgrowth), as well as diarrhoea induced by drugs or diet and managed appropriately. If no specific cause can be found, use of a nonspecific antidiarrhoeal and a fibre supplement to bulk and firm the stool up may be effective in treating incontinence, as a loose stool is far more difficult to retain than a formed stool. If symptoms persist referral for pelvic floor assessment is appropriate, and if that is unhelpful,

Table 2: Structured guide for the GP to help explore psychological aspects of urinary and faecal incontinence.

Urinary incontinence	Faecal incontinence
History and examination **Physical:** Explore the onset of symptoms in relation to risk factors; obstetric delivery, pelvic surgery, neurological conditions. Urinalysis and urine cytology, post-void residual measurement, urodynamic testing and pelvic ultrasonography.[16] Questions that could be asked: *What is the pattern of leakage—exertion related suggesting stress incontinence or associated with nocturia and frequent voiding indicating overactive bladder?* *Is leakage associated with poor warning suggesting a neurological mechanism?* *Is it affecting your choice of activities?* *Do you have to wear heavy pads?* *Day and night?* *Number of pads?* Severe incontinence requires a more urgent plan than mild infrequent incontinence that is not affecting activities of daily living nor requiring pads. **Psychological:** Explore current level psychological distress, and links between psychosocial factors (eg, stress, anxiety, behavioural avoidance) and incontinence. Do you experience fear about not making it to a bathroom in time to urinate? Questions that could be asked: *Are you unable to relax if you feel your bladder isn't empty?* *Are your bladder patterns unpredictable?* *Do you worry about being humiliated in public if you lose control of your bladder?* *How does urinary inconsistence impact on your life (including work, family, social activities, and sex)?* **Treatment recommendations** **Physical:** Conservative approaches are usually recommended at first.[21] Stress incontinence may be remedied with physical interventions which could be discussed using the recent Australian Commission on Safety and Quality in Health Care (ACSQHC; http://www.safetyandquality.gov.au/our-work/transvaginal-mesh/resources/care-pathway-sui/) pathways and patient information.[6] **Psychological:** Referral to mental health professional for psychological intervention. Key psychological strategies likely to be of benefit: *Psychoeducation* (educating the patient about how anxiety influences bladder function), *stress/anxiety management* (managing stress through breathing retraining), *cognitive restructuring* (reappraising unhelpful thoughts regarding bladder function) and *in-vivo exposure* (having patient expose themselves to increasingly anxiety-provoking situations, to allow for extinction response to occur).	**History and examination** **Physical:** Rectal examination with or without abdominal film, pelvic floor assessment, anorectal physiological (eg, manometry) and anatomical (eg, endoanal ultrasound) assessment.[17] Questions that could be asked: *Is your bowel incontinence unpredictable? Does it make a difference to your continence whether the bowel motions are loose or firmer?* *Are you troubled by leaking/soiling of clothes or can you lose a large amount?* **Psychological:** Explore current level psychological distress, and links between psychosocial factors (eg, stress, anxiety, behavioural avoidance) and incontinence. Do you experience fear about not making it to a bathroom in time to defecate? Questions that could be asked: *Are you unable to relax if you feel your bowel isn't empty?* *Are your bowel patterns unpredictable?* *Do you worry about being humiliated in public if you lose control of your bowel? How does faecal inconsistence impact on your life (including work, family, social activities and sex)?* **Treatment recommendations** **Physical:** Psyllium supplementation, surgical intervention.[22] Often management to firm up bowel motions/add bulk will be helpful (eg, fibre supplement, loperamide). Be careful of impaction and leakage—do a PR and/or abdominal film to check and if present start with a clean-out. If medications and pelvic floor physiotherapy are not helpful, consider rectal irrigation (eg, Peristeen; Coloplast Pty Ltd). If life is intolerable, a stoma may not be a bad option, but the patient needs to decide (after talking to the stoma nurse and ostomates). **Psychological:** Referral to mental health professional for psychological intervention. Key psychological strategies likely to be of benefit: *Psychoeducation* (educating the patient about how anxiety influences bowel function), *stress/anxiety management* (managing stress through breathing retraining), *cognitive restructuring* (reappraising unhelpful thoughts regarding bowel function) and *in-vivo exposure* (having patient expose themselves to increasingly anxiety-provoking situations, to allow for extinction response to occur).
Example statement that could be used to normalise distress around incontinence and link to psychological treatments: It is very common for individuals who are experiencing incontinence to also feel some anxiety, shame and frustration with its impact on one's life. We also know that psychological stress can make bladder/bowel problems worse. Given this, along with the physical strategies that we are going to put in place to manage your incontinence, I would like you to consider seeing a mental health professional. Mental health professionals can work with you to identify psychological strategies you can implement to reduce the stress and distress and increase your ability to manage living with incontinence. Note: The role of psychological treatments may be particularly helpful where other treatments have failed. In addition to the ongoing physical problem, patients may have to cope with the disappointment of not having the problem cured despite their efforts and expense.	

Note: Psychological treatment questions from the Bladder and Bowel Incontinence Phobia Severity Scale (BBIPSS).[23]

referral for anorectal physiological (eg, manometry) and anatomical (eg, endoanal ultrasound) assessment may be required to determine whether there are any aspects that may benefit from surgical intervention. For information regarding management of incontinence in a residential aged care (RAC) population, see Guinane and Crone.[17]

Psychopathology and associated psychological mechanisms

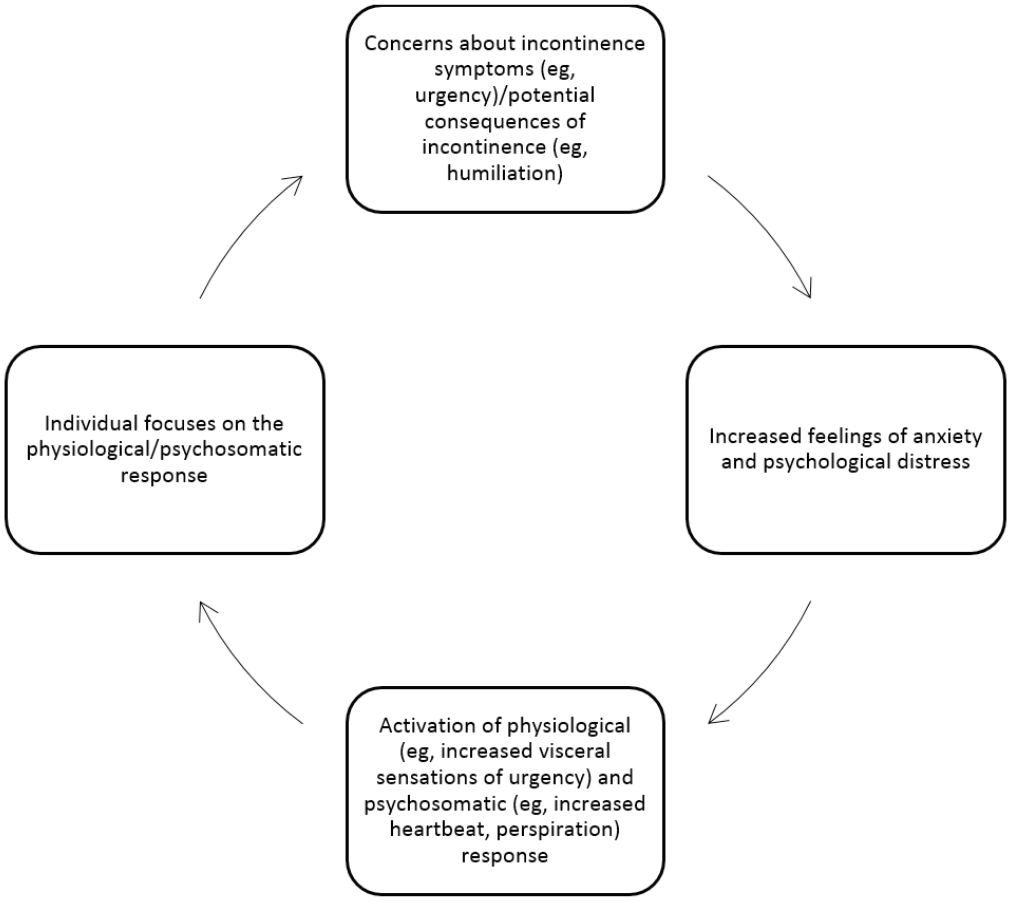
Incontinence is distressing as it is associated with poor health perception, sexual dysfunction and reduced quality of life (QoL).[3,18] Assessment of the psychological impact of incontinence symptoms should be utilised as part of the medical examination for incontinence (see Table 2 for structured guide).[19] In managing these patients, clinicians should also be mindful of associated psychosomatic components of incontinence and the embarrassment and reluctance of patients to seek treatment.[8]

Psychological factors such as depression, anxiety, embarrassment, fear, shame and living with, management of and attitudes about incontinence symptoms have been associated with incontinence.[18,20,21] Literature reviews on the psychosocial impact of UI in women, note that UI is commonly associated with psychological comorbidity.[18,20] In particular, women with severe UI have been reported to be 80% more likely to be significantly depressed, while women with mild to moderately severe UI were noted as 40% more likely to have depression.[22] Likewise, another study found significantly higher levels of major/other depressive syndromes in men and women with UI, compared to individuals who were continent.[21] As for anxiety, a review reported that UI was associated with a 50% increase in risk of anxiety symptoms for both men and women, and a four-fold increase in anxiety prevalence in cases where UI caused functional impairment.[23] A review also found psychosocial factors such as how an individual lives with (eg, the impact of incontinence on intimate relationships, physical activity, social and occupational life), manages (eg, planning and constant vigilance of incontinence symptoms, help-seeking behaviours/disclosure) and their attitudes towards incontinence (eg, negative vs positive perceptions) mediate the relationship between UI and mental health status.[20] Specifically, incontinence patients can better manage their condition by increasing awareness of the psychosocial issues (eg, reframing their attitudes towards incontinence symptoms) that can influence their incontinence and mental health.[20] Conversely, while there are fewer studies which document psychological factors in FI, the depression and anxiety experienced in FI is believed to be greater than that of UI.[23] Indeed, according to a review, individuals with FI are four times more likely to be afflicted with anxiety, and five times more likely to be affected by depression, with FI sufferers also being more likely to report anxiety, frustration and shame.[23] It is apparent that incontinence has a profound negative impact on QoL, whereby sufferers experience humiliation and stigma over their symptoms.[18] Additionally, individuals with incontinence also struggle with anxiety and fear relating to episodes of incontinence in public, and the ensuing consequences.[18] As such, the psychological morbidity associated with incontinence likely stems from reduced QoL due to incontinence symptoms.[18]

During initial examination of incontinence patients, a number of validated measures can be used to assess the nature, severity and impact that incontinence has on QoL. Examples of faecal incontinence measures include the Fecal Incontinence Severity Index (FISI),[24] Cleveland Clinic Florida Fecal Incontinence Score (CCFFIS; also known as the Jorge-Wexner incontinence score),[25] St. Marks Incontinence Score,[26] Comprehensive Fecal Incontinence Questionnaire,[27] Revised Fecal Incontinence Scale[28] and the International Consultation on Incontinence Questionnaire (ICIQ)-Bowels module.[29] As for measures of urinary incontinence severity, examples include the ICIQ-UI Urinary module,[29] the Incontinence Severity Index (ISI),[30] and the Revised Urinary Incontinence Scale (RUIS).[31] Although there are a number of measures available, clinical practice guidelines have recommended commonly used instruments such as the FISI, St. Marks Incontinence Score and CCFFIS.[19] It should also be noted that while several of the abovementioned measures include QoL and lifestyle-based items within their scoring, there are incontinence-specific QoL scales such as the Fecal Incontinence

Quality of Life (FIQL) scale[32] and the Incontinence Quality of Life (I-QOL) instrument[33] for UI. Despite the subjective nature of these self-report instruments, the use of QoL-incontinence measures is recommended as they can assist in selecting appropriate therapies (eg, use of more aggressive, interventional therapies for patients with severe symptoms) and gauge treatment efficacy over time.[19] Consistent with a cognitive-behavioural framework, incontinence patients have been noted to experience dysfunctional thoughts (eg, thinking they are socially undesirable and physically unattractive) along with avoidance behaviours where they avoid social activities which may lead to incontinence or where incontinence would be particularly distressing (eg, exercising, visiting friends).[20] Distress may be significantly increased by of "lack of control or urgency".[20] The relationship between distress and urgency symptoms can be described as a cycle whereby psychological processes perpetuate feelings of incontinence urgency, which lead to development of further psychological symptoms (see Figure 1).[34,35] Concerns about incontinence symptoms (eg, feelings of urgency) and potential consequences of incontinence (eg, public humiliation) can lead to increased feelings of anxiety.[18] This increased anxiety then produces a physiological (eg, visceral sensations of urgency) or psychosomatic (eg, increased heartbeat) response where the individual focuses on somatic stimuli,[36] increasing concerns surrounding incontinence symptoms. Through this cycle, psychological processes exacerbate the physical symptoms of incontinence, which then trigger further anxieties and fears regarding impending incontinence. Accordingly, as well as the physical symptoms of incontinence, associated psychological symptoms should also be monitored.[10] Although there is little formal research about pelvic floor overactivity, there is an increasing awareness of this construct and incontinence may be a manifestation of this anxiety driven disorder.[37]

Figure 1: Cycle of incontinence symptoms and psychological distress.



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A notable psychogenic condition that can result from incontinence is bladder and bowel incontinence anxiety. Bladder and bowel incontinence anxiety refers to overwhelming fear of incontinence in a public setting, in the absence of physical illness.[34] Primary clinical features include overwhelming fear of incontinence; repeated checking of sensations in the bladder or bowel; reoccurring, intense visceral sensations of urgency; avoidance of anxiety-provoking situations (eg, travelling long distances without access to a restroom); and compulsive urination or defecation.[34,38–40] While prevalence rates for incontinence have been reported, the prevalence of bladder and bowel incontinence anxiety has yet to be clearly identified. The recently developed Bowel Incontinence Phobia Severity Scale (BBIPSS)[41] will help better assess fear relating to bowel and bladder incontinence and help to explore the prevalence and severity of psychopathology surrounding incontinence anxiety.

Management recommendations

A systematic review by Forte and colleagues[42] on FI treatment reported low-strength evidence for certain non-surgical treatment (eg, psyllium supplementation), while also noting insufficient evidence on all available surgical treatment. The review concluded that surgical treatment was associated with greater complications and adverse effects compared to non-surgical management, and that limited evidence was present to support treatment beyond three to six months.[42] Conversely, a recent systematic review on UI cure rates noted that surgical intervention was effective for stress UI, with open colposuspension displaying a median cure rate of 32%, and other surgical techniques displaying a cure rate of 82.3%.[6] For urgency UI, pharmacological intervention had a median cure rate of 45.8%.[6] Supervised pelvic floor muscle therapy (PFMT) interventions were noted to display a cure rate of 35% at 12 months.[6] For mixed UI, the median cure rate of surgical intervention in women was 82.3%, with supervised PFMT intervention eliciting a cure rate of 47% in men and 28% in women at six months.[6] While physical characteristics of incontinence are routinely explored in consultations, psychosocial aspects of incontinence tend to be overlooked.[20] Factors such as attitudes towards, living with and management of incontinence have been reported to contribute towards the relationship between incontinence and mental health.[20] Given the significant bi-directional links between distress and incontinence (eg, incontinence causing distress and distress affecting coping behaviours in people with incontinence), evidence-based psychological interventions such as Cognitive Behavioural Therapy (CBT)[43] should be considered in the psychological management of incontinence, especially when symptoms are associated with treatment-resistant incontinence.

Summary

Urinary and faecal incontinence significantly impact the physical health and mental wellbeing of those afflicted. While the prevalence of urinary and faecal incontinence has reported to range between 3.0% to 60.0% and 2.2% to 20.7% respectively, due to the stigma and embarrassing nature of symptoms, patients hesitate to raise incontinence issues during consultations, and these may need to be specifically enquired about. Clinicians should be mindful of risk factors associated with incontinence along with the psychosocial impact of incontinence on mental health and QoL. Treatment interventions should be tailored to the pattern of symptoms, underlying causes/contributors, individual needs and circumstances of each patient. Where appropriate, psychological interventions should be utilised to facilitate patient management of symptoms, especially in cases involving psychological distress and/or treatment-resistant incontinence.

Key points

- There are several forms of urinary and faecal incontinence.
- Due to the stigma and embarrassing nature surrounding incontinence, patients may be reluctant to disclose their symptoms.
- General practitioners should provide a normalising experience for the patient and proactively identify and address incontinence symptoms.
- Urinary and faecal incontinence are often associated with significant psychological symptoms, which may in turn lead to an increase in physical symptoms and reduction in quality of life.

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Nil.

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Patient-reported quality of life for cataract surgery: prospective validation of the 'Impact on Life' and Catquest-9SF questionnaires in New Zealand

Sunny S Li, Stuti L Misra, Henry B Wallace, Lyn Hunt, James McKelvie

ABSTRACT

AIMS: The 'Impact on Life' (IoL) questionnaire is used to prioritise publicly funded cataract surgery in New Zealand, however, it has not been formally validated for ophthalmic use. The Catquest-9SF questionnaire is widely used to assess vision-related quality of life (VRQoL) but has not been validated in New Zealand. This study evaluates the validity of the IoL and Catquest-9SF questionnaires for measuring VRQoL in New Zealand.

METHOD: Formal ethics approval was obtained. Participants completed the IoL and Catquest-9SF questionnaires before and three months after routine cataract surgery. Rasch analysis was used to investigate all qualitative questionnaire responses. Results were correlated with the change in patient visual acuity.

RESULTS: There was a 100% response rate at follow-up (41 participants). Disordered probability thresholds were observed for all IoL questions but no Catquest-9SF questions. All IoL questions demonstrated unsatisfactory mean-square fit statistics. Differences in visual acuity following surgery correlated with the change in total F-score for the Catquest-9SF (P=0.04), but not IoL responses (P=0.17).

CONCLUSIONS: Disordered probability thresholds, poor question-model fit and correlation with visual acuity changes indicate the current IoL questionnaire is poorly suited for assessment of VRQoL. In contrast, the Catquest-9SF demonstrated credible results for assessment of VRQoL in New Zealand.

Cataract surgery is the most frequently performed surgical procedure in New Zealand with approximately 16,500 publicly funded cataract surgeries completed annually.[1–3] With limited resources for publicly funded surgery, prioritising patients for cataract surgery is essential to enable equal access to surgery for all New Zealand residents and ensure those who are most likely to benefit from surgery are prioritised highest. The New Zealand public health system currently utilises a standardised Clinical Priority Assessment Criteria (CPAC) that involves priority scoring to determine patient eligibility for publicly funded elective surgical services including cataract surgery.[4] The CPAC system aims to improve equity of access to surgical services across New Zealand, enhance transparency around prioritisation for surgery and improve certainty regarding treatment for patients who require surgery.[5]

Prioritisation for cataract surgery in New Zealand using the CPAC system is based on weighted scores for patient responses to the Impact on Life (IoL) questionnaire, best corrected visual acuity (BCVA) and cataract morphology.[6] The IoL questionnaire is intended to quantitatively score patient-reported functional status in six qualitative domains that include safety, social interactions, responsibility to others, personal relationships, personal care and leisure activities. The IoL questionnaire was not designed specifically for use with cataract or ophthalmic surgery, and was initially developed for prioritisation in orthopaedic and other surgical specialities.[7] Despite the national adoption of the IoL as an integral component of CPAC prioritisation for cataract surgery in New Zealand, the ability of the IoL questionnaire to assess vision-related quality of life (VRQoL) has not been formally assessed.

The use of patient-reported measures has gained wide acceptance in ophthalmology following development of cataract-related visual disability questionnaires.[8–10] The International Consortium for Health Outcomes Measurement (ICHOM) has convened global groups of experts and patient representatives to outline minimum standard outcomes using a structured process for a variety of specific conditions including cataract based on evidence-based measures to assess quality of life related to vision.[11] The resulting Catquest-9SF questionnaire has been extensively validated as an accurate tool for assessment of patient-reported visual disability for patients undergoing cataract surgery.[12] The Catquest-9SF is well suited for use in clinical practice due to its validity, brevity and ease of use, however, this questionnaire has not been validated in a New Zealand population.[13]

The aim of the current study is to validate and compare the ability of the IoL and the Catquest-9SF to measure VRQoL for New Zealand patients undergoing cataract surgery.

Methods

Formal approval from the New Zealand Health and Disability Ethics Committee was obtained prior to patient recruitment (16/CEN/132), and this study was registered with the Australian New Zealand Clinical Trials Registry (12616001593426). This is a prospective observational cohort study involving patients enrolled for routine cataract surgery at Greenlane Clinical Centre, Auckland District Health Board, New Zealand.

Patients who were referred for publicly funded surgery at Auckland District Health Board were invited to participate in the study. Patients who agreed to participate in the study completed both questionnaires before surgery and at again three months following surgery. All patients completed the IoL and Catquest-9SF questionnaires while the clinician was not in the room and the questionnaires were collected by an independent investigator.

The six-question IoL questionnaire requires patients to score the degree of difficulty that poor vision affected their social interactions, personal relationships, ability to meet responsibilities to others, personal care, personal safety and leisure activities using an ordinal scale (Figure 1). For each question on the IoL questionnaire, patients are required to select one option from a scale labelled 'no difficulty', 'little difficulty', 'some difficulty', 'quite difficult', 'very difficult' and 'extremely difficult'.

The Catquest-9SF is composed of three sections that require patients to select an option from a five-point Likert scale including one option of 'cannot decide' (Figure 1). The questions included: "Do you find that your sight at present in some way causes you difficulty in your everyday life?"; "Are you satisfied or dissatisfied with your sight at present?"; "Do you have difficulty with the following activities because of your sight?". This last question allowed patients to label their satisfaction with vision in various contexts: reading text in newspapers; recognising the faces of people they meet; seeing the prices of goods when shopping; seeing to walk on uneven surfaces eg, cobblestones; seeing to do handicrafts/woodwork; reading subtitles on television; and seeing to engage in an activity/hobby of interest.

All surgery, and assessments before and after surgery, were completed by a single surgeon who performed the operation using standardised surgical technique, intraocular lens and emmetropic refractive target.

Figure 1A: The Impact on Life questionnaire, currently used in the Clinical Priority Assessment Criteria (CPAC) to determine patient eligibility for publicly funded elective cataract surgery in New Zealand.

Patient Impact on Life Questionnaire

We are interested in the degree of difficulty your condition places on your (or your child's) life or how it may limit your (or your child's) quality of life. Please focus on the general concept asked about in each question below. The examples given after each are simply to illustrate what the concept might mean - it doesn't matter that some of these examples don't apply to you. We do not want you to respond to the specific examples, just to think about the general concept, whatever that means for you (or for your child).

Please circle the number, which most represents the impact of your condition on this aspect of your life.

Social Interaction (Meeting friends, going out, joining in groups, going shopping, every day activities **outside** the home)

No difficulty	Little difficulty	Some difficulty	Quite difficult	Very difficult	Extremely difficult
1	2	3	4	5	6

Personal Relationships (Potential intimate social relations; with partner, family members, close personal friends)

No difficulty	Little difficulty	Some difficulty	Quite difficult	Very difficult	Extremely difficult
1	2	3	4	5	6

Ability to fulfill your responsibilities to others
(Do meaningful things for yourself or others; including caring for children, grandchildren, partner, employment (both paid and unpaid), including any impact of dependence on others)

No difficulty	Little difficulty	Some difficulty	Quite difficult	Very difficult	Extremely difficult
1	2	3	4	5	6

Personal care (Looking after yourself, your health, personal hygiene, need for special clothing)

No difficulty	Little difficulty	Some difficulty	Quite difficult	Very difficult	Extremely difficult
1	2	3	4	5	6

Personal safety (Being safe from harm; from yourself, or others, and in your surroundings)

No difficulty	Little difficulty	Some difficulty	Quite difficult	Very difficult	Extremely difficult
1	2	3	4	5	6

Leisure activities (Sporting activities, getting exercise, hobbies, gardening, DIY activities, crafts, travel)

No difficulty	Little difficulty	Some difficulty	Quite difficult	Very difficult	Extremely difficult
1	2	3	4	5	6

Figure 1B: The Catquest-9SF questionnaire, developed by the International Consortium for Health Outcomes Measurement to assess quality of life related to vision as a result of cataracts.

Catquest-9SF Questionnaire

A. Do you find that your sight at present in some way causes you difficulty in your everyday life?

Yes, very great difficulty	Yes, great difficulty	Yes, some difficulty	No, no difficulty	Cannot decide
☐	☐	☐	☐	☐

B. Are you satisfied or dissatisfied with your sight at present?

Very dissatisfied	Fairly dissatisfied	Fairly satisfied	Very satisfied	Cannot decide
☐	☐	☐	☐	☐

C. Do you have difficulty with the following activities because of your sight?

If so, to what extent? In each row place just one tick in the box which you think best corresponds to your situation.

	Yes, very great difficulty	Yes, great difficulty	Yes, some difficulty	No, no difficulty	Cannot decide
Reading text in newspapers	☐	☐	☐	☐	☐
Recognising the faces of people you meet	☐	☐	☐	☐	☐
Seeing the prices of goods when shopping	☐	☐	☐	☐	☐
Seeing to walk on uneven surfaces, e.g. cobblestones	☐	☐	☐	☐	☐
Seeing to do handicrafts, woodwork etc.	☐	☐	☐	☐	☐
Reading subtitles on TV	☐	☐	☐	☐	☐
Seeing to engage in an activity/hobby that you are interested in	☐	☐	☐	☐	☐

Thank you very much for taking part.

Statistical analysis

A group of statistical models termed the Item Response Theory (IRT) have been developed to instrument questionnaire development, evaluation and refinement. This framework analyses individual components of a questionnaire by a set of properties that describe the relationship of the questionnaire with the underlying construct measured by the model, in addition to how well individual questions fit with respect to the underlying construct. IRT is not dependent on the sample of respondents.[14,15] This allows researchers to identify the questions that can most accurately measure the intended purpose of the questionnaire.

The Rasch model is a robust and commonly used form of IRT which can be used to assess functioning of rating scale categories within the Catquest-9SF and IoL questionnaires. This is a mathematical framework that takes into account the ability of participants, the difficulty of questions in the questionnaire, and assumes equal discriminating ability across all questions.[16] In the Rasch model, the probability of a particular response to a specific question can be modelled as a logistic function of the difference between the person's ability (measured by using test questions) and the difficulty of the items being asked.[17]

All IoL and Catquest-9SF question responses were assessed using the Rasch model to assess the validity of the questions in quantifying VRQoL. If responses to a question successfully fit the Rasch model, it provides evidence that this question adequately measures VRQoL. Two types of mean square fit statistics (infit and outfit) were used to evaluate how well patient responses fit the Rasch model for all of the questions within the IoL and Catquest-9SF questionnaires. Infit and outfit statistics have a chi-square distribution and provide an index of magnitude for the degree of misfit of a question with the model. These fit statistics have an expected value of 1 and suggested acceptable lower and upper thresholds of 0.5 and 1.5 respectively.[18] Fit statistics for each question were calculated using an average of the squared residuals between the observed and expected responses from the Rasch model. The infit statistic is an estimate that gives more weight to individual variance of questionnaire responses to minimise the impact of unexpected responses far from the mean. Conversely, the outfit statistic is an unweighted estimate of the average question response variance within the IoL and Catquest-9SF questionnaires, and is more likely to be influenced by unexpected responses.

All statistical analyses were completed using R software.[19] IoL questionnaire data were coded 1–6 representing the options of 'no difficulty', 'little difficulty', 'some difficulty', 'quite difficult', 'very difficult' and 'extremely difficult', respectively. Catquest-9SF questionnaire data were coded 1–5 representing the options of 'no difficulty', 'some difficulty', 'great difficulty', 'very great difficulty' and 'cannot decide', respectively. The *mirt* package was used to fit models for item response theory analysis.[20] Preoperative and postoperative data were combined for model fitting. The corrected Akaike information criterion (AICc) is an estimator of the relative quality of statistical models for a given set of data, and was used to select the best model. The G–test of goodness-of-fit was used to determine if the final model accurately predicted the data. Normalised factor scores for both questionnaires were correlated with visual acuity in the operated eye and age using Pearson's product-moment correlation. Secondary analyses of normalised factor scores by ethnicity and gender were performed using analysis of variance. A qualified statistician reviewed all statistical methodology and analyses used in this study.

Results

Forty-one patients undergoing cataract surgery were enrolled in the study from March to May 2017. All patients who were approached consented to inclusion in the study and completed the questionnaire at both time points. The mean patient age was 77±8 years (sd), with 20 (49%) female participants. Ethnicity included New Zealand European 29 (71%), Māori 3 (7%), Pacific Island 1 (2%), Asian 4 (10%), Indian 3 (7%), and 'Other' 1 (2%). Table 1 shows the preoperative and postoperative visual acuities and spherical equivalent for the patient cohort.

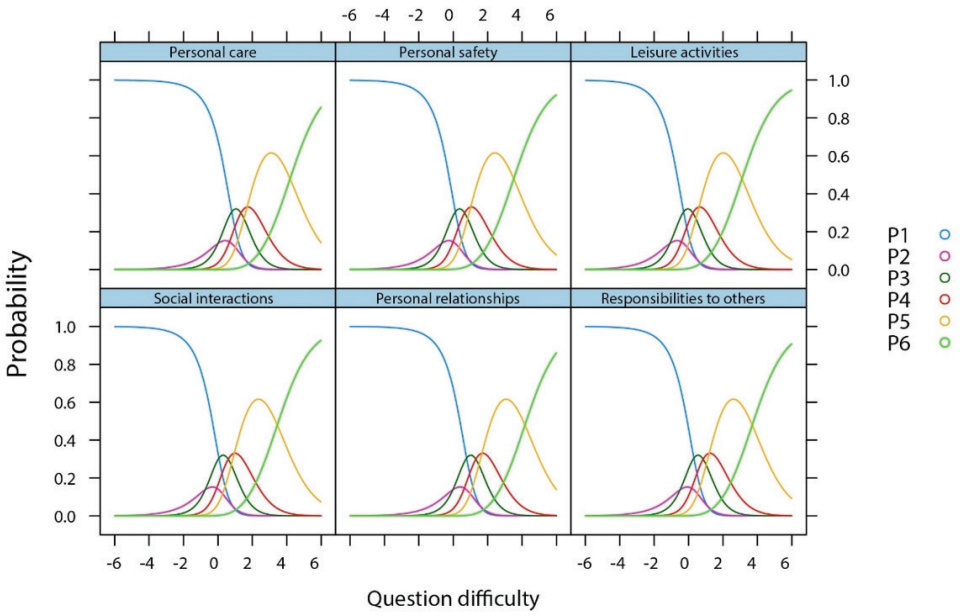
Table 1: Visual acuity and spherical equivalent of 41 patients before and following cataract surgery.

		UCVA	BCVA	SPE
Preoperative	Mean	0.64	0.45	-0.08
	Minimum	0.18	0.18	-11.63
	First quartile	0.40	0.30	-1.16
	Median	0.54	0.30	0.31
	Third quartile	0.88	0.48	1.72
	Maximum	2	2	4.38
Postoperative	Mean	0.06	0.03	-2.07
	Minimum	-0.12	-0.12	-9.13
	First quartile	0	0	-2.34
	Median	0	0	-1.88
	Third quartile	0.1	0	-1.5
	Maximum	0.54	0.18	-0.75

UCVA = uncorrected visual acuity, BCVA = best corrected visual acuity, SPE = refractive error (spherical equivalent) in dioptres. Spherical equivalent = sphere power + (cylinder power x 0.5). Postoperative visual acuity was measured at three months following cataract surgery and all visual acuity was represented in logMAR notation.

Figure 2A: Rasch model category probability curves for the Impact on Life questionnaire.

A



These curves summarise the probability (y-axis) that a patient with visual difficulty (x-axis) would answer with a given response. P1 to P6 represents the question response options; P1 = no difficulty, P2 = little difficulty, P3 = some difficulty, P4 = quite difficult, P5 = very difficult, P6 = extremely difficult.

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Figure 2B: Category frequency responses for 41 patients who completed the Impact on Life questionnaire before surgery (pink) and three months following surgery (blue).

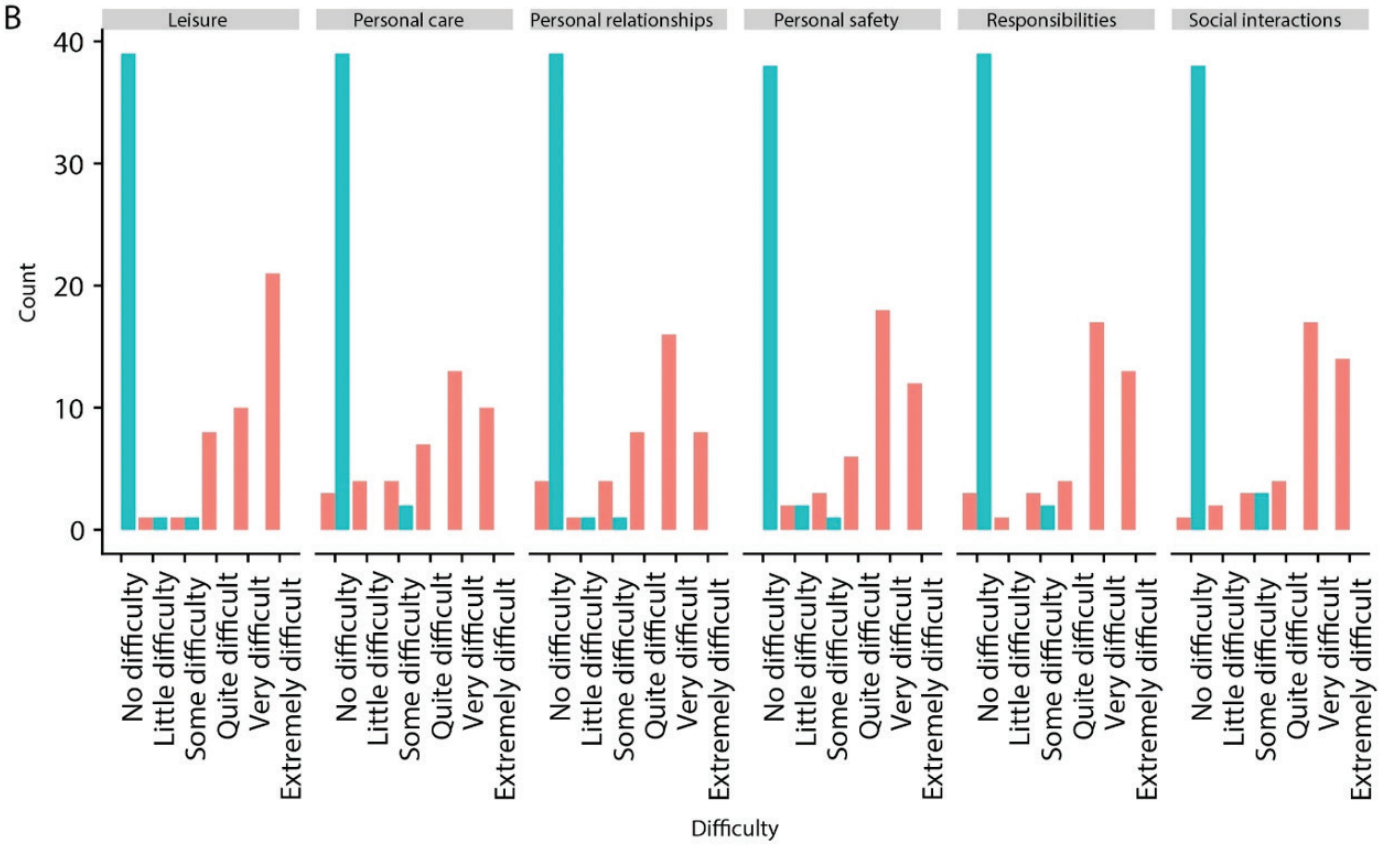


Table 2: Summary of Rasch model fit statistics for the Impact on Life (IoL) questionnaire. The sample includes responses from 41 patients preoperatively and at three months following cataract surgery.

Impact on Life questions	Outfit mean square	Outfit z-score	Infit mean square	Infit z-score
How much does your condition affect your social interactions?	0.29	-2.56	0.47	-3.16
How much does your condition affect your personal relationships?	0.27	-1.61	0.46	-3.38
How much does your condition affect your ability to meet your responsibilities to others?	0.34	-1.98	0.60	-2.21
How much does your condition affect your personal care?	0.22	-1.91	0.38	-4.06
How much does your condition affect your personal safety?	0.29	-2.41	0.44	-3.42
How much does your condition affect your leisure activities?	0.36	-2.54	0.60	-2.21

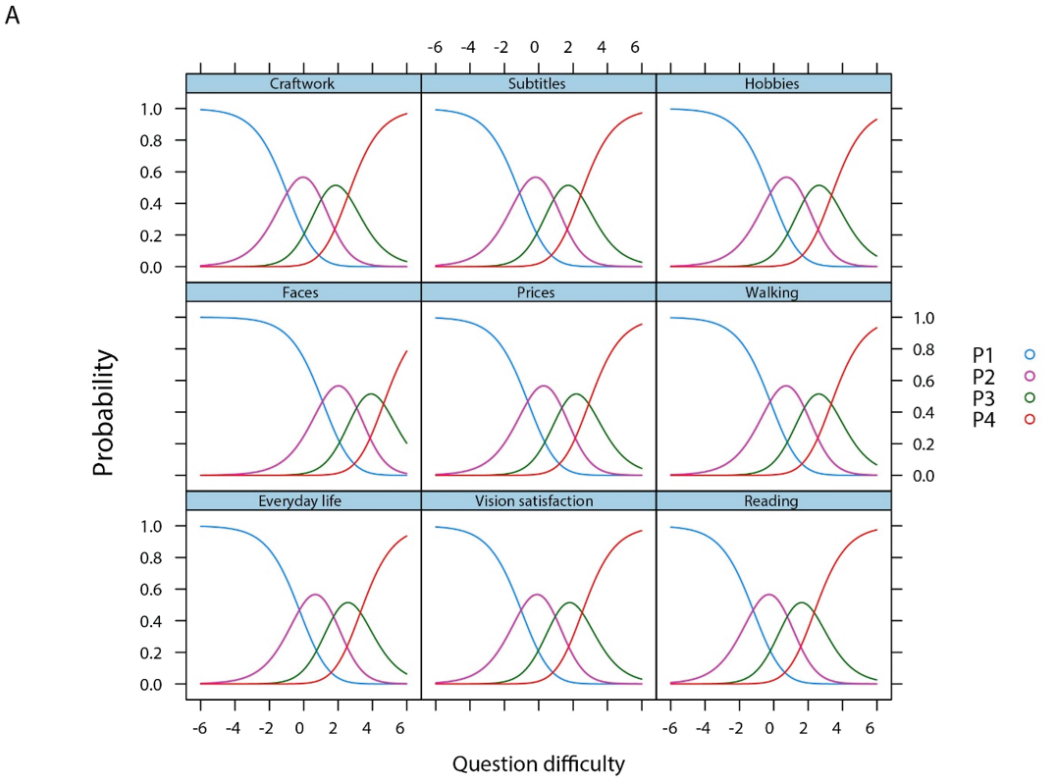
Table 3: Summary of Rasch model fit statistics for the Catquest-9SF questionnaire from International Consortium for Health Outcomes Measurement (ICHOM). The sample includes responses from 41 patients preoperatively and at three months following cataract surgery.

Catquest-9SF questions	Outfit mean square	Outfit z-score	Infit mean square	Infit z-score
Do you find that your sight at present in some way causes you difficulty in your everyday life?	0.57	-1.16	0.75	-1.36
Are you satisfied or dissatisfied with your sight at present?	0.79	-0.64	1.13	0.70
To what extent do you have difficulty with reading text in newspapers?	0.64	-1.37	0.71	-1.59
To what extent do you have difficulty with recognizing the faces of people you meet?	0.43	-0.74	0.67	-1.76
To what extent do you have difficulty with seeing the price of goods when shopping?	0.44	-2.00	0.62	-2.22
To what extent do you have difficulty with seeing to walk on uneven surfaces, eg, cobblestones?	0.55	-1.20	0.74	-1.40
To what extent do you have difficulty with seeing to do handicrafts, woodwork etc?	0.54	-1.71	0.82	-0.92
To what extent do you have difficulty with reading subtitles on TV?	0.48	-2.10	0.67	-1.89
To what extent do you have difficulty with seeing to engage in an activity/hobby that you are interested in?	0.56	-1.17	0.73	-1.47

The model fit statistics for the Catquest-9SF responses are summarised in Table 3. 'Cannot decide' responses on the Catquest-9SF questionnaire represented 7 of 738 responses (0.95%) and were assumed equivalent to data missing at random for analysis. Apart from 'recognising faces', 'seeing price of goods when shopping' and 'ability to read TV subtitles' (mean-square fit statistics 0.43, 0.44 and 0.48 respectively), all other Catquest-9SF questions were within the range suitable for measurement (mean-square outfit statistic 0.5 to 1.5). The graphical Rasch categorical probability curves for the Catquest-9SF questions are summarised in Figure 3A. The category frequency of each response in the IoL questionnaire is summarised in Figure 3B.

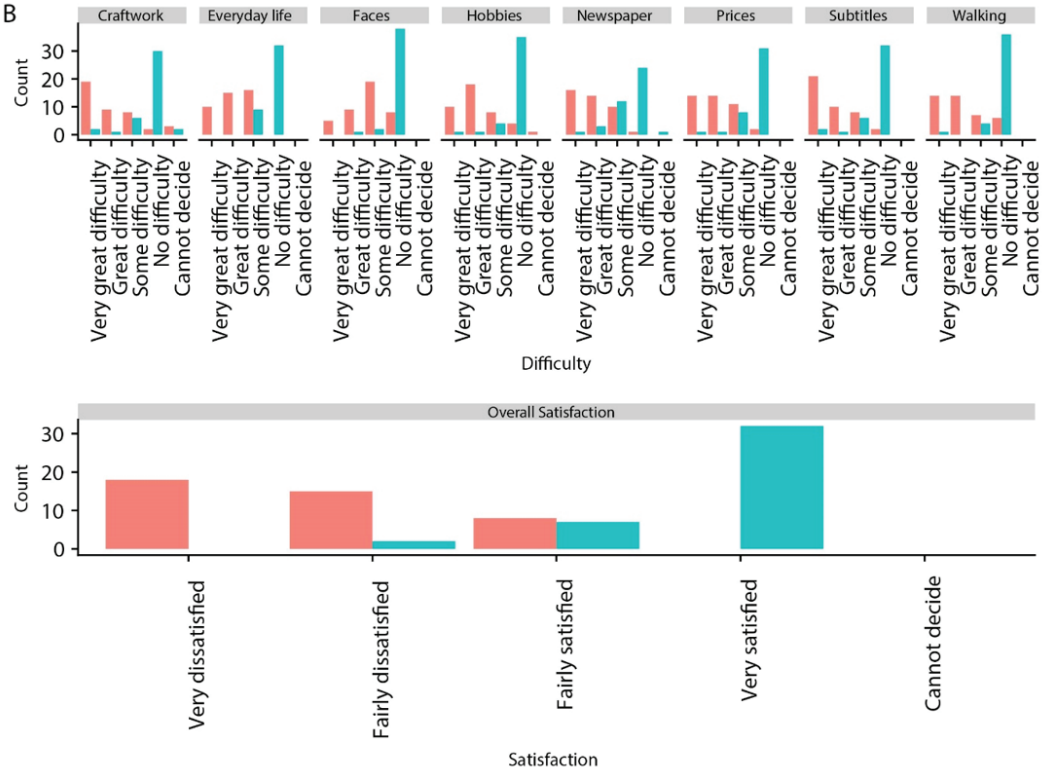
The difference in visual acuity before and after surgery correlated with the change in total F-score for the Catquest-9SF responses (P=0.04), but not the IoL responses (P=0.17). The overall questionnaire score in both IoL and Catquest-9SF questionnaires correlated with worsening visual acuity (P<0.001). There were no statistical differences in quality of life scores between ages or ethnic groups for both questionnaires. The change in F-score was not significantly different for patients who received cataract surgery on their first eye or second eye.

Figure 3A: Rasch model category probability curves for the Catquest-9SF questionnaire from International Consortium for Health Outcomes Measurement.



These curves summarise the probability (y-axis) that a patient with visual difficulty (x-axis) would answer with a given response. A higher number of question difficulty indicates greater disability (6 = extremely difficult; -6 = no difficulty). P1 to P4 represents the question response options; P1 = no difficulty; P2 = some difficulty; P3 = very difficult; P4 = extremely difficult.

Figure 3B: Category frequency responses for 41 patients who completed the Catquest-9SF questionnaire before surgery (pink) and three months following cataract surgery (blue).



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Discussion

The current study uses Rasch analysis to evaluate the validity of the IoL and Catquest-9SF questionnaires for quantifying VRQoL for cataract surgery patients in New Zealand. As far as the authors are aware, this is the first study to statistically assess the validity of the IoL questionnaire for use in cataract surgery, and the first study to compare the IoL with any other questionnaire to assess VRQoL.

The unequal peaks noted in the Rasch analysis for the IoL questionnaire suggest that the response options of 'no difficulty', 'little difficulty', 'some difficulty', 'quite difficult', 'very difficult' and 'extremely difficult', are too numerous and ideally should be collapsed into fewer options with more consistent probability thresholds. This finding was consistent for all six questions in the IoL questionnaire. In contrast, the Catquest-9SF demonstrated relatively uniform peak height for the question response options that remained consistent for all questions in the Catquest-9SF questionnaire, similar to previous studies.[21]

The IoL questionnaire demonstrates category disordering on Rasch analysis. Category disordering occurs when the ordinal numbering of categories (response options) does not correspond with their substantive meaning. The IoL questionnaire ordered response options are substantively defined to represent increasing levels of disability in VRQoL. In all six questions, there is substantive and step disordering such that 'little difficulty' consistently locates below 'no difficulty' in the Rasch analysis. This finding suggests that the response options used in the IoL questionnaire are not able to accurately discriminate increasing impairment in VRQoL as intended.

The IoL questionnaire demonstrated unsatisfactory statistical fit of almost all questions (mean-square fit less than 0.5). This finding indicates less variation in participant responses than expected, and that responses are more predictable than the Rasch model expects. The high predictability of responses to IoL questions and overfit to the Rasch model suggests sub-optimal question wording resulting in non-discriminatory patient responses.[22] This finding suggests that the IoL questionnaire is likely to lack the required sensitivity to accurately rank patients based on VRQoL.

Catquest-9SF questions demonstrated satisfactory mean fit squares and appropriate category response curves with monotonic increases and decreases in the category thresholds (Figure 3A). This finding was consistent with other studies evaluating the Catquest-9SF using Rasch analysis in Europe and Australia.[21,23] These results confirm that the Catquest-9SF questionnaire is valid tool for the assessment of VRQoL in a New Zealand population and can accurately rank patients based on VRQoL.

Questionnaire scores for the Catquest-9SF and the IoL improved with the improvement in visual acuity following surgery. Only the Catquest-9SF questionnaire, however, demonstrated significant correlation between the change in visual acuity and change in questionnaire F-scores following surgery. The F-score is a single indicator that summarises the variance (accuracy and recall ratio) of data points around the mean, which can be used to evaluate and compare the fit of multiple linear models.[24] Based on these results, the IoL questionnaire responses appear to be independent to VRQoL and poorly suited for predicting which patients will experience quality of life gains as a result of improved vision following cataract surgery.

There are several limitations to this study. Firstly, patient bias may influence questionnaire responses. Patients may suspect that preoperative questionnaire responses could affect their eligibility for surgery and bias towards over-reporting poor quality of life prior to surgery or after surgery where second eye surgery is required. The lack of significant difference in F-scores between patients receiving first or second eye cataract surgery, however, suggests similar degrees of variance in responses indicating no such bias exists in this data. Secondly, the current study has a relatively small sample size. Reports of Rasch analysis results are considered to be robust to smaller sample size.[25] In addition, despite the small sample size, the current study was able to replicate similar findings to previous, larger studies evaluating the Catquest-9SF.[21,23]

The primary strength of this study is analysis of the qualitative responses using Rasch analysis. The importance of Rasch analysis has been well-recognised for the evaluation of questionnaire quality and there have been numerous requests for the development of Rasch-approved questionnaires within ophthalmology.[26–28] The current study offers the first Rasch assessment of the IoL questionnaire. This questionnaire is currently in widespread use to assess eligibility for all patients in the New Zealand public health system that require cataract surgery.

In summary, the current study compared the ability of IoL and Catquest-9SF questionnaires to accurately measure VRQoL. The results of this study demonstrate that the IoL does not accurately assess VRQoL for patients that require cataract surgery in New Zealand. The Catquest-9SF is a domain-specific assessment tool that can accurately measure VRQoL in New Zealand. The convenience of using a single tool, such as the IoL, to allocate healthcare resources across multiple specialities must be carefully weighed against the risk of not allocating resources where they are needed the most.

Despite its widespread use, the current study highlights inadequacies of the IoL questionnaire for the assessment of VRQoL for cataract surgery in New Zealand. In addition to any role in surgical prioritisation, it is increasingly important for quality improvements in healthcare delivery to use standardised patient reported outcome tools, such as the Catquest-9SF. These standardised tools enable international benchmarking and direct comparison with other studies. In conclusion, the Catquest-9SF questionnaire provides a more accurate assessment of VRQoL than the currently used IoL questionnaire for New Zealand patients that require cataract surgery.

Competing interests:
Nil.

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Infectious pulmonary tuberculosis in a New Zealand cancer centre

James Chancellor, Julianna Lees, Kate Grimwade, Neil de Wet, Lynnette Borissenko

ABSTRACT

This report details the investigation of oncology and haematology patients, as well as cancer centre staff, friends and family who were exposed to an oncology patient with reactivated pulmonary tuberculosis (TB) in a New Zealand cancer centre. A total of 46 patients, seven staff members and 14 family and friends were identified as being exposed to the index case of TB (Mr K). These people were screened for TB infection by the use of a symptom questionnaire, Qiagen QuantiFeron (QFT)® Gold Plus test and, if potentially immunocompromised, a chest x-ray (CXR). There were no confirmed secondary cases of TB in any of the groups screened for infection, but surveillance for signs and symptoms of TB disease in those with significant risk is ongoing. In this article we discuss the public health response to TB in a cancer centre and potential preventative strategies for the future.

Mr K is a 67 year old Māori male who was a heavy smoker and presented with substantial weight loss (15kg in six months), central abdominal pain and melaena for two weeks. He had no significant past medical history or known TB contact. He was diagnosed with gastric cancer on gastroscopy. A staging positron emission tomography-computed tomography (PET-CT) scan showed the cancer was confined to the stomach without any lymph node involvement. The PET-CT scan also demonstrated some non-specific inflammatory changes in the left lung upper lobe, which were thought to be due to a concurrent chest infection at the time of the PET-CT. A staging laparoscopy confirmed no spread of the cancer outside the stomach. He commenced neoadjuvant FLOT (5-Fluorouracil, Folinic acid, Oxaliplatin, Docetaxel) chemotherapy, administered fortnightly at the hospital's cancer centre, with the aim of curative intent following a gastrectomy.

He tolerated the first cycle of chemotherapy well. However, the second cycle of chemotherapy was delayed due to worsening of his chronic 'smoker's cough'. This cough partially improved without further investigation or intervention. He received two further cycles of chemotherapy. A repeat PET-CT scan to assess treatment response revealed reduction in the size of the gastric cancer but worsening parenchymal change and new cavitating lesions in the left upper lobe, suggestive of pulmonary TB. He underwent an urgent bronchoscopy. Spontaneously produced sputum and bronchial washings were both strongly positive for acid fast bacilli on Ziehl–Neelsen stain, and cultures grew *Mycobacterium tuberculosis* within four days. He was commenced on anti-TB therapy while awaiting sensitivities. Sensitivities later showed the organism to be fully sensitive to first-line agents. He went on to have an uneventful and successful treatment of his pulmonary TB. His gastric cancer initially responded to the chemotherapy and surgery, with no evidence of disease recurrence a year after his surgery. However, in May 2019 he presented again to hospital with abdominal pain. A repeat CT abdomen demonstrated recurrence of his gastric cancer with intraabdominal metastatic disease. Mr K sadly died from metastatic gastric cancer in June 2019.

Public health investigation

The risk of healthcare-associated infection and the vulnerability of the exposed patient population was immediately recognised. The Medical Officer of Health was notified and an interdepartmental response group was formed to manage the incident.

The aim of the response was to minimise the risk of further exposure to TB, and also identify, screen and test for TB infection in anyone with significant contact. Contacts were also provided with information and advice about the symptoms of TB, and what to do should they experience these symptoms.

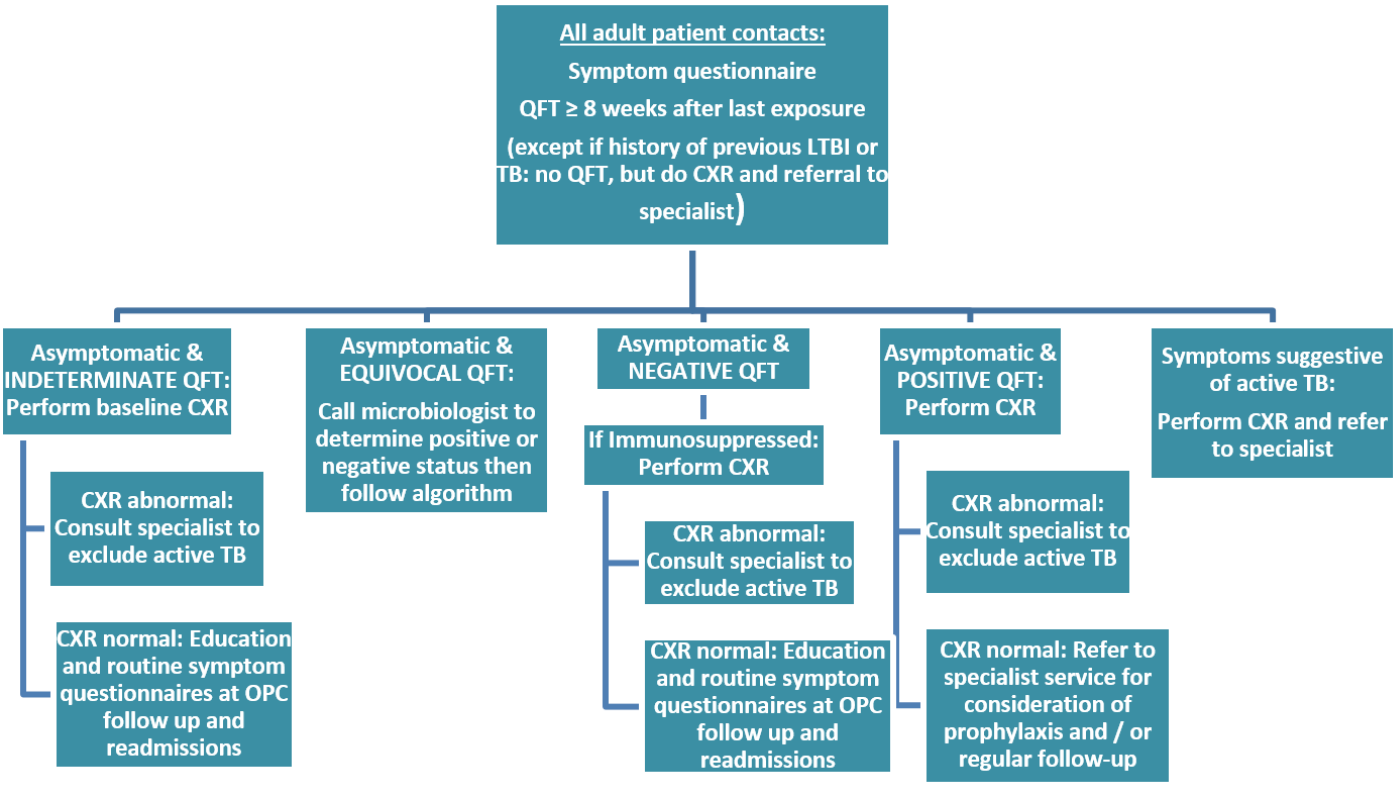
The cancer centre is an open ward with dimensions of 21 metres long by 5 metres wide and 2.4 metres high. It has 10 armchairs and one bed for patients, which encircle the perimeter of the room. Each armchair is separated by approximately two metres. Patients sit in these armchairs while receiving chemotherapy. There are curtains surrounding one of the armchairs and the bed, but these are seldom used.

Patient and staff records were sourced to establish the estimated duration of exposure to Mr K by staff and patients. An algorithm used in a previous similar incident (see Figure 1 for testing algorithm) was used to decide who warranted testing for TB. The contact tracing of friends and family was commenced immediately.

The following definition of a 'contact' was created based on the *Guidelines for Tuberculosis Control in New Zealand 2010*.[1] The time period for identifying potential contacts was set at three months prior to Mr K's diagnosis of TB, as recommended by the guidelines when the date of cough onset is not known (as was the case). In order to clarify those at elevated risk of acquiring TB we used the following contact definition:

"A person with greater than eight hours of cumulative exposure to the case, in a closed environment during the three months prior to the case's Tuberculosis diagnosis OR an immunocompromised person with more than three hours of cumulative exposure to the case, in a closed environment, during the three months prior to the case's Tuberculosis diagnosis."*

Figure 1: Tuberculosis exposure screening and testing algorithm.[2]



(*A single dose of chemotherapy or a blood transfusion was estimated to take an average of 3 hours; therefore any patient who had received chemotherapy or blood products on the same day as the index case was considered to be at risk and qualified for screening.)

All family and friends (immunocompetent) of Mr K with significant exposure were identified and screened with an immediate and an eight-week post-exposure QFT test if they met the contact definition. Some contacts lived outside the local public health unit's catchment area, therefore other public health units assisted with contact tracing.

Staff members (immunocompetent) who met the contact definition were screened with a symptom questionnaire and an eight-week post exposure QFT test.

All oncology and haematology patients undergoing treatment at the cancer centre were assumed to be immunocompromised. An algorithm (Figure 1) for appropriate investigation of these contacts was adapted from another district health board, who had responded to a similar incident among immunocompromised patients exposed to TB.[2] Given the lower sensitivity of QFT in immunosuppressed hosts,[3] exposed patients were screened using both QFT test and a CXR.

All patients who met the contact tracing threshold were phoned by a clinician to discuss the situation and provide an opportunity for questions. A letter outlining the situation and management was also sent to patients and their general practitioner (GP) and oncologist or haematologist. All patients were phoned with results as these became available, with explanation of the test results and any further action required. A final summary letter containing individual contacts' test results and public health recommendations was sent to all patient contacts, their GPs and their oncologist or haematologist, with advice to remain vigilant for TB signs and symptoms for at least two years.

All staff who met the exposure threshold were identified and informed of the situation and testing requirements by the occupational health and safety department. The test results were reported to each staff member by occupational health and safety.

Results

Family

Fourteen family and friends of Mr K met the contact definition and were screened by their local public health unit. One adult underwent serial Mantoux® testing by his GP, and the remainder were tested using an immediate and eight-week post-exposure QFT. All family and friends were asymptomatic for symptoms of TB disease and QFT negative.

Staff

There were a total of 15 staff members, identified by occupational health and safety, who had been in contact with Mr K during his infectious period. Only four of these staff members met the contact definition criteria. These staff members were screened with a symptom questionnaire and an eight-week post-exposure QFT test.

A further three staff members, who did not meet the contact definition threshold requested to be tested for reassurance. All seven of the screened staff members were asymptomatic for symptoms of TB disease, and all had negative QFT tests.

Patients

There were 55 patients who were identified as being present in the cancer centre on the same days as Mr K. Of these people, 46 met the contact definition.

Four patients passed away in the period between exposure and screening of contacts. After discussion with their respective oncologists or haematologists, none of these deaths were thought to be caused by TB disease, nor were there any concerns of active TB symptoms prior to their death.

The remaining 42 patients were screened with both a symptom questionnaire, eight-week post exposure QFT test and a CXR. Of these 42 patients, five had symptoms which may have been consistent with TB disease. Of these five patients, four had stable symptoms that either preceded their exposure or their symptoms were thought to be a manifestation of their underlying malignancy. In all four cases the eight-week post-exposure QFT tests were negative, and their CXRs did not have features suggestive of TB. One of the five symptomatic patients had developed a new non-productive cough

since being exposed, however their QFT test was negative and their CXR showed indeterminate right upper lobe focus. Close monitoring for signs suggestive of TB and a repeat CXR in three months was advised after discussion with an infectious diseases specialist. The repeat CXR demonstrated slight enlargement in the indeterminate right upper lobe focus, which was further evaluated using a computed tomography chest scan and reported as a new primary lung cancer.

The 37 asymptomatic patients all had negative eight-week post-exposure QFT tests. One patient had right upper lobe interstitial changes/fibrosis on CXR, and after discussion with an infectious diseases specialist a repeat CXR was advised in three months, with close monitoring for symptoms of TB. The repeat CXR showed an increase in the right upper lobe interstitial changes/fibrosis, which was also further evaluated using a computed tomography chest scan and reported as progressive right upper lobe post-radiotherapy fibrosis. See Figure 1 for the flow chart of the screening and results.

Discussion

Diagnosis and management

The management of malignancies is rapidly changing. Many cancer treatments cause immunosuppression, increasing the risk of opportunistic infections.

Reactivation of latent pulmonary TB or progression of TB disease is a known complication among people receiving chemotherapy.[4] In the case described, the combination of chemotherapy and the marked malnutrition from gastric malignancy most likely led to the reactivation of latent pulmonary TB: there was progression of a chronic cough and worsening appearance of lung disease on repeat PET-CT scanning following the initiation of chemotherapy.

TB is a relatively uncommon disease in New Zealand. There is an incidence of 7–10 cases of TB disease per 100,000 people per year.[1] Notably, TB often presents with signs or symptoms that may be attributed to other diagnoses (including malignancy). Consequently, it is not always at the forefront of a physician's mind. This situation was unusual and unfortunate in terms of both the large number and the susceptibility of the contacts involved. Due to the open plan of the cancer centre and the insidious nature of our case's symptoms, a number of immunosuppressed patients were exposed before the diagnosis of TB was made.

A key to the successful management of this situation was the collaborative approach across departments and the clear lines of communication. Colleagues from Public Health, Infectious Diseases, Infection Prevention and Control, Oncology, Occupational Health and Safety were involved in this response. This group included clinicians, managers and also a communications expert with experience in risk communication. Clear communication was a priority in this challenging situation and involved both internal communications with the response team, and also communication with affected staff, patients and the public if necessary. Regular team meetings, shared files and collated email updates were used to ensure everyone was working with the same information and that relevant stakeholders were kept informed. Furthermore, every patient involved in this incident was phoned by a doctor or TB nurse specialist and sent written information; including the contact details for a clinician should they have questions. This information was also communicated to primary care, and the relevant oncologist or haematologist. Information was also recorded in occupational health records for affected staff.

Investigation of the event

The standard TB symptom screening questionnaire among this patient population was of limited value, as the systemic symptoms of TB are similar to those of malignancy and haematological disorders. Fatigue, fevers, night sweats and weight loss may reflect progression of malignancy rather than development of TB disease. Even respiratory symptoms such as cough, haemoptysis and shortness of breath may be a manifestation of a primary lung cancer or pulmonary metastases as opposed to pulmonary TB. Interpreting symptoms in this patient population was difficult. Therefore the timing of the patient's symptoms and their known exposure date was important to distinguish between the possibility of TB and the patient's known malignancy. A further complicating factor among this patient

population was that the QFT test used for screening of contacts is less sensitive due to the depletion of lymphocyte populations with chemotherapy.[2] Due to this recognised loss of QFT test sensitivity, immunocompromised patients were also screened with a CXR to help improve the reliability of detecting TB. This issue was well illustrated in one immunocompromised contact who had received ablative chemotherapy prior to a bone marrow transplant. Their QFT test result was reported as indeterminate, likely due to a lack of interferon production (T-cell response) from a demonstrable lymphopaenia.

Mr K had many features of high infectivity (smear positive pulmonary disease, cough longer than 10 weeks and cavitating lesions on CXR), yet to date there have been no confirmed secondary cases of TB. However, surveillance of patient contacts by their oncologists, haematologists and GPs is ongoing. A possible reason for this lack of transmission may be Mr K's reserved nature: many of the staff in the cancer centre noted that he tended to "keep to himself". Given that there is no evidence of transmission in any of the identified contacts, the risk of transmission is likely to have been overestimated and a less extensive contact tracing may have been appropriate, however because Mr K did not live in the same household as any of his close contacts, an estimation of his infectivity was not able to be determined, and therefore broad contact tracing was undertaken.

This incident occurred among a group of patients who are often (understandably) already stressed and anxious due to their cancer diagnosis and treatment. The team managing this event was mindful of the potential for psychological harm by both alerting cancer patients to this TB exposure and screening for TB infection. However, it was felt that honest communication and transparency was important in managing this situation, and that patients were entitled to have clear information about their exposure to TB and the potential risks to them. Overall it was believed that the benefits of identifying any TB infected patients outweighed the potential psychological harms to the patient group from anxiety related to the TB exposure and any distress related to false positives identified in the initial screening process. Importantly, in managing this event the patient concern and anxiety was managed by reassuring patients that their total exposure was likely to be small and that early identification of an infection would reduce the risk of harm. Furthermore, each patient was phoned with the results of their TB screening to provide additional reassurance, with the proviso that they remain vigilant for any new symptoms suggestive of TB.

Risk assessment and screening of patients undergoing chemotherapy

This situation raises the question of whether TB risk-assessment and consideration of pre-treatment screening should be performed among oncology patients as part of routine work-up prior to chemotherapy. In other medical specialties where immunosuppressive monoclonal antibodies are used, clinicians routinely screen for TB in all patients prior to commencement of these therapies.[5] However, it is not currently routine practice for cancer patients to undergo TB screening before starting chemotherapy.

A 2017 systematic review from the European Respiratory Journal confirms that chemotherapy patients have an increased risk for developing TB compared to the general population.[6] The authors recommend that given the limited period of immunosuppression in cancer patients and the reduced cumulative lifetime risk of TB disease (due to reduced life expectancy) patients with cancer undergoing chemotherapy do not warrant screening for latent TB infection. However, this recommendation does not extend to children with curable cancers who have a longer life expectancy. The authors of this review advise that adult cancer patients with risk factors for latent TB (family history, previous exposure or birth in a country with high rates of endemic TB) and paediatric cancer patients should be considered for QFT testing before starting chemotherapy. However, detailed guidance on how to quantify risk or what process of screening should be followed does not exist in the published literature.

In 2005–2009 in New Zealand the incidence rate of TB among Māori was five times that of Europeans and 10 times more common among Pacific peoples than in

Europeans. In Asian ethnic groups the rate is 25 times greater than in Europeans, however the TB incidence by ethnic group is confounded by place of birth.[1] It therefore may be sensible to target TB screening for pre-chemotherapy patients towards Māori, Pacific people and Asian ethnic groups, particularly those born outside of New Zealand, who are at higher risk of having TB. This will not only assist in the diagnosis and treatment of TB but also reduce the risk of complications during treatment, increasing the likelihood of improved survival and quality of life.

It is important to recognise that screening for TB has both potential harms and benefits. A systematic approach to TB screening in pre-chemotherapy oncology patients needs to weigh up the potential costs, both financial costs and patient harms (invasive investigation following false positive results, psychological harm of false positives and inappropriate reassurance in the case of false negatives), against the importance of preventing the spread of infection among other patients and the public. Further research is required to develop and validate a screening tool that will assist clinicians to determine the risk of latent TB in a prospective chemotherapy patient and ensure that QFT testing is used appropriately.

Another lesson from this incident is that close attention to cancer centre design and infection control policy may be important to minimise the risk of communicable disease spread among vulnerable patient populations and healthcare staff. Importantly, the investigation of this case did not identify any secondary cases of TB despite the multiple features, high infectiousness in our case, and the prolonged exposure of many immunocompromised patients in a small open-plan cancer centre. Open-plan healthcare facilities are important for social interaction and patient wellbeing, during what is often a stressful and socially isolating time, with frequent and sometimes lengthy treatments in hospital. However, social interaction may come at the cost of an increased risk of the infectious disease spread. The trade-off between these two aspects of patient health is an important discussion, and not one with a clear-cut answer. Going forward, this case also highlights the responsibility of both patients and staff to follow their respective cancer centre's infection control policy when patients present with symptoms that could be from an infectious illness.

Conclusion

Incidents with potentially significant public health consequences, such as the situation described, necessitate the collaboration of a multi-disciplinary team of health professionals to ensure a rapid and coordinated response to identify and minimise risk to the public. Effective communication between all responders involved is crucial to a desired outcome.

Chemotherapy often creates a state of immune compromise, increasing the risk of either acquiring or reactivating infectious diseases, including TB. Reactivation of infectious diseases in chemotherapy patients can have serious negative consequences for both the patient and also family, staff and other immunosuppressed patients.

Current evidence points us to the importance of vigilance for symptoms, infection prevention and control strategies and public health management of TB. However, there is a lack of evidence and protocols for evidence-based decision making on how to risk-assess and manage screening of TB in pre-chemotherapy cancer patients.

Competing interests:
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The projected burden of knee osteoarthritis in New Zealand: healthcare expenditure and total joint replacement provision

Ross Wilson, J Haxby Abbott

ABSTRACT

AIM: To estimate the healthcare costs and demand for total knee replacement (TKR) associated with knee osteoarthritis in New Zealand over the period 2013–2038 and the contribution of increasing obesity rates to these costs.

METHOD: We used the NZ-MOA computer simulation model of knee osteoarthritis in the New Zealand population. Osteoarthritis-related healthcare costs and TKR incidence were modelled for a 25-year horizon, for a starting cohort drawn from the 2013 New Zealand population. Population obesity projections were used to estimate the life-course of cohort obesity. Per-person projected outcomes were multiplied by national demographic population projections to obtain total population projections.

RESULTS: Healthcare costs of knee osteoarthritis were projected to increase from NZ$199 million in 2013 to $370 million in 2038. Annual TKR incidence was projected to increase from 5,070 to 9,040 over the same period. Projected increases in population obesity rates (above the obesity prevalence seen in 2013) accounted for 25% and 47% of the projected increase in per-capita healthcare costs and TKR provision rates, respectively.

CONCLUSION: The healthcare burden of knee OA will continue to increase for the foreseeable future. Public health measures to reduce further increases in population obesity rates would contribute to slowing this rising burden.

Osteoarthritis (OA) is a common and debilitating chronic disease and one of the leading causes of disability in New Zealand and worldwide.[1–3] Knee OA is the most common form of OA, affecting as much as one-third of the population at some point in their lifetime. Globally, OA is responsible for more than 16 million disability-adjusted life years (DALYs) and is the 12th leading cause of worldwide disability.[4] In New Zealand, osteoarthritis accounted for more than 15,000 DALYs in 2018.[5] In addition to the health losses associated with OA, it also accounts for a substantial economic burden on the health system and the wider economy. In New Zealand, the total annual financial cost of arthritis (of all types) is estimated to be $4.2 billion, including health system costs of $990 million; productivity costs of $1.2 billion, through reduced employment, time off work and impaired performance at work; and other costs, such as non-health sector care and aids and modifications to support independent living for people with arthritis, of $2 billion.[5]

Total knee replacement (TKR) surgery is a common and successful operation to reduce pain and improve HRQoL in patients with advanced knee OA.[6,7] Provision of TKR has been increasing across the world

in recent decades.[8–11] However, TKR is a costly procedure and high provision rates place strain on limited public healthcare resources. Furthermore, access to TKR, particularly in the public healthcare system, is limited by capacity constraints due to the availability of a suitably-trained workforce and surgical facilities.

The two most important risk factors for incidence and progression of knee OA are age and obesity. In New Zealand, as elsewhere, the combination of an ageing population and increasing rates of obesity is therefore expected to result in continuing increases in demand for OA healthcare.[8,10,12–15] The population aged over 65 is expected grow by 40 percent over the next decade,[16] while obesity rates are projected to increase to close to 50% of the adult population by the late 2030s.[17] Understanding the implications of these population changes is critical for successful health system and workforce planning.

The aims of this study are (1) to estimate the projected healthcare costs of osteoarthritis care in New Zealand for the period 2013–2038, (2) to estimate the demand for TKR surgery in New Zealand over the same period, and (3) to assess the contribution of projected increases in population obesity to future healthcare expenditure and TKR demand.

Methods

We used the New Zealand Management of Osteoarthritis (NZ-MOA) model, a state-transition microsimulation model of the incidence, progression, health impact and healthcare costs of knee OA in New Zealand.[18] The model generates a hypothetical cohort drawn from the 2013 New Zealand population distribution; runs each simulated individual through a sequence of annual health state transitions, defined by obesity, knee OA status (Kellgren-Lawrence grade), health-related quality of life (HRQoL) outcomes and treatment pathway; and computes the resulting per-capita healthcare costs, quality-adjusted life years (QALYs) and treatment utilisation. By running the same cohort through multiple scenarios, the incremental change in outcomes attributable to knee OA prevalence, change in risk factors or change in treatment patterns can be estimated.

We computed model outcomes under two scenarios: continuation of projected trends in population obesity levels[17] and holding population obesity constant at 2013 levels. We generated simulation cohorts of 10,000 individuals for each age- (in five-year age groups), gender- and ethnicity-specific population subgroup. For each subgroup, we ran each scenario for a modelled 25-year time horizon (2013–2038) and recorded the age-, gender- and ethnicity-specific OA-related healthcare expenditure and TKR incidence in each year. Projections of healthcare costs and joint replacement provision at the population level were calculated by multiplying the age-, gender- and ethnicity-specific per-person projected outcomes from the simulation model by Statistics New Zealand's published national population projections for each future period.[19] This whole process was repeated 1,000 times, each with a new random draw from the distribution of obesity projections, resulting in a total simulated population of 760 million individuals to provide stable and precise estimates of the outcomes. We calculated the mean healthcare costs and joint replacement incidence in each year across the 1,000 cycles to provide the projected point estimates for each outcome, and the 2.5th and 97.5th percentiles to construct 95% uncertainty intervals for the contribution of increasing obesity levels (ie, undertaking probabilistic sensitivity analysis).

Baseline population model input parameters and sources have been described previously,[18] and are summarised in Appendix A. Costs of treatment were based on provision of usual publicly and privately provided medical care as practiced in New Zealand,[20] valued with New Zealand-specific reference prices[21] (see Appendix Table A5). TKR incidence rates in the New Zealand population were obtained from the New Zealand Joint Registry,[22] which covers almost all privately and publicly funded joint replacement surgeries in New Zealand, and used to calibrate the baseline modelled TKR provision rates. Projected increases in population obesity rates, stratified by age, gender and ethnicity, were obtained from a previously published age-period-cohort model of body mass index (BMI) in the New Zealand population.[17]

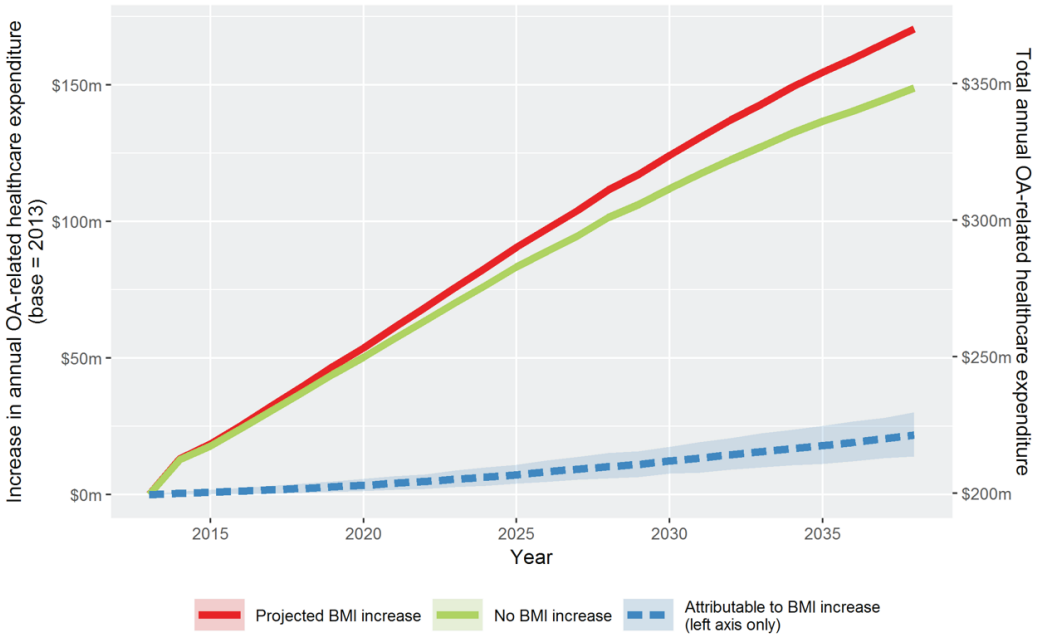
Cross-model validation was conducted by comparing our projected increases in the provision of TKR with those previously published in the *Journal* by Gary Hooper and colleagues (2014).[13] Those estimates were based on different inclusion criteria than our model: all TKR were included for any primary diagnosis, whereas our model includes only one OA knee per person (ie, only the first primary TKR performed), and includes only TKR performed for a primary diagnosis of knee OA. The total number of TKR performed annually should therefore be lower in our model projections; to allow direct cross-model comparison, we normalised all estimates to an index value of 100 in 2011 (the base year in Hooper et al's projections), to compare the total percentage increase in TKR provision between models. (The observed increase in TKR provision between 2011 and 2013 was used to determine the baseline (2013) index value for the NZ-MOA model, as the model was calibrated to observed 2013 data.)

Results

In 2013 (the base year for the NZ-MOA model), the total direct healthcare costs of knee OA were estimated to be NZ$199 million (1NZD≈0.82USD), and 5,070 patients had a first total joint replacement for knee OA. Women accounted for $110 million (55%) of the total costs and 2,460 TKR (48%); Māori for $18 million (9%) of the total costs and 490 TKR (10%).

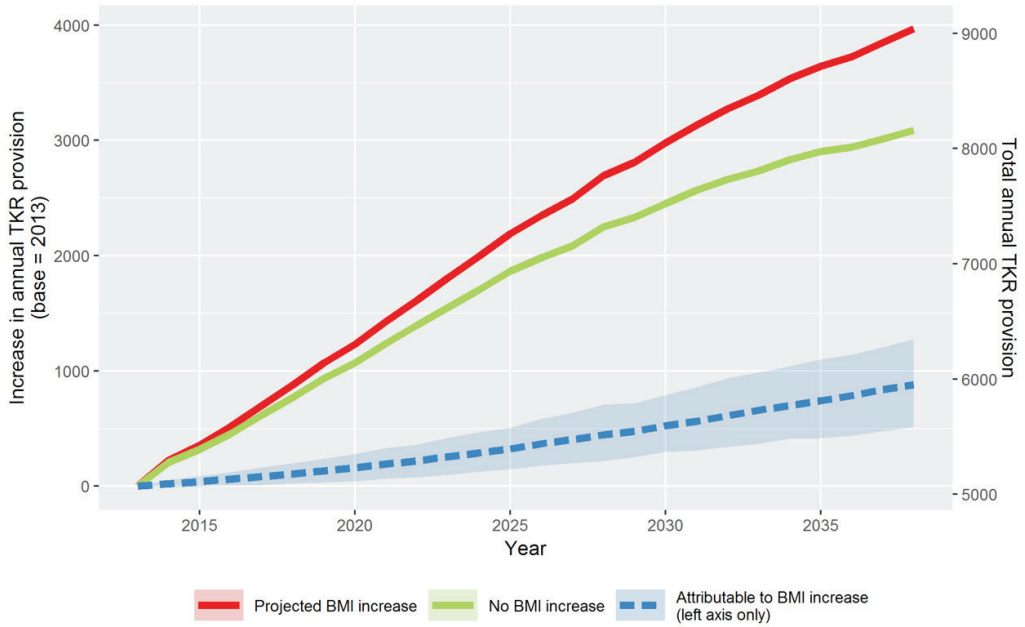
The healthcare costs associated with OA treatment were projected to increase to $370 million per year in 2038 (at constant 2013 prices; Figure 1), an increase of 85%. Per-capita treatment costs (for the adult population aged 25 and over) were projected to increase from $69 to $90. TKR incidence was projected to increase to 9,040 per year

Figure 1: Projected healthcare costs of knee osteoarthritis in New Zealand, 2013–2038.



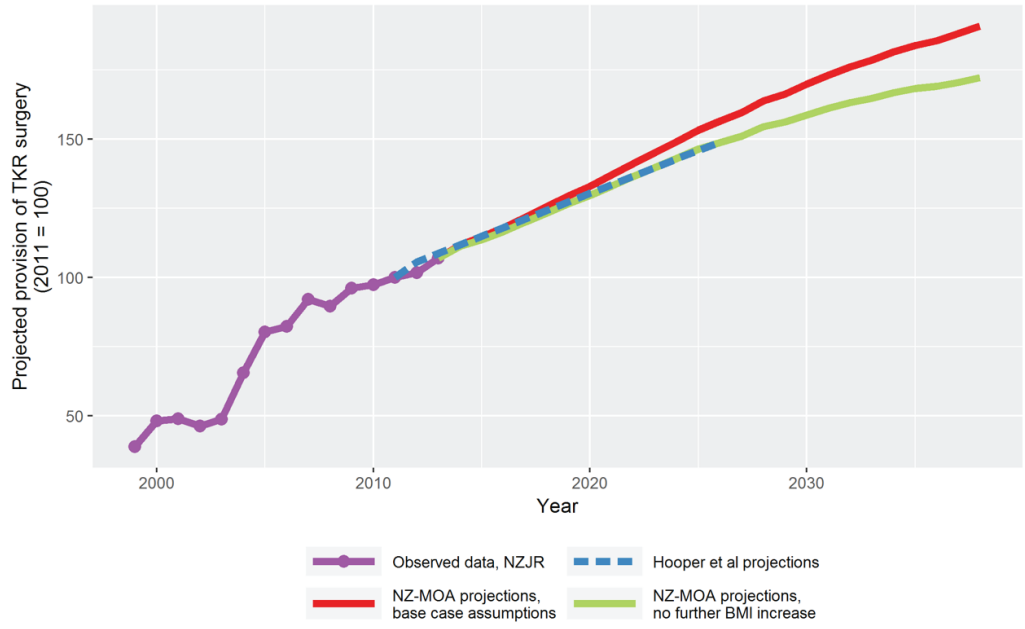
Source: NZ-MOA simulation model. Lines show the projected increase in annual healthcare expenditure on OA treatment under the base case scenario (ongoing increase in population BMI based on current trends) and with no further increase in population BMI (ie, maintaining 2013 BMI distribution), relative to 2013 baseline level. 'Attributable to BMI increase' is the difference between the two lines, representing the incremental OA-related healthcare expenditure attributable to continued increases in population BMI relative to the 2013 level. The shaded uncertainty interval represents the 95% confidence interval for projected annual increase in population BMI. Right-hand axis shows total projected annual healthcare expenditure in each period for the base case and no BMI increase scenarios.
BMI indicates Body Mass Index; OA, Knee osteoarthritis.

Figure 2: Projected demand for first total knee replacement for knee osteoarthritis in New Zealand, 2013–2038.



Source: NZ-MOA simulation model. Lines show the projected increase in annual provision of TKR under the base case scenario (ongoing increase in population BMI based on current trends) and with no further increase in population BMI (ie, maintaining 2013 BMI distribution), relative to 2013 baseline level. 'Attributable to BMI increase' is the difference between the two lines, representing the incremental TKR provision attributable to continued increases in population BMI relative to the 2013 level. The shaded uncertainty interval represents the 95% confidence interval for projected annual increase in population BMI. Right-hand axis shows total projected annual provision in each period for the base case and no BMI increase scenarios.
BMI indicates Body Mass Index; TKR, Total knee replacement surgery.

Figure 3: Observed and projected demand for total knee replacement in New Zealand, 1999–2038, cross-model comparison.



Source: NZ-MOA simulation model; NZJR 2016;[22] Hooper et al 2014.[13] Points show observed provision of TKR 1999–2013; dashed line the published projections from Hooper et al 2011–2026; and solid lines the new model projections 2013–2038, under the base case scenario (ongoing increase in population BMI based on current trends) and with no further increase in population BMI (ie, maintaining 2013 BMI distribution). The absolute numbers in each series differ due to different inclusion criteria: all values are normalised to 2011 = 100 for consistent comparisons.
BMI indicates Body Mass Index, in kg/m^2; NZJR, New Zealand Joint Registry; TKR, Total knee replacement surgery.

in 2038 (Figure 2). The provision rate was projected to increase from 174 to 221 per 100,000 population per year.

In 2038, women were projected to account for $210 million (57%) of the total healthcare costs and 4,760 TKR (53%); Māori for $44 million (12%) of the total costs and 1,120 TKR (12%). Full results for projected costs and TKR incidence for each year 2013–2038, including ethnic and gender breakdowns, are reported in Tables B1 and B2 in the Appendix.

Further increases in population BMI, relative to the baseline distribution in 2013, accounted for 25% of the projected increase in per-capita OA-related healthcare costs and 47% of the increase in TKR provision rates between 2013 and 2038. By 2038, this accounts for an additional $22 million and 880 TKR per year. Over the 25-year time horizon, projected increases in BMI, relative to baseline levels, will result in an additional $231 million in OA healthcare costs and 9,880 TKR required.

The increase in TKR provision projected by our model, in the absence of further increases in population obesity, was very close to that previously reported, using a different modelling approach, by Hooper et al (2014) (Figure 3).[13] Between 2011 and 2026, TKR provision was projected to increase by 48.8%, compared to 49.0% reported in the previously-published estimates. Allowing for projected increases in population obesity, this increased to 56.6% in our model, and 90.8% by 2038. The total numbers of projected TKR (without normalisation) from both models are shown in Figure B1 in the Appendix.

Discussion

Treatment of knee OA cost the New Zealand healthcare system $200 million in 2013, an amount projected to increase to $370 million over 25 years. Demand for TKR is projected to increase by almost 80% over the same period, requiring an additional 4,000 surgeries to be performed annually by 2038. After adjusting for population growth, projected increases in obesity rates account for one-quarter of the increase in per-capita costs and almost half of the increase in TKR provision rates over 25 years.

These results highlight the need for effective—and cost-effective—treatment of OA throughout the disease course. Our projections were calculated under the assumption that patients' access to TKR (and other treatments) remains at the same level as in 2013. Access to TKR is already rationed through the public health system, with many local health systems unable to offer surgery to all patients who would benefit;[23,24] improving access to TKR would require further resourcing beyond that suggested by our projections. Effective, low-cost, early interventions, such as exercise therapy, can alleviate symptoms, improve patients' quality of life and reduce the need for costly treatment, such as TKR, later in the disease course.[25,26] Improving access to such treatments may help to mitigate the increasing burden on the health system associated with rising rates of OA.

There is limited existing research on the future healthcare costs of OA. Our projected increases in costs are very similar to those reported recently for Australia,[27] which had a projected increase in direct OA healthcare costs of 2.2% per year between 2015 and 2030, based on the changing age and gender distribution of the population (ie, excluding the effect of changes in population obesity). For comparison, we projected the same 2.2% annual increase between 2013 and 2038 when holding obesity rates constant at the 2013 level. A study in Canada projected increases in costs of OA treatment of 4.7% per year between 2010 and 2031;[28] these higher rates are at least in part explained by differing assumptions about the course of future healthcare prices.

There is more literature on projected provision of TKR, although previous studies have reported widely-varying results due to differences in context, modelling assumptions and statistical methodology. Our projections (2.3% per year, or 1.9% excluding the effects of increasing obesity, which have often not been captured in past studies) are at the low end of published projections for the US (between 1.9% and 8.5%[14,29]), similar to those for the UK (1.6% to 2.8%[30]) and the Netherlands (1.7% to 2.7%[32]), and higher than those for Sweden (0.9%[8]). In the local context, our results are consistent with those of Hooper et al,[13] when excluding the effect of increasing obesity rates, providing external validation of our model, and demonstrate the additional

burden being placed on the health system by the continuing obesity epidemic.

The study has limitations relating to model structure and availability of data. The estimated costs associated with knee OA are not stratified by disease severity (other than the cost of TKR for end-stage OA), due to a lack of available data on the relationship between disease progression and treatment costs. As obesity is associated with both incidence and progression of knee OA, this limitation may have resulted in our projections underestimating the effects of increasing obesity on healthcare costs of OA. We have also modelled direct healthcare costs only, excluding non-health costs such as time off work or reduced productivity, informal care outside the health system, or equipment and aids to assist with daily living. These other costs may be substantial in OA; for example, a recent report on the costs of (all types of) arthritis in New Zealand found that productivity losses associated with arthritis were 125% of direct healthcare costs, and other non-health financial costs a further 202% of healthcare costs.[5] These suggest that the healthcare costs reported here may represent only one-quarter of the total societal cost of knee OA. Lastly, the NZ-MOA model captures the most severely OA-affected knee only for each individual; the projections of TKR provision therefore relate only to the first TKR surgery per patient. According to our data from the New Zealand Joint Registry, these account for approximately 75% of all TKR in New Zealand.

Strengths of the study include the use of a validated, state-of-the-art computer simulation model, populated with comprehensive and reliable national-level data on disease prevalence, risk factors and TKR provision.[18] By modelling the underlying drivers of future TKR incidence—initial prevalence of OA across the population, and ongoing disease incidence, structural progression and symptom severity—this approach may provide more reliable projections than statistical models relying on linear or exponential extrapolation of observed trends in TKR incidence rates far beyond the period of observed data. The sensitivity of data-driven statistical projections of TKR incidence to modelling assumptions about the ongoing trend is apparent in the wide variability in previously published estimates. Our projected increases in TKR incidence were generally higher than previously published estimates assuming constant incidence rates (within demographic strata), but (often substantially) lower than those assuming the continuation of observed short-run increasing trends.

The consistent results found in our cross-model validation exercise demonstrate the validity of the model for predicting future outcomes based on current practice patterns and risk factor distributions and reliable estimates from Statistics New Zealand of projected demographic change. The impact of increasing population obesity, additional to these validated projections based on demographic change, was derived from published estimates, for the New Zealand population, of future trends in population BMI, and international evidence on the relationship between BMI and OA incidence and progression. By combining these reliable sources of data, using our well-validated computer simulation model, we have been able to provide well-grounded, coherent and reliable projections of the increasing healthcare burden of knee OA in the New Zealand population.

Conclusion

The healthcare burden of knee OA in New Zealand will continue to grow over the next 25 years due to population ageing and increasing rates of obesity. Without changes in the provision of effective and cost-effective care throughout the disease course, the annual direct healthcare costs of knee OA will increase by 85% to $370 million by 2038, and an additional 4,000 TKR surgeries per year will be required.

Appendix A

This appendix describes the sources and derivations of the NZ-MOA model input parameters used in this study. For further details refer to Wilson & Abbott (2018)[33] and the NZ-MOA Technical Manual, version 1.4.0 (available on request from the authors).

Demographic characteristics

Baseline age, gender and ethnicity are drawn from the discrete joint probability distribution of the New Zealand population, obtained from the 2013 New Zealand Census.[34] The model uses an annual cycle, so age is incremented by one year each period; gender and ethnicity are assumed to be fixed throughout the lifetime of each individual. Mortality rates, stratified by age, gender and ethnicity, were obtained from the New Zealand Period Life Tables 2012–14,[35] and further adjusted for the relative risk of mortality associated with obesity using data from the US population.[36] Mortality rates were assumed to decrease by 1.75% per year for non-Māori and 2.25% per year for Māori until 2026 and remain constant thereafter.[37]

Body mass index

Baseline BMI is drawn from an age-, gender- and ethnicity-specific log-normal distribution (Table A1). Future trajectories of BMI are assumed to follow the population-average age trajectory of BMI, plus an annual trend increase reflecting increases in population obesity.[38] The ongoing trend increase was drawn, in each loop of the PSA process, from a normal distribution with gender- and ethnicity-specific mean and variance (Table A2).

Table A1: Mean of population baseline BMI distribution, by age, gender and ethnicity.

	Non-Māori		**Māori**	
	Men	**Women**	**Men**	**Women**
Constant	20.30	20.54	20.21	19.94
Age	0.3141	0.2824	0.4356	0.4825
Age^2	-0.00279	-0.00247	-0.00401	-0.00455

Table A2: Trend increase in population BMI distribution.

	Non-Māori		**Māori**	
	Men	**Women**	**Men**	**Women**
Mean	0.0763	0.1049	0.0590	0.0919
Std. Error	0.0150	0.0169	0.0287	0.0373

Structural (radiographic) knee osteoarthritis

Baseline radiographic knee OA status is drawn from the age-, gender-, ethnicity- and obesity-specific prevalence of self-reported doctor-diagnosed all-site OA, derived from the New Zealand Health Survey 2013/14 (Table A3), and further adjusted for the ratio of knee OA to all-site OA[39] and the ratio of radiographically-defined knee OA to self-reported diagnosis.[40] Incidence was derived to be consistent with baseline prevalence rates, assuming no case fatality or remission in radiographic knee OA.

Table A3: Baseline prevalence of self-reported doctor-diagnosed all-site OA.

	Coefficient
Constant	-11.27
Age	0.2245
Age^2	-0.00121
Female (Male = reference)	0.5938
Overweight (Underweight/Healthy weight = reference)	0.0362
Obese I	0.3764
Obese II	0.4405
Obese III	0.8243

Values are coefficients from a logistic regression model (ie, log(Odds(OA))). Further adjustments to estimate radiographically-defined knee OA prevalence are: ratio of knee to all-site OA (men = 0.713, women = 0.665), odds ratio of radiographically-defined knee OA to self-reported diagnosis (1.30).

Annual progression of radiographic knee OA (defined by K-L grade 2/3/4) was obtained from US- and UK-based prospective cohort studies,[41–43] stratified by gender, obesity and prior K-L grade (Table A4).

Table A4: Annual progression of radiographic knee OA.

	Non-obese		**Obese**	
	Men	**Women**	**Men**	**Women**
K-L grade 2 to 3	5.58%	4.00%	12.26%	8.95%
K-L grade 3 to 4	1.29%	1.95%	2.94%	4.27%

Health-related quality of life impacts of radiographic knee osteoarthritis

The HRQoL impacts of knee OA are modelled on each of the six dimensions of the SF-6D, which are then valued using the SF-6D preference-based utility scores.[44] The average health utility loss associated with knee OA is 0.02 at K-L grade 2, 0.05 at K-L grade 3, and 0.10 at grade 4.

OA healthcare costs

The direct healthcare costs of OA treatment were based on the assumed provision of usual medical care as practiced in New Zealand (consisting of GP consultations, analgesic medication, and referrals to physical therapy for some patients),[45] valued with New Zealand-specific reference prices sourced from PHARMAC's Cost Resource Manual for HTA in New Zealand (Table A5).[46]

Table A5: Annual costs of OA-related healthcare.

Treatment	**Annual cost (per user)**	**Utilisation**	**Annual cost (average)**
Office (GP) visits	$131	50%	$66
Physical therapy	$750	20%	$38
Devices	$50	20%	$10
NSAIDs	$123	32%	$39
CBC and electrolytes lab test (for 50% of NSAID patients)	$22	16%	$4
GI-protective medication	$57	14%	$8

Acetaminophen/paracetamol	$25	45%	$11
Liver function test (for 50% of acetaminophen patients)	$20	23%	$4
Other OA medications	$124	53%	$66
Mood medications	$25	14%	$4
Neutraceuticals	$247	36%	$88
Total			$337

Appendix B

Table B1: Projected healthcare costs and TKR provision, by year.

Year	Healthcare costs ($million)		TKR provision		Population
	Base case	Constant BMI distribution	Base case	Constant BMI distribution	
2013	199.5	199.5	5,070	5,070	2,905,900
2014	212.6	212.2	5,295	5,276	2,959,400
2015	218.0	217.2	5,429	5,390	3,025,930
2016	224.8	223.6	5,589	5,529	3,104,230
2017	231.9	230.3	5,770	5,687	3,179,440
2018	239.1	236.8	5,950	5,842	3,251,610
2019	246.4	243.6	6,139	6,007	3,318,160
2020	253.2	249.8	6,300	6,141	3,380,210
2021	260.6	256.5	6,499	6,308	3,436,950
2022	267.8	263.1	6,686	6,468	3,486,141
2023	275.2	269.6	6,879	6,623	3,532,690
2024	282.4	276.0	7,066	6,777	3,576,110
2025	290.0	282.8	7,262	6,938	3,619,780
2026	296.8	288.5	7,418	7,051	3,660,840
2027	303.4	294.2	7,564	7,158	3,697,870
2028	311.0	300.8	7,765	7,320	3,734,030
2029	316.8	305.7	7,880	7,403	3,770,450
2030	323.7	311.4	8,048	7,523	3,805,593
2031	330.2	317.0	8,201	7,639	3,841,320
2032	336.6	322.1	8,346	7,733	3,879,110
2033	342.4	326.8	8,465	7,807	3,918,510
2034	348.6	331.8	8,605	7,906	3,957,120
2035	354.0	336.1	8,714	7,974	3995,790
2036	359.0	339.9	8,796	8,011	4,032,330
2037	364.6	344.1	8,921	8,083	4,067,150
2038	370.0	348.3	9,041	8,160	4,100,230

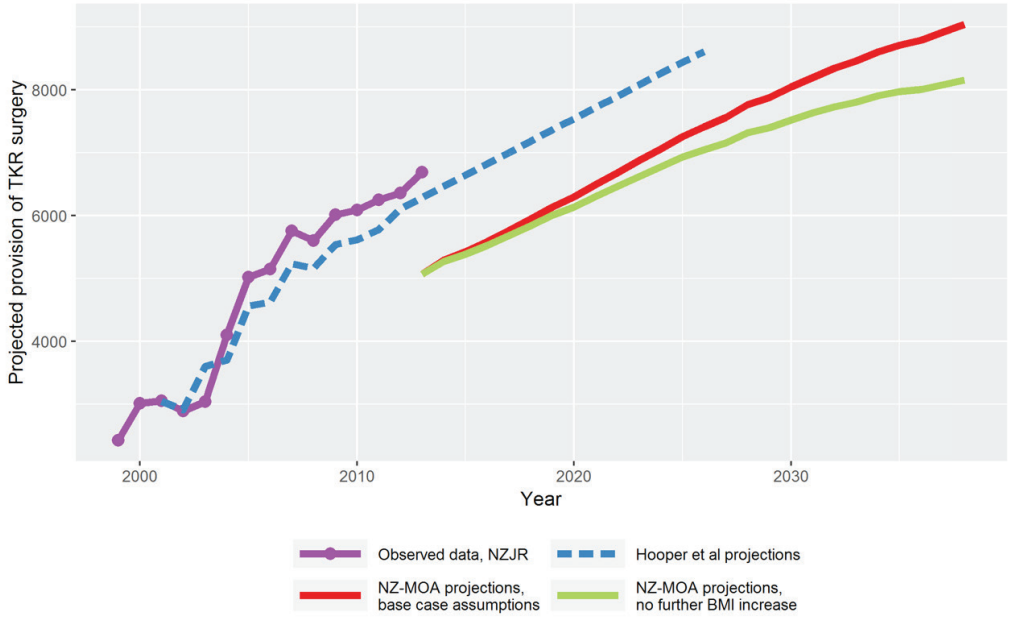
All values refer to the New Zealand adult population aged 25–99.

Table B2: Projected healthcare costs and TKR provision, by year, sex and ethnicity.

Year	Healthcare costs ($million)				TKR provision			
	Non-Māori		Māori		Non-Māori		Māori	
	Men	Women	Men	Women	Men	Women	Men	Women
2013	81.2	100.1	7.8	10.4	2,374	2,211	239	246
2014	85.7	107.1	8.4	11.4	2,407	2,372	248	270
2015	87.3	110.1	8.7	11.9	2,437	2,453	253	286
2016	89.7	113.6	9.0	12.5	2,484	2,543	263	299
2017	92.5	117.0	9.4	13.0	2,560	2,623	273	314
2018	95.1	120.6	9.7	13.6	2,627	2,711	283	329
2019	97.9	124.1	10.1	14.2	2,704	2,798	294	343
2020	100.3	127.5	10.6	14.8	2,762	2,874	306	359
2021	103.1	131.1	11.0	15.4	2,839	2,966	318	376
2022	105.9	134.5	11.4	16.0	2,916	3,047	330	392
2023	108.6	138.1	11.8	16.7	2,990	3,139	341	409
2024	111.3	141.6	12.2	17.4	3,063	3,224	353	425
2025	114.1	145.3	12.6	18.0	3,142	3,314	365	441
2026	116.5	148.6	13.0	18.7	3,199	3,383	377	459
2027	118.7	151.9	13.5	19.3	3,246	3,455	388	475
2028	121.8	155.4	13.9	20.0	3,331	3,546	398	490
2029	123.4	158.5	14.2	20.6	3,362	3,606	407	505
2030	125.9	161.9	14.6	21.2	3,425	3,687	417	520
2031	128.1	165.2	15.0	21.9	3,475	3,763	427	536
2032	130.5	168.1	15.4	22.6	3,535	3,821	436	553
2033	132.3	171.0	15.8	23.3	3,567	3,886	445	567
2034	134.7	173.9	16.2	23.9	3,628	3,945	453	578
2035	136.3	176.7	16.5	24.5	3,659	4,001	461	592
2036	138.1	178.9	16.9	25.1	3,689	4,028	472	607
2037	139.7	181.8	17.3	25.8	3,723	4,099	479	620
2038	142.0	184.0	17.7	26.4	3,789	4,133	487	632

All values refer to the New Zealand adult population aged 25–99.

Figure B1: Observed and projected demand for total knee replacement in New Zealand, 1999–2038, cross-model comparison.



Source: NZ-MOA simulation model; NZJR 2016;[22] Hooper et al 2014.[13]
Points show observed provision of TKR 1999–2013; dashed line the published projections from Hooper et al 2001–2026; and solid lines the new model projections 2013–2038, under the base case scenario (ongoing increase in population BMI based on current trends) and with no further increase in population BMI (ie, maintaining 2013 BMI distribution).
Inclusion criteria differ between data sources, resulting in the discontinuity between observed and modelled TKR provision in 2013. See the main manuscript for further discussion of modelling assumptions and inclusion criteria.
BMI indicates Body Mass Index, in kg/m^2; NZJR, New Zealand Joint Registry; TKR, Total knee replacement surgery.

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Mate wareware: Understanding 'dementia' from a Māori perspective

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ABSTRACT

AIM: To investigate Māori (Indigenous people of Aotearoa New Zealand) understandings of dementia, its causes, and ways to manage a whānau (extended family) member with dementia.

METHOD: We undertook kaupapa Māori research (Māori informed research) with 223 kaumātua (Māori elders) who participated in 17 focus groups across seven study regions throughout Aotearoa New Zealand and eight whānau from the Waikato region. We audio recorded all interviews, transcribed them and then coded and categorised the data into themes.

RESULTS: *Mate wareware* (becoming forgetful and unwell) ('dementia') affects the wairua (spiritual dimension) of Māori. The findings elucidate Māori understandings of the causes of *mate wareware*, and the role of aroha (love, compassion) and manaakitanga (hospitality, kindness, generosity, support, caring) involved in caregiving for whānau living with *mate wareware*. Participants perceived cultural activities acted as protective factors that optimised a person's functioning within their whānau and community.

CONCLUSION: Whānau are crucial for the care of a kaumātua with *mate wareware*, along with promoting healthy wairua for all. Whanau urgently need information to assist with their knowledge building and empowerment to meet the needs of a member affected by *mate wareware*. This requires collaborative healthcare practice and practitioners accessing the necessary mātauranga Māori (Māori knowledge) to provide culturally appropriate and comprehensive care for whānau.

Similar to other countries, Aotearoa New Zealand is experiencing a growing number of people living longer. Numbers of kaumātua living beyond 65 years and 80 years of age have almost doubled in the last decade. In 2011, there were 1,928 Māori estimated to have dementia, and this number is projected to reach approximately 4,500 by 2026.[1] A recent study found Māori were significantly younger when the diagnosis of dementia was made. Māori are 8.5 and 3.3 years younger than Pākehā (English person of European descent) and Pasifika, respectively.[2] Current epidemiological estimates assume that Māori and Pākehā have the same rates of dementia.[3] However, the actual incidence of this disease for Māori could be higher due to older Māori being: less likely to access primary care services; less likely to utilise mental health services; and more likely to be cared for within the whānau rather than reside in long-term care facilities where they are more visible.[4] In addition, Māori have a high prevalence of health conditions, such as diabetes, cardiovascular disease, stroke, and a history of traumatic brain injuries, which are risk factors for the onset of dementia. Further, Māori experience differential access to determinants of health, access to health services, and quality of healthcare compared to others living in Aotearoa New Zealand, which also increases their risk.[5–8]

The literature regarding Māori and dementia is lacking. As a result, dominant Western biomedical views influence the current understandings of dementia. For example, dementia affects the whole whānau, not just an individual, yet there are no explanations or descriptions of the

impact on whānau in the current literature. Furthermore, current protocols and tools used in the diagnosis of dementia have not included Māori in their development and validation, and are therefore culturally biased, inappropriate and lack accuracy for this population.[9] A growing understanding of the importance of including Māori worldviews in healthcare together with the increasing impact of dementia for Māori signals the need for a dementia care pathway informed by mātauranga Māori. The current study 'Kaumātuatanga ō Te Roro (The Ageing Brain)' aimed to develop (1) a Māori understanding of dementia, and (2) a Māori-responsive assessment tool for the diagnosis of dementia ready for a full validation study. This paper reports Māori understandings of dementia, its causes, and ways the whānau manage a whānau member with dementia. An inclusive approach was adopted when referring to kaumātua. A broad definition of kaumātua as older people (men and women) within whānau, hapū (subtribe), iwi (tribe) and Māori communities was applied. This paper reports our findings related to the first aspect of the study, Māori understandings of dementia.

Method

A qualitative design using kaupapa Māori research methodology was used. Two hundred and twenty-three kaumātua from across Aotearoa, and eight whānau from the Waikato rohe were recruited using whanaungatanga (relationship building) as a form of purposive sampling. Kaumātua participated in 17 focus groups across seven study locations throughout Aotearoa (Kaitaia, Auckland, Hamilton, New Plymouth, Whakatane, Wellington and Christchurch). Kaumātua were given the option to participate in a focus group in te reo Māori or English. The whānau interviews were conducted in English. All interviews were semi-structured and the same prompt questions were used across all focus groups with a different set of questions for the interviews, which were audio-recorded. Following the transcription and translation (for te reo Māori focus groups) of recordings, transcripts were checked for accuracy. Transcripts were coded and categorised into five key categories using Mahi ā-Roopū (a Māori collective qualitative analysis approach),[10,11] with the guidance of kaumātua. These five categories reflect the commonality of understandings, causes and management approaches of some with *mate wareware* that emerged across the dataset in both (focuucs groups and whānau interviews).

Results

Overwhelmingly, participants found the words 'dementia' and 'Alzheimer's' evoked feelings of despair and confusion. A clear preference for utilising kupu Māori (Māori words) to describe changes in behaviours such as absentmindedness and forgetfulness was evident. Participants used terms including wareware (forgetful), pōrangi (mad), rorirori (crazy), wairangi (unbalanced), māharatanga (remember), maumahara (reminisce), rangirua (confused) and whakapakeketanga (adulthood). Following whakawhiti kōrero (discussion) with the rōpū kaitiaki (kaumātua advisory group), *mate wareware* (pronounced phonetically *ma-te* wah-ree-wah-ree) lent itself for universal use among Māori across Aotearoa New Zealand. *Mate* refers to being sick, ill, ailing, unwell and diseased; while *wareware* means to forget or be forgotten. While participants used a variety of terms for a whānau member's forgetfulness and problems with thinking, for the most part their understandings of *mate wareware* were surprisingly similar.

Te Oranga Wairua (spiritual wellbeing) is the central and unifying category that emerged from the data. Living and functioning in Te Ao Māori is critical for *te oranga wairua* of whānau. *Mate wareware* does not just affect an individual, it impacts whānau, hapū and communities Māori live within. One important aspect of te oranga wairua was for kaumātua to continue to undertake their cultural roles, such as kaikaranga (caller) or whaikōrero (formal speech), despite any perceived changes in memory or behaviour. Whānau who embraced changes in behaviour, accommodated and adapted to the changing needs of kaumātua because they understood the importance of culture, environments, community and social contact for the ongoing functioning of whānau. The following is an example of *te oranga wairua* in action:

"I believe [be]*cause of our way of life, our acceptance, our extendedness they were just drawn into the whānau, you know, and just cared for and just looked after* [others]*…"*

"We got her to the doctors and [she] *had a few assessments and scans. That's when they came up with the vascular dementia. So we sort of got into a bit of a study and research and had a look at what that meant and things like that. We've sort of a built a little solid whanau around aunty."*

Whānau treasured and valued continuance of kaumātua roles, and therefore accepted changes and ensured the maintenance of familiar environments for optimal kaumātua engagement in daily life and cultural activities. For some whānau, changes compromised their cohesion when challenged by geographical distance and different views and understandings about *mate wareware*. This lack of cohesion appeared to negatively affect the oranga wairua of the whānau.

"…the impact that it had on my cousins, at the time, [be]*cause even they started fighting against each other, saying 'This is the best thing' and 'No she's not* [got dementia]*.' 'Yes, she has. Well you don't live near. You only come home every so often. You didn't see her, when it* [mate wareware] *really started…'"*

Five sub-categories explain *mate wareware* from a whānau Māori perspective, which are necessary for their te oranga wairua (Figure 1): *Ngā Pūtake* (causes); *Ngā Rongoā* (protective factors); *Aroha and Manaakitanga* (acceptance of illness and behaviour change); *Kaitiakitanga* (caregiving); and *Ngā Ratonga* (dementia services). Table 1 provides examples whānau conveyed for each sub-category.

Ngā Pūtake (causes)

Whānau held different understandings of *mate wareware*. Many whānau understood *mate wareware* to be a debilitating disease that had serious adverse effects on both the individual and the whānau. These beliefs were evident in the tone and manner in which they described the behaviours.

"…she'd go wandering and you couldn't lock her in the house, she'd always find a way out. Jump out the window. Put her clothes on, put her coat on outside, and that was sad to see, such a forceful woman like that and suddenly she's reduced to nothing. Yeah that's the hard bit to watch. Nearly burnt the house down. Put her food on, forgot about it."

According to whānau, the *Ngā Pūtake* (causes) of *mate wareware* related to the loss or change in socially oriented activities in a person's life. *Ngā Pūtake* was also seen as occurring within the broader context of the ongoing intergenerational effects of colonisation, such as loss of rongoā (Māori medicine), introduction of Pākehā medicines, loss of tohunga (traditional Māori healer), changes in cultural practices and lack of access to traditional foods for many Māori whānau.

"She had dementia because of loneliness. My father died and she had all her grandchildren, but it wasn't enough."

Often whānau interpreted the causes of *mate wareware* within historical, cultural and social contexts rather than as a physical illness or disease.

"I do think that the Pākehā environment has impacted on Māori memory and also the pills they give us to take. We are part of the Pākehā world. It's a world that we can't escape from and we're victims of it. We have to live in it."

Some whānau did not perceive *mate wareware* as an illness or disease, but rather as part of a spiritual journey and as a normal consequence of growing old and preparing to join their tūpuna (ancestors).

"I remember my aunties and uncles saying they were talking to the old people. They are with them. They are over on the other side. They are between two worlds. So, don't worry about them, they are okay."

Ngā Rongoā (protective factors)

Ngā Rongoā describes the protective factors that slow down or prevent *mate wareware*. Kaumātua reported that engagement in cultural activities were crucial protective factors. Listening to te reo Māori (the Māori language) and being engaged in a range of cultural activities promoted wellbeing and maintained a person's ability to be socially active (Table 1).

"This is the hinengaro [psychological dimension]*. We can sit here, close our eyes, comprehend everything that is being said, because we are listening not just with our ears, but with our minds, with our souls and whole physical being."*

Some whānau reported those with *mate wareware* demonstrated increased use of te reo Māori, which was their first language but suppressed in early childhood.

"They miss the reo because that is their first language."

The value of te reo Māori was consistently highlighted as a vital healing and comforting factor for those who suffer from *mate wareware*.

"te reo Māori is a gift, it is a medicine. It is health for our thoughts."

and

"My husband, he used to go in there and the minute he spoke in te reo, my father was there and for the whole hour they used to talk. You'd think that my father had nothing wrong with him, he remembered everything! But the minute you spoke English, that was it. He just didn't want to know."

Being able to utilise te reo Māori enabled those with *mate wareware* to engage more fully in cultural activities and events—in these ways engagement in cultural practices are seen as rongoā that slowed or prevented the progression of *mate wareware*.

Aroha and Manaakitanga (compassion and caring)

Many whānau appear driven by an inherent collective obligation to care for others with their sense of compassion and caring that enables their acceptance and tolerance of changes brought about by illness and disease. They do this by absorbing the changes that occur, and work around and with the person to ensure they are fully included in daily activities and life.

"I find Māori accept that either koro (grandfather), *or nanny, or sister, or aunty or whoever have this unwellness, and the family just absorb it and deal* [with it] *and work around it.."*

Thus, because some whānau did not always view changes resulting from *mate wareware* as something pathological, they accepted and accommodated these new behaviours as part of normal ageing.

"It pains me when I see so many elders told by tauiwi (non-Māori) *that there is something wrong with them."*

Instead, *mate wareware* involved whānau doing things differently in order to maintain a person's independence and involvement in activities for as long as possible.

Kaitiakitanga (caregiving)

Kaitiakitanga occurs within a Māori collective cultural context and is a critical role in te oranga wairua of the whānau, especially in respect of children and older members.[12] The obligations to care for others, and the notion that Māori ways of doing things is best practice.

"Initially, koro (grandfather) *was quite depressed and down. I said to him, 'Just do what you want to do, be who you want to be.' So every day he would say karakia* (prayer) *and work on the vegetable garden. It's the sense of whānau, purpose* (and) *being productive…he knows where he belongs."*

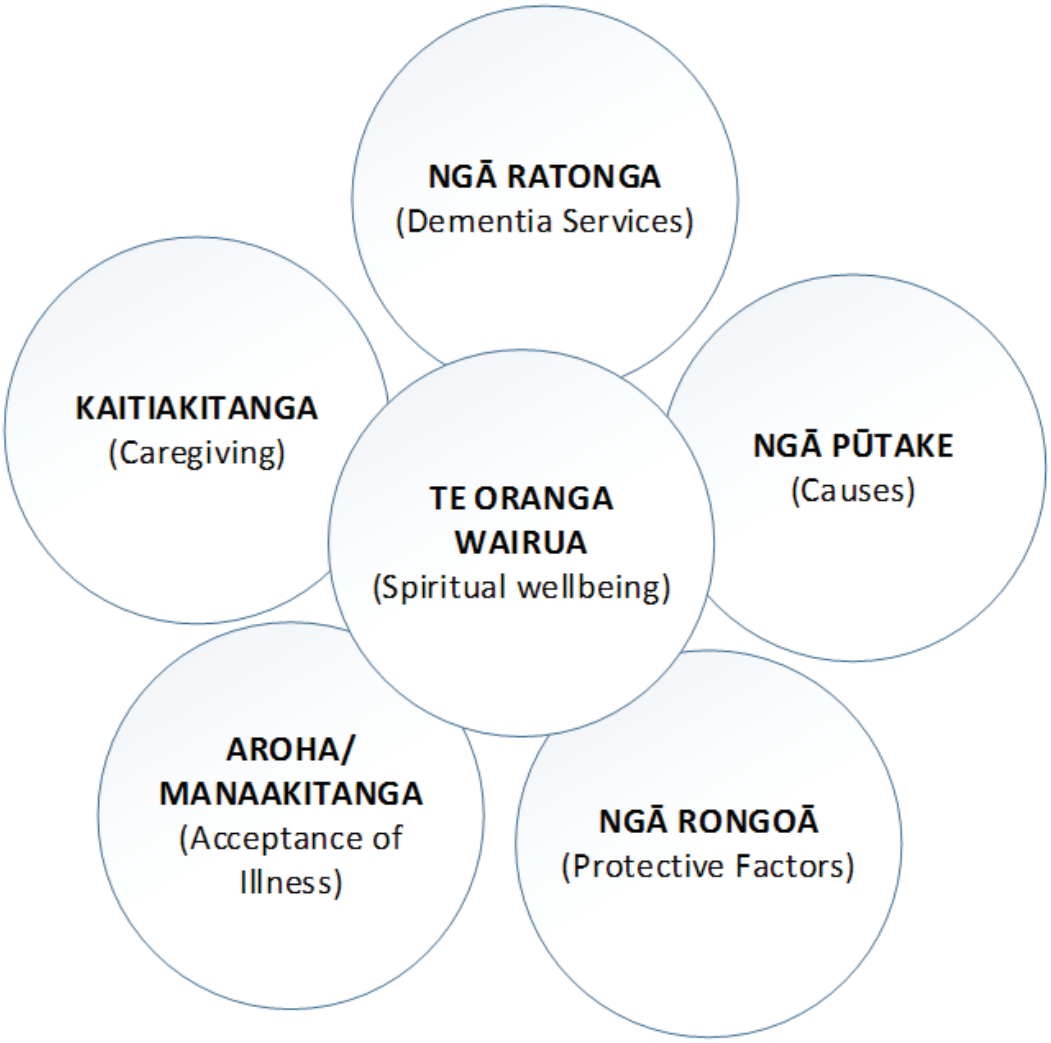
Ngā Ratonga (dementia services)

Ngā Ratonga are important to reduce the burden and stress on those whānau caring for their kaumātua with *mate wareware*. Clearly, whānau needed good support and advocacy to help them understand *mate wareware* and the growing needs of their kaumātua, and accessing necessary services. Often whānau needed practical help and resources, such as paid care-giving, home help, physical alterations to homes, equipment for activities of daily living (eg, hand supports for showers, toilets and beds), caregiver respite, social activities and access to resources such as continence products. While most whānau firmly believed in keeping their kaumātua at home and out of residential care facilities, there came a time when they needed to access greater support and care. Obvious in participants' kōrero was their need for more information about available services and how to access them. However, whānau expressed concerns about the cultural competence of service providers and the monocultural nature of many residential care services when they did access services.

Table 1: Sub-categories: examples of whānau activities.

Sub-category	Examples
Ngā Pūtake (causes)	• Enduring effects of colonisation • Social isolation and loneliness • Loss of significant whānau member • Retirement • Lack of social and physical activity
Ngā Rongoā (protective factors)	• Te reo Māori • Waiata (song) • Whakapapa (genealogy) • Whaikōrero (formal speaking on marae) • Kapa Haka (song and dance) • Roopū Kaumātua (kaumātua groups) • Marae • Cariving, raranga (weaving), etc
Aroha and Manaakitanga (compassion and caring)	• Treating kaumātua with respect and aroha • Whānau working together • Pooling resources • Adapt the environment, when needed • Willing to alter own lives and daily routines in response to changes and to care for a person with *mate wareware*
Kaitiakitanga (caregiving)	• Collective cultural obligations • Māori ways of doing things is best practice • Whānau is optimal caregiving environment so avoid 'mainstream' residential care • Encountering challenging behaviours: such as hitting, swearing, wandering, arguing, aggressive, driving unsafely, frustration, abusive, paranoia • Encountering guilt when unable to fully care for a person with *mate wareware*
Ngā Ratonga (dementia services)	• Cultural competency of clinicians and dementia service providers • Lack of Māori services for *mate wareware* • Referral and access to specialist services that work in partnership with whānau • Advocacy to assist whānau • Sufficient to address kaumātua and whānau needs • Residential care facilities not including whānau in the care

Figure 1: Achieving Te Oranga Wairua in the presence of *mate wareware*.



Discussion

Māori understandings of *mate wareware*, commonly referred to as dementia, differs from the predominate Western conceptions. We noted respectful tolerance and acceptance of a whānau member displaying forgetfulness and problems with thinking. Whānau were generally inclusive of their whānau member's changes in their daily functioning and new emerging behaviours. They often talked about honouring their identity as older Māori and ensuring they were able to continue to participate in various activities like pōwhiri (traditional welcoming), waiata (singing), kapa haka (Māori performing group), and raranga (weaving). Te Oranga Wairua, the spirituality of older Māori with *mate wareware* is also a key difference in the understanding of *mate wareware*.

Whānau are crucial for the care of a kaumātua with *mate wareware*, along with promoting healthy wairua for all. The collective obligations of whānau are important for their wairua, and the care of those affected by *mate wareware*. Mana-enhancing (upholding whānau status) relationships with whānau are vital, and need to be informed by cultural concepts such as aroha, manaakitanga, whakapapa (geneology) and whanaungatanga (relationships/connections). This highlights the need to not just work with an individual 'patient' but with whānau, and recognise the value and positive ways whānau make to the optimal wellbeing of someone with *mate wareware*.

These findings highlight the importance of whānau and their contribution to the health and wellbeing of all involved. Indeed, for some whānau experiencing isolation,

this resulted in loneliness with a profound impact on te oranga wairua. We found the wairua of whānau with *mate wareware*, as a collective and individuals, must be considered for their experiences and positive functioning.[13,14,15] Elder has reported that insults to the brain have both physical and wairua elements, such wairua 'injuries' impact on individuals' and the collective whānau as a whole.[14,15] These cultural 'injuries' necessitate culturally informed assessment and interventions.[9]

Whānau varied in their abilities to function as caregivers, from those who function cohesively to those whānau compromised by factors such as geographical distance and competing commitments. Despite the commitment by many whānau to care for a person with *mate wareware*, kaitiakitanga (caregiving) can be challenging. Poor knowledge and understanding about *mate wareware*, a lack of resources and necessary support services all contributed to difficulties in providing day-to-day care. Although on the one hand, it appeared that rural whānau were more likely to pool resources, on the other hand these whānau were more likely to encounter a lack of services available to them in the community. A lack of resources to support whānau in their kaitiakitanga role, forced them to make difficult choices about going into mainstream long-term care facilities.

We advise some caution in applying the findings to iwi and hapū outside the Waikato rohe where whānau data was collected. However, whānau-related information was collected in the course of the kaumātua interviews undertaken across Aotearoa. This research nevertheless reinforces the significance of mātauranga Māori informing the provision of comprehensive care for whānau with someone with *mate wareware*. This signals the need for the collaboration of medical and health professionals with whānau in recognising the vital role cultural knowledge has in working with and planning care for whānau. It also indicates the need for health professionals to access mātauranga Māori, and accessing local cultural advisors to assist in developing collaborative healthcare practice that integrates Māori cultural concepts and practices. The Meihana Model[16] is one approach that positions whānau centrally during assessment and intervention planning activities, and provides clinicians with a structured process for bringing together cultural and clinical concepts. This multidimensional model of practice promotes a collaborative approach to practice.

We found an urgent need for information sharing and knowledge building for whānau that empower them to manage *mate wareware* within their unique contexts. This involves building their health literacy, in culturally relevant and meaningful ways so they can utilise the information to their benefit. We also found whānau were challenged when accessing services for a range of reasons, indicating whānau access to resources is a crucial consideration.

Conclusion

This research is the first to describe Māori understandings of the ageing brain and 'dementia' in particular. Mate wareware has emerged as the preferred term for what might be termed 'dementia' and the manifestations of the ageing brain, although for Māori these changes are likely to occur at younger ages than for Pākehā. This cultural concept clearly positions the importance of using te reo Māori (the Māori language), and is underpinned by mātauranga Māori. These findings strongly support use of the term *mate wareware* in place of dementia along with other preferred kupu (words) in te reo Māori, and approaches informed by mātauranga Māori. This should occur in all contact with whānau who may be experiencing changes in memory, behaviour, thinking and emotions.

Te Oranga Wairua has been identified as central to Māori thinking (Figure 1). Five key themes were identified from kaumātua around Aoteaora New Zealand: *Ngā Pūtake* (causes); *Ngā Rongoā* (protective factors); *Aroha and Manaakitanga* (acceptance of illness and behaviour change); *Kaitiakitanga* (caregiving); and *Ngā Ratonga* (dementia services). Te Oranga Wairua can be considered a deeply spiritual and uniquely Māori experience of connectivity. This links to previously published work emphasising the indication for cultural intervention when there is disruption to wairua.[9,14,15]

Effective care for someone with *mate wareware* must therefore include cultural practices to strengthen wairua of the whole whānau. In addition, whānau require information, support and collaborative relationships with healthcare providers to ensure delivery of culturally appropriate and comprehensive assessment and care. Healthcare providers need a more in-depth understanding of the ways in which Māori comprehend *mate wareware* and how whānau manage a member. This research contributes new knowledge to help bridge the gaps that exist for whānau and healthcare providers.

Competing interests:
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Availability of automated external defibrillators in Hamilton, New Zealand

Peter A O'Callaghan, Janice Swampillai, Martin K Stiles

ABSTRACT

BACKGROUND: Last year, there were 2,000 out-of-hospital cardiac arrests (OHCA) in New Zealand, 74% received CPR but only 5.1% accessed an automated external defibrillator (AED). The average survival rate of OHCA is 13%. The aim of this study was to visit all 50 AED locations shown on www.hamiltoncentral.co.nz to assess their true availability and visibility to the public in the event of an OHCA.

METHOD: All premises were visited and the first staff member encountered was asked if they were aware an AED was onsite, its location, hours of availability, if restricted access applied and whether it had been used.

RESULTS: Of the 50 locations, three sites no longer exist and two AEDs were listed twice. Therefore, only 45 AEDs exist. Two sites had grossly inaccurate locations. Three AEDs (7%) were continuously available. Nine AEDs were accessible after 6pm at least one day of the week. Thirteen AEDs were available on weekends; however, five required swipe card access. None of the AEDs were located outdoors.

CONCLUSION: Far fewer than 50 listed AEDs are freely available to the public, especially after 6pm and on weekends. Lack of signposting and restrictions to access would lead to delayed defibrillation. This important health issue needs addressing.

In New Zealand, there are close to 2,000 out-of-hospital cardiac arrests (OHCA) per year.[1] Cardiac arrests fall into two categories; shockable rhythms (ventricular fibrillation (VF), pulseless ventricular tachycardia (pVT)) and non-shockable rhythms (pulseless electrical activity (PEA), Asystole), which ultimately determine their management. For shockable rhythms, performing defibrillation as soon as VF/pVT are identified greatly increases the likelihood of achieving return of spontaneous circulation (ROSC) and thus survival.[2,3]

If VF is defibrillated within the first minute of collapse, the patient's chances of survival are approximately 90%.[1] For every minute that defibrillation is delayed, survival is reduced by 10–12%.[4,5] If it is delayed by more than 10 minutes, the chance of survival is less than 5%.[1] The median response time for emergency services called to a cardiac arrest call in New Zealand is six minutes in an urban community, and nine minutes in a rural/remote community.[1] Therefore, if solely relying on an ambulance to provide a defibrillator, chances of survival will have dramatically decreased by the time paramedics have arrived. These statistics show how important early defibrillation is for shockable rhythms in OHCA cases, and therefore the importance of readily available AEDs in local communities.

In 2018, 74% of OHCA patients received cardiopulmonary resuscitation (CPR) by a bystander but only 5.1% were defibrillated by a public access automated external defibrillator (AED).[1]

The low number of public AED use in OHCA is not unique to New Zealand. This global problem has been recently reviewed by Delhomme et al, who listed the contributing factors to this issue under two categories; AED deployment issues (low public AED numbers, limited AED visibility and limited AED accessibility) and bystander-related issues (education and training in basic life support (BLS) manoeuvres and the willingness to initiate CPR).[6]

Improvements in all of these areas are hoped to increase the rate of public AED use in OHCA, and therefore survival. In this study, we focus on the AED accessibility and visibility in the city centre area of Hamilton, New Zealand. We test if these issues exist here and discuss what we can do to improve this.

Aims/objectives

There are a number of different ways of locating public AEDs—for example various apps which can be downloaded to a smart phone, and also community websites. At the time this study was carried out there were 50 AED locations listed on www.hamilton-central.co.nz in the Hamilton urban area, a website freely accessible to the public.

The aims of this study were to:

1. Visit all 50 locations in person to assess their true availability
2. Identify the precise AED location within these premises
3. Review restrictions, if any, to device access
4. Assess the visibility of the AED to the public as well as signposting for the device

Methods

A questionnaire was formed prior to visiting the AED locations, containing all pertinent questions to achieve the objectives above. All 50 sites listed were visited between 1 May 2018 and 22 August 2018.

The following questions were put to the first member of staff encountered to simulate an emergency. They were asked:

1. If they were aware an AED was onsite
2. Its precise location
3. Hours of availability
4. If restricted access applied (ie, key/PIN/staff member/swipe card access required to access AED)
5. If the AED had ever been used.

Additionally, the visibility and signposting of the AED was assessed.

Results

AED location accuracy and AED use

Of the 50 locations listed, three sites no longer existed due to relocation or closure and two locations were duplicate listings. Therefore, only 45 AEDs existed out of 50.

The location of two AED sites grossly differed from the location described on the website. One of the AEDs was incorrectly listed as inside one of the retailers in a shopping centre, when in fact it was kept behind the information desk. As for the other inaccurate listing, the company had relocated to another part of the city taking its AED with it. Therefore, there was no AED at the location specified.

Four of the AEDs had been used or attempted to be used; two by the urgent care centre and the fire department. In the other two attempts, the pads were applied but it turned out not to be a cardiac arrest.

Additionally, two locations were identified that had AEDs on their premises but were not listed on the website. This was co-incidental while searching for AEDs listed on the webpage.

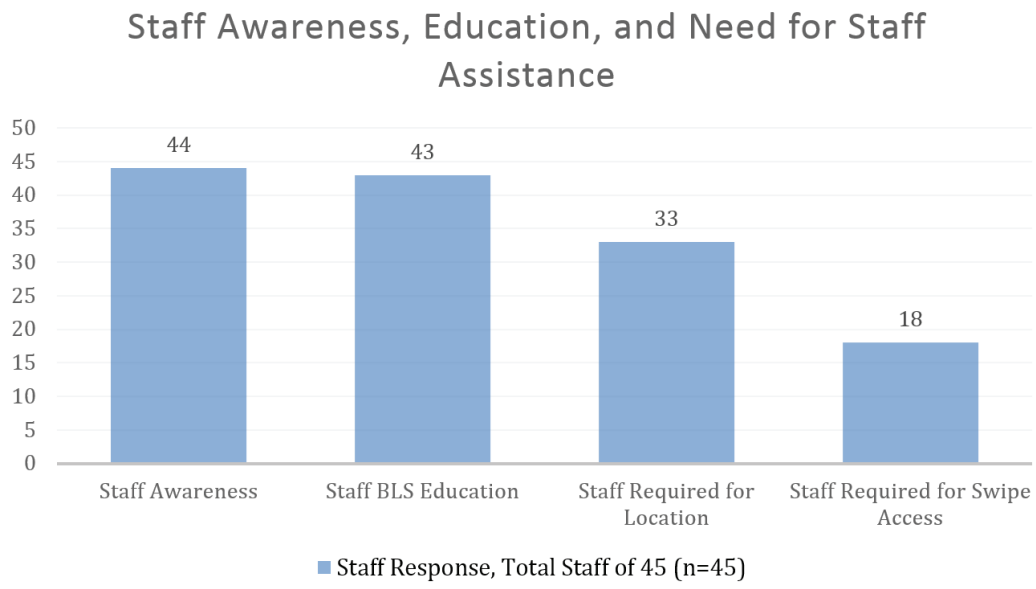
Staff awareness, education and accessibility

Of the first staff members encountered, 44 out of 45 knew that an AED was onsite and were able to identify the location of the AED without assistance. All but one of the 44 stated that they, or other staff members within the building, had received BLS and/or AED training.

For 33 out of 45 AEDs, a staff member was needed to help identify the location of the AED, 18 of which also supplied swipe card access which was needed to get to the device. Several AED locations were within office blocks with the office located above ground level. In these situations, access was only available via the lift as access to the stairs required a swipe card.

The majority of AEDs listed on the website were located at private companies, purchased with the primary intention of staff use. This was a common response when asked why they located their AED inside, or

Figure 1: Graph illustrating the responses of the first staff members encountered at all 45 AED locations.



From left to right; (i) The number of staff aware that an AED was onsite (ii)The number of locations having at least one member of staff BLS trained (iii) The number of locations staff members are required to help locate device (iv) The number of locations a staff member is required for swipe card access to get to device.

on a floor above ground level, rather than outside the premises. However, they also chose to list them on a public website as an accessible AED for the Hamilton community.

Times of accessibility

In total, just three AEDs (7%) were available 24 hours a day, seven days a week. These were located at an urgent medical care centre, a fire station and a petrol station. Within the fire station, the AED was not located in the building itself, but on the fire trucks. The building is usually closed to the public and would require a phone call to the emergency services to alert the fire-fighters inside of the emergency.

In addition, there were three AEDs located within a college campus that are accessible to staff and students continuously, but not to the public. A student or staff swipe card would be required to enter the campus buildings outside of office hours as well as to open the locked case storing the device. For this reason, they were not deemed continuously available to the public.

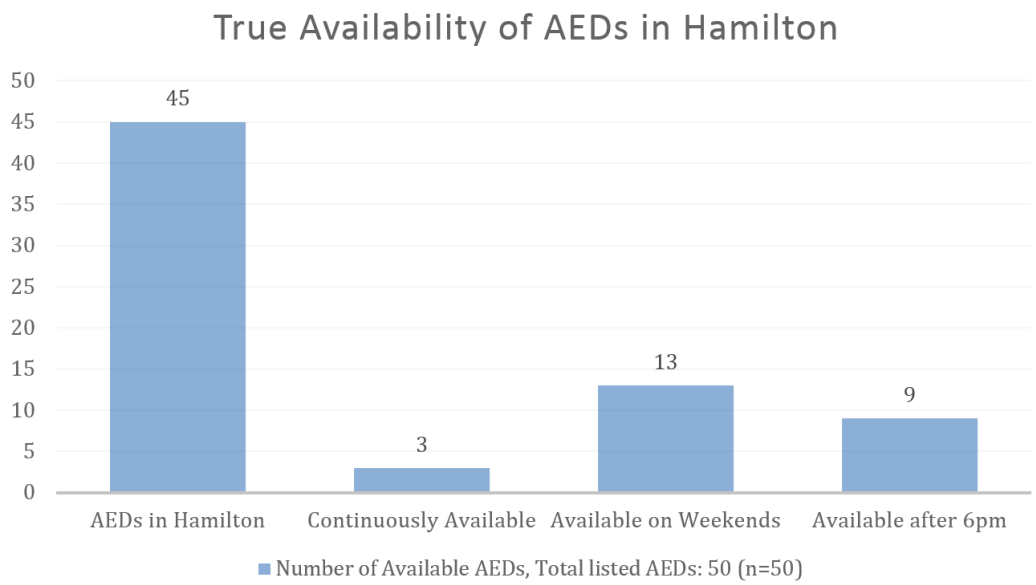
Nine AEDs were accessible after 6pm on at least one day of the week. These include the six AEDs discussed above, it also includes one AED accessible for only one hour per week after 6pm. Thirteen AEDs were available on weekends; however, five of these would require swipe access to the building or to contact a member of staff to gain entry.

AED location, visibility and signposting

None of the 45 AEDs were located outside. Of the staff members surveyed, the most common reason quoted was due to fear of vandalism or theft. As many of these locations were in office blocks rented by the occupier, some of the staff surveyed felt they would not be able to securely encase their AED outside the building easily as that would require modifications approved by the landlord. Consequently, none of the AEDs were clearly visible to the public from the outside and only 10 were deemed visible from within the premises.

AED signage was also rare. Only eight premises had a sticker or sign on the outside identifying that an AED was located within the building. Typically, this was identified by placing a 20cm by 15cm sticker on the entrance doorway, a sign that would only be visible at close proximity. Six locations had signage within the building, while one had both.

Figure 2: Graph illustrating the true availability of AEDs listed in Hamilton.



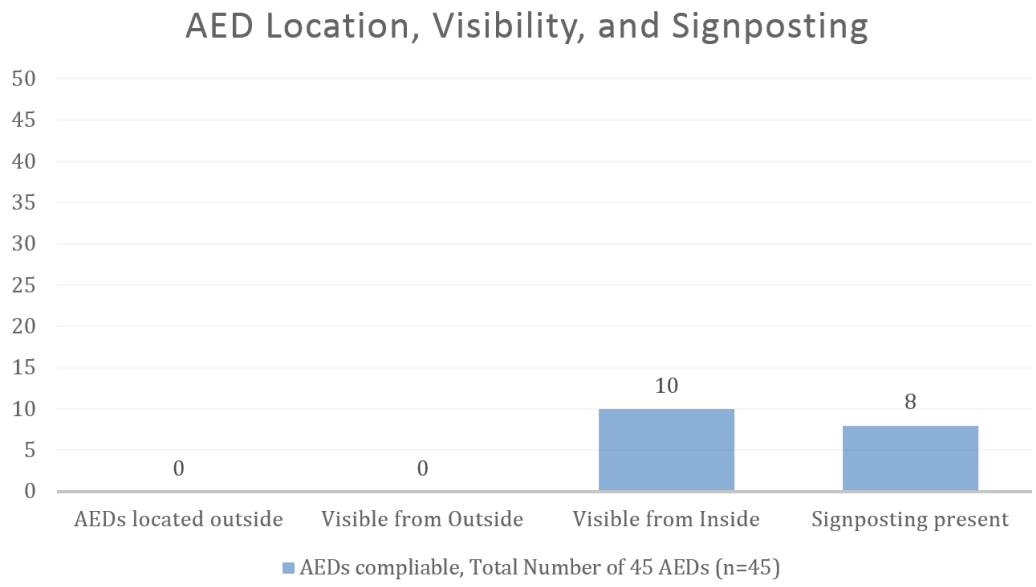
From left to right; (i) The actual number of AEDs in Hamilton (ii) Number of AEDs available continuously (iii) Number of AEDs available on the weekends (iv) Number of AEDs available after 6pm for at least one day of the week.

Discussion

Far fewer than the original 50 listed AEDs are freely available to the public, particularly after 6pm or on weekends. There are errors on the website that could potentially waste time in a life-threatening situation. These include duplicate listings, sites that no longer exist and inaccurate descriptions of locations provided on the website. The website was contacted and the appropriate corrections have been made.

There are no outdoor AEDs available, with none of the AEDs listed clearly visible from the outside. Combined with the lack of signposting, there would be an inevitable delay in obtaining an AED in an OHCA. Access is further limited as many AEDs require assistance for location, swipe card access or both

Figure 3: Graph illustrating the number of AEDs located outside, those that are visible from outside and inside the premises and those with outdoor signposting accompanying the AED. This is out of a total of 45 AEDs.



in order to obtain the defibrillator. Issues with accessibility were not unexpected as this has been identified as an issue in other studies. For example, a study was performed by Sun et al in 2016 investigating the AED accessibility issues in OHCA in Toronto, Canada. They found that between 2006 to 2014, one in five OHCAs occurred near an inaccessible AED at the time of the arrest, and that 61% of all OHCAs occurred during the evening, night and weekends.[7] Similar findings would be expected to found if the same study was performed here in Hamilton given the results of our research.

There are likely more AEDs within the community that could be listed online, as evidenced by the coincidental finding of two AEDs. Only one of the AEDs listed is located within a sports complex. More AEDs could be identified by reaching out to sports clubs and training facilities within Hamilton informing them of the website.

We would recommend the following in order to improve the issues with accessibility and visibility:

1. Increase the number of outdoor AEDs

There needs to be more publicly available AEDs located in more visible outdoor locations. One possible solution would be to convert old/unused telephone booths into secure AED locations as seen in Ireland.[8] Telephone booths are becoming increasingly obsolete and are usually located in focal points within a town or city. Therefore, converting old telephone booths to an AED location would provide a highly visible and secure defibrillator to the public (Figure 4).[9]

To ease the public concern of vandalism and theft, outdoor AEDs can be housed in secure casings that require a pin code from emergency services. An example of such is provided in Figure 5 below, seen on Waiheke Island, New Zealand.

Figure 4: Telephone booth converted to contain an AED in Killarney, Ireland.

Image used with permission by Heart of Killarney, http://heartofkillarney.ie/fossa/

Figure 5: Example of secure outdoor AED casing on Waiheke Island, New Zealand.

Photo taken by author.

2. Increase signposting of AED locations

We recommend that all premises should highlight that an AED is within the building. Ideally with a sticker or sign that is larger than the current ones provided as they are only visible at close range.

3. Use of smartphone applications to locate AEDs

Even though the Hamilton Central website is useful in locating AEDs, it is not the website's primary function. There are smartphone applications dedicated solely to listing AED locations as well as alerting trained bystanders to help in an OHCA. These apps also have a larger number of devices listed compared to the website.

The GoodSAM smartphone app was introduced to New Zealand in 2018, originally designed in London.[10] The app alerts the three closest registered users to an OHCA at the same time the ambulance services are alerted. Registered users can also alert bystanders using the 'Alerter' function. All users of the app must prove that they are BLS trained before registering. Responders have 20 seconds to accept the alert, otherwise it moves onto the next nearest bystander. The responder that is closest to a listed AED is directed to collect the device and bring it to the arrest.[10] The aim of the app is to improve the morbidity and mortality of OHCA sufferers by decreasing the time to first shock as well as time to commencing CPR.

There is no scientific evidence yet that this particular app is proven to be beneficial; however, similar alerting systems have shown to improve survival rates. A text message-based alert system in the Netherlands showed that OHCA victims were 2.8 times more likely to survive if their arrest was attended by an alerted rescuer versus those that were not.[11] Hopefully, similar findings will support the GoodSAM application when audited.

Another application is available in New Zealand that solely lists the locations of all nearby AED devices. 'AED Locations' is an app created by Gareth Jenkin, a resuscitation coordinator at Auckland City Hospital, which has over 9,000 AED locations listed.[12] In this app, the option is also available to include the hours each AED is accessible, which could avoid wasting time in attempting to obtain a defibrillator.

4. Regular audits of AED applications and websites

As applications and websites expand, and AED lists become longer, the potential for inaccuracies grows as it becomes more difficult to regularly audit. In our study alone, there were errors in seven out of the original 50 listed (duplicate listings, no longer exist or inaccurate locations), 14% of our relatively small sample size. The responsibility has to be shared with those who list their device to maintain the accuracy of its location and accessible times, especially as these applications continue to grow.

5. Only show the available AEDs at the time the list is accessed

With all AED listing websites and applications, we strongly recommend that the times that the device is available should be added to the information accompanying the device. If possible, the lists should only show the AEDs that are truly available at the time the list is accessed.

6. Use of alternative AED sources and technologies

Alternatives to fixed location public AEDs have been investigated with the potential for success. The use of drones to deliver AEDs has the potential to reduce the time of first shock in OHCA. In Sweden, they recreated previous OHCA events and used drones to deliver an AED to those exact locations. They then compared the dispatch to arrival time of the paramedics that had arrived versus the drone. The median time from dispatch to arrival of the paramedics was 22:00 minutes vs 5:21 for the drone ($P<.001$). The drone was also quicker in all cases with a median reduction in response time of 16:39 minutes ($P<.001$).[13] Even though this study showed large reductions in defibrillator arrival times, there would be multiple difficulties in implementing a system like this, including cost, training, weather and airspace restrictions to name a few.[13]

Other technologies that may be beneficial include battery-operated pocket defibrillators carried by members of appropriate services such as police officers.[14] More research is needed to see if these are beneficial and practical in real life scenarios.

Limitations

In retrospect, there are additional questions that could have been asked during the study that would have been of value. The accurate number of AEDs that required lift access would have been of interest as it was a noticeable obstacle in some cases. An opportunity was missed to question if all AEDs were operational and up to date with servicing. Previous knowledge of the website could have been assessed by surveying the staff members encountered. All would be valuable information in a re-audit in the future or a similar study in another city.

Conclusion

During office hours there is a reasonable number of accessible AEDs in Hamilton. Access to public AEDs is limited outside office hours, with only 7% of AEDs available 24 hours, seven days a week. This is mainly due to restrictions to access. Simple measures could increase availability and public awareness of this life-saving equipment.

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Nil.

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Tailoring a rapid autopsy protocol to explore cancer evolution: a patient collaboration

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ABSTRACT

Genomic analysis of tissues from rapid autopsy programmes has transformed our understanding of cancer. However, these programmes are not yet established in New Zealand. Our neuroendocrine tumour research group, NETwork!, received a request from a patient wishing to donate tumour tissues post-mortem. This viewpoint article summarises the ethical, logistical and social process undertaken to accept this patient's generous donation, and highlights the scientific and educational value of such a gift.

Tumours and their genomes are neither homogenous nor static; it is appreciated that they may change and evolve with time.[1] This process might contribute to the failure of clinical systemic treatments, and therefore remains an important clinical challenge to overcome, and biological phenomenon to understand.[2] During tumour evolution, changes to the genome (mutations) and its gene expression lead to metastatic spread and promotes the survival of the 'fittest' of a genomically heterogenous mix of cancer cell 'clones' that can be disseminated across the body. Research into tumour evolution has been enabled by the advent of next-generation sequencing providing a better appreciation of the genomic complexity of the tumour cells that are present within an individual patient. This builds on an already appreciated histological understanding of morphological heterogeneity between a primary tumour and its seeded metastases.

Tumour heterogeneity can occur between different lesions from a single patient, but also within each lesion with different cells within the tumour evolving different genotypes and having varying potential to metastasise.[3] Important advancements in understanding the genomic landscapes of many tumour types have been made through global sequencing programmes such as the International Cancer Genome Consortium.[4] However, these programmes have been less valuable for understanding the genomic heterogeneity of tumours within individual patients. Nevertheless, in the clinic, understanding tumour heterogeneity within each patient can sometimes contribute to appropriate treatment decisions. For example, the presence of multiple distinct tumour cell clones within the tumour(s) of an individual could lead to treatment resistance where the 'fittest' cells survive and evade therapy or require a different treatment approach. Similarly, specific clones may selectively metastasise to areas of the body that are less amenable to systemic therapy, such as beyond the blood brain barrier. However, these processes remain incompletely understood.

Researchers appreciating the clinical importance of tumour heterogeneity within individual patients have made significant gains in the laboratory. Approaches often involve the analysis of multiple solid tissue samples from an individual, for example for pancreatic or renal carcinomas, taken

at different times during their care and/or from different sites in their body.[5,6] This temporal and spatial information has been invaluable in better understanding the molecular changes that occur as a tumour evolves to evade therapy.[7,8] However, solid tumours, particularly within internal organs, are a challenge to sample unless surgically resected. Invasive tissue biopsies are seldom taken for purely research purposes due to the risks to the patients, making the study of progressive disease difficult in patients where surgical intervention is no longer clinically helpful. Circulating free DNA (cfDNA) has been proposed as a surrogate for multi-organ sampling, but it is unknown whether cfDNA can represent all tumours in the body, or if there is a selective elucidation of individual clones or favouring of particular anatomical locations. To facilitate study of metastastatic cancer in single patients, research hospitals and biobanks around the globe have established routine 'Rapid Autopsy' programmes, allowing patients to donate tissues through autopsy at their point of natural death for use by research groups to better understand tumour heterogeneity and evolution. Such established programmes at over a dozen institutes worldwide have collected invaluable samples, leading to improved understanding across the spectrum of cancers.[9,10] Several well-documented programmes are located in the US (eg, Johns Hopkins Legacy Gift Rapid Autopsy Programme,[11,12] Fred Hutchinson Institute at University of Washington[13] and University of Michigan[14]) and Australia (CASCADE programme, Peter MacCallum Cancer Centre[15]). No established programme of this kind for cancer research exists in New Zealand.

Our New Zealand-based research group, NETwork!, brings together clinical, epidemiological and genomic information to build improved biological understanding of neuroendocrine tumours (NETs). The NETwork! programme was established in 2012 and works closely with patients, collecting tissues for use in research with the ultimate aim of improving care for people diagnosed with NETs in New Zealand. The team is truly multidisciplinary with expertise ranging from clinical oncology through to computational biology. In early 2016, a patient with a metastastic broncho-pulmonary NET made a direct approach to her oncologist, a principal investigator of the NETwork! team. The patient had multiple metastases from her original tumour, and wished to donate her tumour tissues through rapid autopsy on her natural death. Her hope was to contribute to biological understanding which might help those who followed her. Initially, the research team were reluctant to pursue this request and declined, not having established the ethical or logistical framework to effectively conduct such a procedure. However, the patient was persistent and returned on her next appointment accompanied by two of her children, who were both highly supportive. Given this level of determination on the part of the patient, and the strong support from her immediate family, the team felt that they had a duty to at least ascertain whether or not such a procedure would be possible.

In this viewpoint article we summarise the considerable efforts taken to develop and coordinate a process that could meet the challenge initiated by this selfless act. This undertaking has allowed us to assemble and analyse a unique tissue resource, and has given us a valuable understanding of the legal, ethical and logistical considerations needed to carry out rapid autopsy research in New Zealand. We also highlight the value of this partnership between patient, family and researchers to better understanding the biology of neuroendocrine tumour evolution.

Feasibility assessment

After the initial approach from the patient to her treating oncologist, the first step was to assess the feasibility of sample collection through a rapid autopsy procedure. Considerations were made on scientific, logistical, ethical and financial bases. This was performed in parallel through multiple discussions with the lead of the Forensic Pathology Department at Auckland City Hospital, with the Health and Disability Ethics Committee (HDEC), DHB clinicians responsible for her care, and with the laboratory researchers within the NETwork! group. These discussions took a number of months, with ongoing consultation needed throughout the pre-autopsy period in order to plan and later refine the processes. A further consideration for the research team was to balance the scientific value of the

samples with the financial cost of collection and subsequent analysis. The study, the autopsy, sample collections and processing were funded as part of the existing NETwork! programme. A research project was clearly designed around the potential use of the samples before committing to the autopsy to ensure a scientifically beneficial study was possible with the types of tissues that could be collected. These consultations concluded with the decision to proceed with organising the rapid autopsy process, promising best efforts to the family to collect the samples on the day of her natural death. Ongoing communication with the family was important to clarify expectations and balance the likelihood of the autopsy going ahead.

Ethical and legal consent

Upon confirmation from all parties that the process was feasible, ethical approval was sought as an amendment on an existing ethical approval for prospective collection of NET tissue from clinically indicated medical procedures (eg, surgery and biopsy). The patient and their family described their wish to participate with no issues raised during this conversation regarding religious or cultural beliefs. Informed signed donor consent was obtained for the tissues to be collected, stored and used for genomics research after death via an autopsy process and was co-signed by family members. Legal consent was also received to perform an autopsy. The HDEC amendment was submitted alongside letters of support from the donor and her family. This step in the approval followed extensive previous community consultation regarding tissue collection for other parts of the project, and took just three weeks to obtain. When obtaining this approval, we undertook to ensure that the patient's participation in this study would have no impact on her clinical care.

Sampling documentation plan

Spatial information is vital to meaningfully model and interpret tumour metastasis and clonal evolution. In order to accurately map every lesion and site sampled, a documentation process was developed in conjunction with a radiologist and an anatomical pathologist. Cross-sectional images from computed tomography (CT) scans conducted as part of clinical care or follow-up were carefully interrogated prior to the autopsy, and every visible individual lesion localised and anatomic location stated and mapped. This information would then be adjusted according to findings made by the forensic pathologist and technician during the autopsy. The plan would require the manual completion of paper-based forms to record anatomical specimen location, assign naming codes and to sketch diagrams of where each sample was taken from within a specimen. A coding system was developed whereby each excised specimen was assigned a number, and the individual samples derived from this specimen were assigned either a letter or numerical code if to be stored as formalin fixed paraffin embedded (FFPE) or fresh frozen tissues respectively; to be recorded using the paper forms. Further, a photography plan was developed to incorporate *in-situ* and resected large-scale photographs of each specimen and the samples derived from it. As we wanted to use samples for genomic analysis in combination with morphological analysis it was imperative that the quality of the nucleic acids was maximised in the stored tissues. The decision was made to store both formalin fixed and snap frozen tissues in order to 'future-proof' the collection for use in multiple downstream molecular analyses.

Preparing the team

In order to ensure that enough people were available on the day of autopsy, remembering that it could happen at any time of any day, a roster was established to ensure that all areas of expertise would be available. A hierarchical phone-call system was also established to be used to contact people when needed. The autopsy required people with clinical training; oncologists, surgeons and pathologists (forensic and anatomical); as well as tissue banking scientists from the Auckland Regional Tissue Bank and the NETwork! laboratory team experienced in preparation of samples for genomic analyses. All members of the team generously volunteered their time to assist with the project.

Assembling the kit

The collections required extensive surgical and laboratory consumables and ready access to liquid nitrogen and dry ice stores. Documentation forms and sampling tubes (fresh frozen samples) and formalin-filled

pots (FFPE samples) were pre-labelled with alpha-numeric codes. All items were assembled on a large trolley ready to be transferred from the research laboratory at the University of Auckland Grafton Campus across the road to the Auckland City Hospital Mortuary when required.

The autopsy

On an early morning in mid-2017, now 14 months following her initial request, our donor passed away from a natural death. She had since moved from her own home to care in a private nursing hospital, and further discussions and collaboration had been fostered with her carers, GP and institution administrators. The family had chosen a funeral director with whom they had an existing relationship, and discussion and planning for the process required had been made in advance. The treating oncologist received a phone call from the private hospital nurse at 4am and the roster phone calls were initiated and cascaded to pathologists and the research team. A member of the patient's family met with the oncologist at the bedside, acknowledged her life and her gift, farewelled their mother, and the process began. End-of-life paperwork was completed.

The timing was fortuitous; a quiet early weekday morning allowed easy access to the mortuary and a complete, experienced group of people were available to assist. The donor arrived at the mortuary two hours after her passing. Eleven people worked for six hours to collate over 300 carefully annotated tissue samples. The team was divided into two key groups: the post-mortem team and the sampling team. The post-mortem team included a forensic pathologist, an oncologist, a surgeon and a forensic technician. Another research team member was the link between the two teams, moving between the autopsy room to courier samples and information to the sampling team. The sampling team was led by an anatomical pathologist, alongside two sampling excision staff, two annotation/recording staff and one sample preservation staff member. The sampling team were located in a separate laboratory, away from the autopsy. This enabled separation for non-clinical staff and allowed for the donor's privacy and dignity to be preserved.

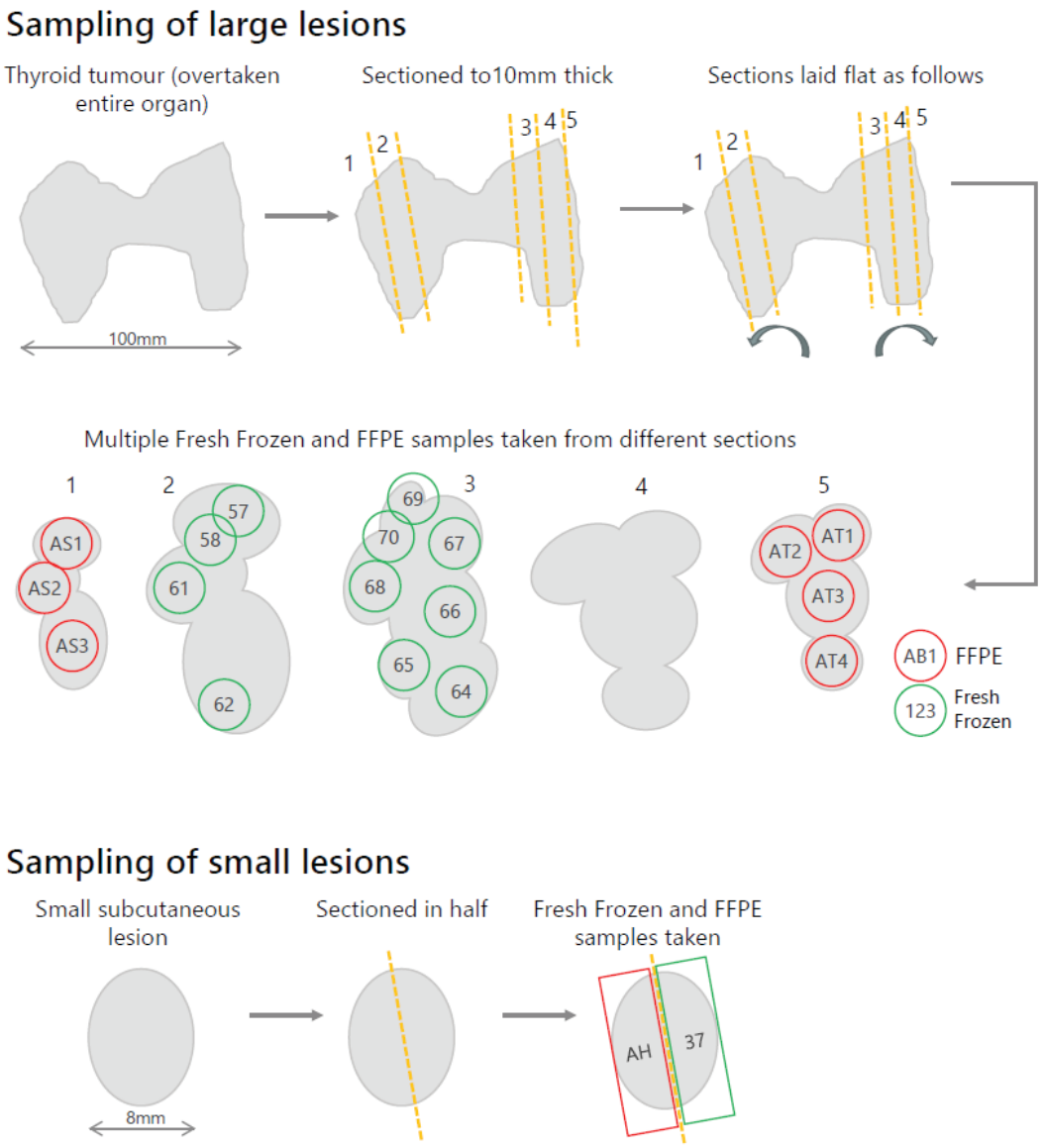
At the donor's last CT imaging scan, over 90 distinct lesions had been identified, ranging from small 5mm subcutaneous nodules to replacement of complete organs with tumour tissue. All lesions but one were successfully sampled. Prior to removal, each lesion was photographed by the team member acting as courier, labelled with a unique number, excised and placed in a pre-labelled dish with orientation noted, before being transferred to the sampling team in an adjacent laboratory. Here, the excised lesions were again photographed and sampled into small cubes for snap freezing or placed into formalin for fixation. Where tissues were large and potentially heterogeneous, multiple samples from different regions were taken; see Figure 1 for an example of the complex sampling in the thyroid gland, compared to sampling of a smaller subcutaneous lesion. Every sample code was noted onto the specimen documentation forms (in written and diagramatic form) in order to record the location of each specimen relative to the others. The stored samples averaged $5mm^3$ for the frozen tissues and $20mm^3$ for the formalin fixed tissues. No tissues were stored that would be unlikely to be used in later research and all surplus tissues were 'returned to the body' for cremation, which had been the donor's wish. Participation in the autopsy did not change the timing or nature of her funeral arrangements.

Sample processing

After the day of autopsy, 141 small specimen containers of tissues fixed in formalin were transferred into ethanol after adequate fixation. Where too large to be blocked individually, tissues were divided, totalling 187 samples, and blocked in paraffin with further photographs taken to record specimen orientation and relative location. This process took a number of weeks, and was carefully documented. A small number of vertebral specimens required decalcification and were placed into a gentle EDTA buffer for up to 12 weeks in order to try and retain the nucleic acid quality and tissue morphology, following an appropriate decalcification protocol to optimise preservation of nucleic acids.[16] Finally, all data and photographs were transferred to digital storage on a password-secured server and stored in a non-identifiable manner.

Speed was essential to maximise the quality of nucleic acids for later genomics.

Figure 1: Comparison between sampling methods for large and small lesions.



For large lesions, such as the thyroid tumour shown, the lesion was first sliced into 10mm thick sections, sections were carefully laid flat in order, photographs were taken of all sections lying flat and individual sections were sampled, taking some samples for fresh frozen and some for FFPE fixation. All sites were carefully annotated on paper drawings, which were later transferred onto the photographs of sections, and unused tissue was returned to the body. For small lesions, such as the 8mm subcutaneous lesion shown here, the lesion was bisected, photographed, and each side received either fresh frozen or FFPE fixation.

The samples were collected over the course of six hours and timing of freezing or fixation carefully documented as samples were sequentially collected. The complexity of the case, ie, the extensive number of sampled lesions throughout the body defined the timeframe. This extended timeframe to fixation could affect sample quality, causing hypoxia and necrosis driven changes within the RNA and methylation profiles in the tissues.[17] Careful documentation of sampling has been important to monitor for these effects in resultant genomic data.

Invaluable tissue samples

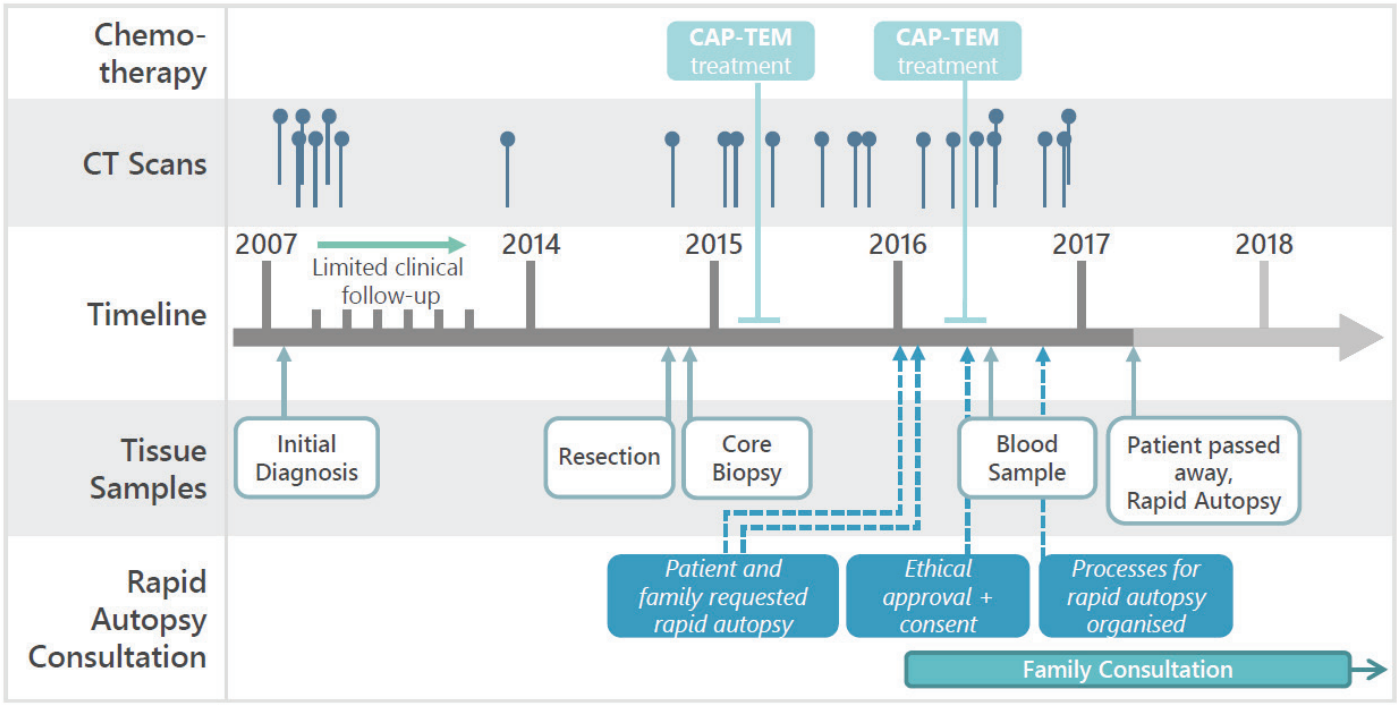
Tissue samples are only as valuable as their annotation. This includes the histopathology, the spatial and organ location as well as a detailed summary of clinical features. The clinical history of the donor is summarised in Figure 2, alongside a summary of the breadth of information collected during this project in Figure 3. The donor's tumour progression and clinical care is shown overlaid with the samples collected both for diagnostics and for research, imaging dates, and the research project consultations and collaborations. Since its inception, this project has required input from close to 100 people, each contributing their expertise in areas including pathology, radiology, surgery, oncology, tissue banking, genomics and evolutionary mathematics. It has provided a valuable training opportunity for a PhD student who is working to coordinate new collaborations with evolutionary biologists to better model the progression of the lesions. Indeed the experience was a profoundly moving and unique experience for all members of the laboratory research team. A year and a half after her passing, the NETwork! group presented the first preliminary results of the evolutionary genomics model to the audiences at the New Zealand Society of Oncology and Queenstown Research Week annual meetings. The overwhelming feedback from these presentations has highlighted the generosity, value and incredible opportunity provided from the donation. The patient's family continue to provide advice, undertake lab visits and receive project updates. It is interesting to consider processes we may alter, should we complete another similar study. Our collection resulted in a large number of tissue samples from a range of complex tissue types, all found to be suitable for the prespecified genomic analyses. We believe the strengths of the project are the relationship with the patient and family, the focus on carefully designing the types of analyses to be undertaken prior to tissue collection, and completing necessary process personalisation with respect to the clinical case, geographical location and timing. Above all, research value, impetus and research time to analyse the samples must be considered in order to accept invaluable patient donations.

The New Zealand context

While this work may be the first tumour collection tissue banking rapid autopsy of its kind in New Zealand, or at least the most extensive effort documented thus far, it is certainly not the first research tissue rapid autopsy collection in New Zealand. Among other initiatives, the now-named Neurological Foundation Douglas Human Brain Bank has been collecting donated human tissue at post-mortem for over 20 years, and underpins many of the research successes of the Centre for Brain Research at University of Auckland, like providing new evidence that adult human brain cells were capable of regeneration.[18] The success of the Brain Bank, and indeed our one-off rapid autopsy collection, indicate that it is possible to undertake rapid autopsy tumour collections for use in research, but extending this out to a routine tumour collection rapid autopsy programme for our small country is still a large leap. Limitations in New Zealand include the facilities and resources available for completing a research autopsy as well as the funding required to staff, process and suitably conduct research around the collected specimens.

Our programme was tailor-made in response to this individual donor and her family, with the research project designed around the tumour tissues to be collected—an unorthodox way to design a research programme in the era of competitive funding driving research. While we envy permanent rapid autopsy programmes in operation in the northern hemisphere and Australia, we believe that there are key advantages to the personalised approach we have employed here. The number of samples collected, the extent of sampling of each lesion, the degree of annotation of these samples, the bespoke preservation strategies for unusual sample types, the close relationship with the donor and her family, and the commitment from the entire team to honouring the wishes of our donor, we believe are all important aspects to what makes this tumour collection unique and valuable; and indeed more difficult to achieve as part of a large formal programme. We argue that there is great value in the tailoring that is possible with one-off programmes, even when accounting for the increased time investment. In

Figure 2: Overall clinical and research history of the donor.



The top two rows indicate the patient's clinical history, including chemotherapy regimes (CAP-TEM refers to combination Capecitabine and Temozolomide chemotherapy), and computed tomography (CT) scan timings, overlaid on the timeline in row three. Row four indicates the tissue samples collected for clinical care and research. Row five and six show when the rapid autopsy consultation occurred in relation to clinical events, and the initiation of consultations and collaborations currently underway.

small countries like New Zealand, hoping to contribute on the same scale as large laboratories and institutions across the world will always be challenging, but instead of focusing on throughput, perhaps an emphasis on quality, completeness and annotation proves the real value that our approach can provide.

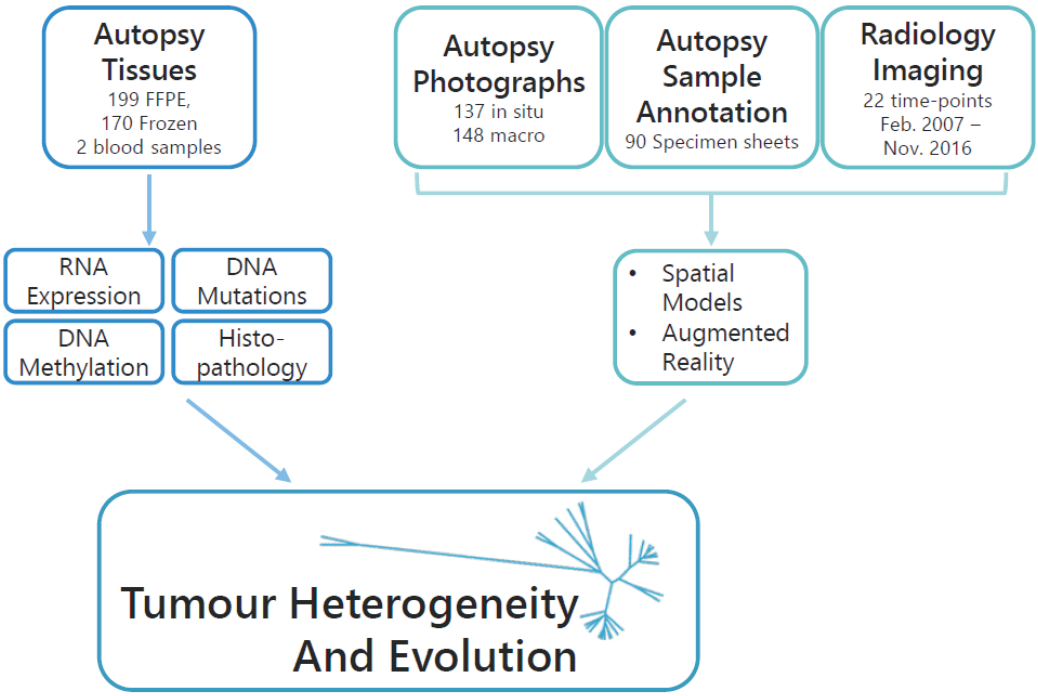
Digital developments

This bespoke project has provided our research group with experiences beyond the value of the tissue itself. Aside from providing the opportunity for student training within the genomics field, the study has also initiated a unique collaboration between the NETwork! team, the School of Architecture and the Centre for eResearch at the University of Auckland to build an augmented reality model of the donor's tumours and how they changed over time, to enable interpretation of the genomic and evolutionary patterns in 3D and improve our spatial appreciation of complex genomic data. Further, it has provided impetus for members of the research team to develop a digital application for enhanced recording of sampling for use during tissue banking; one of the changes that we might implement if the process was repeated.

Reflection from patient's family (anonymous)

When our mother first suggested donating her tumours to medical research on her death, we were all very supportive of her decision to hopefully benefit others in the future who contract the type of cancer that had slowly ravaged her body—and we still are. The team that undertook this task have been fantastic right from Mum's initial donation suggestion and we can't thank them enough for not only the work they are currently doing, but also ensuring we have been kept in the loop as Mum's tumours have been analysed. Late last year we saw the first virtual replication of Mum's body and her tumours and it was mind-blowing—she would have been (and may still be) thrilled to see what her donation has led to and there is still a long way to go. We are all very proud of Mum's decision and hope the ongoing study of her tumours by a great team of specialists will help to increase the understanding of her cancer, making a difference in the future.

Figure 3: Summary of all data types collected and available for integration in evolutionary analyses.



The collection of tissues at autopsy enabled generation of a wealth of genomic and histopathological data, which will be interpreted alongside clinical imaging, photographs and sample annotation to form spatial models and augmented reality representations to better understand tumour evolution in this donor.

Conclusion

Donated human tissue is a valuable resource in medical research, and post-mortem tissue is particularly valuable when it allows collection of tissues not usually available through standard clinical procedures. This generous donation will enable the study of fundamental questions plaguing cancer biology, tumour evolution and heterogeneity, and leave a legacy in the form of a unique tissue resource. Here we have outlined the process by which a post-mortem collection procedure can be built from the ground up. While considerable effort is required to coordinate the legal, ethical, scientific and logistical considerations needed to carry out a bespoke rapid autopsy in New Zealand, the value of tissue collected and its scientific utility well outweigh these considerations when collected as part of a carefully designed research study. The latter point is the key to balancing whether to undertake a bespoke autopsy process; to ensure that the gift is indeed used for the purpose that it was given. The donor handed responsibility to the research team to use this gift for the good of others, and this ethos forms the basis for our ongoing work. We honour the incredible foresight and generosity shown by the donor and her family in championing this research.

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Pelvic mesh in colorectal pelvic floor surgery—implications of recent developments

Rowan J Collinson, Andrew R Moot

ABSTRACT

The use of mesh prostheses in pelvic surgery is under significant scrutiny. There are justifiable concerns around the transvaginal use of mesh products for POP surgery. The latter part of 2017 saw the announcement of wide-ranging regulatory actions relating to transvaginal mesh products, by the Therapeutic Goods Administration in Australia and subsequently Medsafe in New Zealand. In colorectal surgery, pelvic mesh is predominantly used in the treatment of rectal prolapse, with ventral mesh rectopexy (VMR) becoming popularised in recent years. The available evidence suggests that despite the current mesh controversy, VMR is an acceptable procedure, with functional advantages over other colorectal prolapse procedures. With only short-term outcome data available however, comparative studies and longer follow-up are required to answer the question of long-term mesh safety. In the meantime, there are areas where surgical practice can be optimised, in particular around reporting, training and patient education. The aims of this paper are to summarise the current status of pelvic floor mesh surgery and examine how this will impact colorectal pelvic floor surgery.

The use of mesh prostheses in pelvic surgery is under significant scrutiny. Recent developments in gynaecological pelvic floor surgery have led to a broad reappraisal of mesh-related procedures in many health jurisdictions worldwide. Gratifyingly for patients and surgeons, we are now entering a phase of greater accountability, clearer surgical indications, more collaborative decision-making, and prospective monitoring of outcomes. The overall goal remains the successful treatment of patients with pelvic organ prolapse (POP) with the most effective, durable and safe techniques available.

A major Australasian shift in the latter part of 2017 was the announcement of wide-ranging regulatory actions relating to transvaginal mesh products, by the Therapeutic Goods Administration (TGA) in Australia and subsequently Medsafe (New Zealand Medicines and Medical Devices Safety Authority) in New Zealand. Widely reported as a 'ban' on surgical mesh implants for POP, there has been uncertainty among colorectal surgeons regarding the implications of this.

This perspective paper has two aims. The first is to summarise the current status of pelvic floor mesh surgery and put it into a New Zealand practice context. The second is to examine how this will impact colorectal pelvic floor surgery. The paper is not a systematic review of the literature, but an appraisal of what are considered by the authors to be the most salient recent publications for those working in this field.

Use of mesh in colorectal pelvic floor surgery

Products described as surgical 'mesh' fall broadly into two categories—synthetic or biologic. The commonest synthetic product in use is polypropylene—widely utilised in hernia surgery, abdominal wall reconstruction and pelvic floor surgery including suburethral slings. Biological products (often referred to as 'graft' rather than 'mesh') are generally an acellular allograft or xenograft

collagen matrix, with the latter being the most commonly-used variant (usually of porcine or bovine origin). Most of the publications discussed in the next section do not make a distinction between these products, unless stated in this paper.

In colorectal surgery, pelvic mesh is predominantly used for the treatment of rectal prolapse. In particular, ventral mesh rectopexy (VMR) is an operation performed by some colorectal surgeons to correct the posterior pelvic compartment disorders which form part of the POP spectrum. This includes rectal prolapse (both external and internal), enterocele and rectocele. There are technical similarities to gynaecological sacrocolpopexy. VMR in New Zealand is currently performed with either a synthetic mesh (usually polypropylene) or a biologic graft situated between the rectum and the vagina, and sutured to the anterior rectal wall and sacral promontory, and to the vagina in some cases. The mesh is placed from an abdominal approach (usually laparoscopic), with no breach of the vagina, and is completely covered with peritoneum, thus isolating it from the viscera of the peritoneal cavity. While first described using synthetic mesh in 1971,[1] the procedure has been popularised over the last 15 years, as it appears to address some of the undesirable functional bowel sequelae of other procedures, based on reports of uncontrolled case series from high-volume centres.[2–6] As part of the POP spectrum, it is unsurprising that VMR is most commonly performed on women (>90%), and the median patient age is in the range of 50–60 years old,[7,8] although the operation is considered suitable for patients over 80 years of age who are fit for general anaesthesia.[9] While there are two randomised studies comparing mesh with non-mesh rectal prolapse repairs, they focus on functional outcomes, and are not powered to address the question of mesh safety.[10,11]

Background to the current pelvic mesh situation

The global reappraisal of surgical mesh usage has come about through the persistence of patients and their advocates—clinicians, consumer groups, media and government agencies. The process was given momentum in 2011 when the US Food and Drug Administration (FDA) published its report into the safety and effectiveness of transvaginal mesh placement for pelvic organ prolapse (POP), based on adverse event reports and a review of the literature.[12] This report made two broad points, which challenged the enthusiasm for pelvic mesh repairs:

- *"serious complications associated with surgical mesh for transvaginal repair of POP are not rare"*; and
- *"it is not clear that transvaginal POP repair with mesh is more effective than traditional non-mesh repair".*

The report made the following observations about safety:

- *"Based on data from 110 studies including 11,785 women, approximately 10% of women undergoing transvaginal POP repair with mesh experienced mesh erosion within 12 months of surgery."*
- *"More than half of the women who experienced erosion from non-absorbable synthetic mesh required surgical excision in the operating room."*
- *"Transvaginal surgery with mesh to correct vaginal apical prolapse is associated with a higher rate of complication requiring reoperation and reoperation for any reason compared to traditional vaginal surgery or sacral colpopexy."*
- *"Abdominal POP surgery using mesh (sacrocolpopexy) appears to result in lower rates of mesh complications compared to transvaginal POP surgery with mesh…"*

The report makes the distinction that the problems with pelvic mesh seem to be associated with mesh placed via a *transvaginal* route. It also casts doubt on the benefit of mesh repair over traditional native tissue repair of POP. In the most recent (2016) Cochrane review of this,[13] the authors concluded that *"The risk-benefit profile means that transvaginal mesh has limited utility in primary surgery. While it is possible that in women with higher risk of recurrence the benefits may outweigh the risks, there is currently no evidence to support this position."* It went on to recommend *"…newer transvaginal meshes should be utilised under the discretion of the ethics committee".*

In 2014 the Scottish Government declared a suspension of *all* mesh surgeries pending the results of its own enquiry. The release of this report in March 2017 made some broad recommendations, but stopped short of a continued ban on mesh usage.[14] In England, the National Institute of Health and Care Excellence (NICE) produced their updated guideline in December 2017.[15] This concluded that transvaginal mesh repair of anterior or posterior vaginal wall prolapse should be used only in the context of research, effectively banning its routine use. It is unclear in the document whether this also includes urethral sling procedures.

The Australian TGA was widely praised when it issued its own actions on 28 November 2017.[16] Based on a review of the latest published international studies and the 2014 TGA review into urogynaecological surgical mesh implants, the TGA concluded that *"the benefits of using transvaginal mesh products in the treatment of pelvic organ prolapse do not outweigh the risks these products pose to patients. As a result, the TGA has taken a series of regulatory actions in relation to transvaginal mesh products and single incision mini-slings"*.

In practical terms, these actions constitute a 'ban' on the use of some POP mesh products (cancellation from the Australian Register of Therapeutic Goods (ARTG)), and tighter conditions around the use of others, effective January 2018. A full list appears on the TGA website. Some examples of permitted products with tighter controls include:

- the polypropylene *Upsylon Y-Mesh Kit* (Boston Scientific Pty Ltd), which cannot be used transvaginally, but can still be used transabdominally for sacrocolpopexy.
- Biologic grafts, such as the bovine dermis allograft *Xenform Tissue Repair Matrix* (Boston Scientific Pty Ltd), which must alter its instructions for use and labeling to include *"This device is not intended for any pelvic organ prolapse repair via a transvaginal approach"*. *Biodesign 4 Layer Tissue Graft* (Cook Biotech Inc) has had its conditions of use limited to non-urogynaecological procedures
- A number of polypropylene mid-urethral slings used for stress urinary incontinence (SUI). They remain on the ARTG on the basis that they include additional precautions in the instructions for use and labeling, effective 17 January 2018.

Medsafe in New Zealand issued a statement of its own regulatory action following the TGA announcement.[17] It has taken the view that the *"Australian outcome has given sufficient reason to consider that the products involved in the Australian action may not be safe. As a consequence, continued use of these products is considered inadvisable"*. To this end, the Medsafe position is fundamentally the same as that of the TGA.

Background to the New Zealand mesh situation

In 2014 the New Zealand Parliament Health Select Committee considered a petition submitted by Carmel Berry and Charlotte Korte, two patients who had experienced adverse outcomes from pelvic mesh surgery, requesting an inquiry into the use of surgical mesh in New Zealand. The petition raised several issues around the quality of surgical mesh, the standards of care for patients and the need for a surgical mesh registry. Among those who provided submissions were the petitioners, the Accident Compensation Corporation (ACC), Pharmaceutical Management Agency (PHARMAC), the Ministry of Health, and the Royal Australasian College of Surgeons (RACS) and the Royal Australian and New Zealand College of Obstetricians and Gynaecologists (RANZCOG). The Select Committee's report in June 2016 included seven recommendations in three areas:[18] the investigation of options for a surgical registry, improvement in medical practice and the role of the regulator in pre-market medical device approval. The Government supported all of the Committee's recommendations in a response tabled in August 2016,[19] specifically recommending:

- That the Government work with relevant medical colleges to investigate options for establishing and maintaining a centralised surgical mesh registry.

- That the Medical Colleges review best practice around informed consent for mesh procedures. That health providers are encouraged to ensure that coding for mesh surgery is consistent.
- That the Government encourages utilisation of the adverse events reporting system as applicable to medical devices.
- That the Government endorses the provision of ongoing education for surgeons on the use of surgical mesh and mesh removal surgery.
- That the Government considers expanding Medsafe's role over time to assess the quality and safety of a medical device before it can be used in New Zealand.

Following the Government support of the above recommendations New Zealand has had a general election and a change of Government, and it remains to be seen what priority will be given to these, in particular the establishment of a surgical mesh registry.

The scope of the problem within New Zealand has been difficult to quantify, in part due to a lack of a prospective registry, and a reliance on adverse event reports. The 2015 *ACC Surgical Mesh Review* states that 56,508 mesh devices were sold in New Zealand between 1 January 2005 and 31 October 2014.[20] Fifty-eight percent were sold for hernia repair, while 30% were for POP repair and 11% were for SUI repair.

The 2017 ACC review *(Surgical Mesh-Related Claim Data Report)* provides a breakdown of surgical mesh-related claim data, covering claims over 12 fiscal years from 1 July 2005 to 30 June 2017.[21] The report covers adverse events reported following the use of mesh for POP and SUI surgery (470 claims), hernia surgery—including inguinal and ventral (290 claims), and others (50 claims). Of the 470 claims for POP/SUI surgery, 91% were in the gynaecology treatment context, followed by Urology (7%) and General Surgery *(eg, VMR)* eight cases (2%). Two-thirds of 470 POP/SUI claimants presented with the primary symptom of mesh erosion, with the commonest secondary symptoms being sexual dysfunction, pain and infection.

Mesh safety in colorectal pelvic floor surgery

Where does this leave VMR? What can we tell our patients about mesh safety?

Three systematic reviews of VMR have been published since 2010, and demonstrate a mesh-related complication rate of 0.5–3.1%.[7,8,22] This includes the complications of vaginal erosion, bowel erosion and mesh detachment. In the systematic review from Gouvas et al, effect of surgery on sexual function was also examined.[8] Three studies compared pre- and post-operative sexual function for 152 patients. There was no statistically significant between-study heterogeneity. Pre-operatively 98 patients (64.5%) were considered to have sexual dysfunction, compared with 21 (13.8%) post-operatively. In the review by Samaranayake, the rate of chronic abdominal and pelvic pain after VMR is <1%.[7]

Two case series are useful to discuss, as they have large numbers with adequate follow-up, from recognised high-volume centres. The first is 919 consecutive patients (869 women; 50 men) in a combined Belgian and Dutch series.[23] Median follow-up was 34 months. Mesh-related complications were recorded in 18 patients (4.6%). However, in nine patients this represented mesh detachment from the sacral promontory, a mechanical failure presenting with deterioration of initial good functional result. These cases were treated by reoperation and mesh reattachment. Erosion of the mesh to the vagina occurred in seven (1.3%) patients. In five of these patients, VMR had been combined with a perineotomy to suture the mesh to the perineal body, a modification of technique which the authors no longer advocate. This leaves two cases only of true vaginal erosion from what is considered to be standard technique, representing an erosion rate of <1%. The rate of chronic abdominal or pelvic pain was <1%.

The second study is the pooled experience of five centres, over a 14-year period.[24] A total of 2,203 patients underwent VMR, 80% of whom received a synthetic mesh and 20% of whom received a biologic graft. At the time of data analysis, median length of time since operation was 36 months (range, 0–162 months). Forty-five patients (2.0%)

had mesh erosion. Of these 45 patients, 50% required minor treatment for minor erosion morbidity and 40% required major revisional surgery such as mesh removal for major erosion morbidity. Erosion occurred in 2.4% of synthetic meshes and 0.7% of biological meshes. The median time to erosion was 23 months, but up to a quarter of erosions were documented to occur 40–80 months after surgery. Using the Kaplan-Meier method the erosion rate for synthetics was 2.3% at five years. There were three patients with erosion after use of the biological graft, a rate of 0.7% at five years. Synthetic mesh was not significantly associated with an increased incidence of erosion compared with biological graft. The study was limited by its retrospective nature, and included some patients with very short-term follow up.

In summary, when these studies are considered, the risk of a major mesh-related complication with VMR would seem to be in the 1–2% range. This is significantly less than that of transvaginal mesh surgery. It also compares favourably with what is considered the analogous gynaecological procedure (sacrocolpopexy). In the systematic review of Jia et al (27 studies involving nearly 3,000 patients), the risk of a mesh erosion with sacrocolpopexy was 0–12%, median 5.4%.[25] In the case of VMR, the ideal mesh prosthesis is not clear, as synthetic and biologic products have differing characteristics.[26] This is an area where practice is certain to evolve in the next decade as further data become available.

An international perspective on the current status of VMR

In the UK, The Pelvic Floor Society (TPFS) is an affiliate of the Association of Coloproctology of Great Britain and Ireland (ACPGBI), and is a surgical special interest group with a multidisciplinary membership. TPFS has recently released a position statement on the use of mesh in VMR, authored by recognised authorities in the field and endorsed by TPFS.[27] The summary recommendations are consistent with much of the foregoing commentary. They make the following conclusions:

- Mesh morbidity for VMR is far lower than that seen in transvaginal procedures, and lower than laparoscopic sacrocolpopexy.
- Ventral mesh rectopexy should be performed by adequately trained surgeons who work within a multidisciplinary team framework.
- Clinical outcomes of surgery and any complications should be recorded in a registry.
- There should be a move towards accreditation of UK units performing VMR and an enhanced structured training programme.
- Enhanced consent forms and patient information booklets are being developed.
- It may be possible to optimise technical aspects of the procedure to reduce morbidity rates, eg, suture material choice.

Why VMR?

VMR has been popularised for two main reasons. Firstly it may improve some aspects of post-operative bowel function compared to other procedures, as in the case of external rectal prolapse. Second, it offers a treatment option where previously these were lacking, ie, in high-grade internal rectal prolapse, particularly where it relates to faecal incontinence. However, it represents only one treatment option, and is by no means a 'gold standard' procedure. The choice between use of synthetic material or a biologic may ultimately come down to a balance between the risks of erosion and recurrence.[26] This must form the basis of an informed discussion between the operating surgeon and the patient. It must be recognised however that we do not have high-quality long-term safety data for synthetic mesh in this procedure, as it is possible that mesh complications could occur over 10 years after mesh implantation. This is particularly relevant to patients who are contemplating VMR at a young age. Similar question marks surround the long-term recurrence rate with the use of biologic grafts.

Conclusion

There are justifiable concerns around the transvaginal use of mesh products for POP surgery, and the international reappraisal of this is important and timely. However, there are significant differences between this type of surgery and the use of abdominally-placed pelvic mesh for VMR. Available evidence suggests that VMR is an acceptable procedure, with some functional advantages. Comparative studies and long-term follow-up however are required to answer the question of long-term mesh safety. The current regulatory environment does not contraindicate the use of synthetic mesh in VMR, but recommendations around its optimal use have been developed. These are centred around reporting, training and patient education. This will ultimately be to the advantage of both patients and surgeons, with the shared aim of effective, durable and safe treatment of pelvic organ prolapse.

Competing interests:
Nil.

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Perforation of cecum caused by chicken bone under the guise of Crohn's disease

Yury Kitsenko, Olga Tashchyan, Aleksandr Pogromov, Sergey Efetov, Petr Tsarkov, Marina Mnatsakanyan, Ksenia Kolosova, Maria Popova

Diagnosis of inflammatory bowel disease is an important issue in gastroenterology. Even with use of the most modern diagnostic methods, it is not always possible to give an unequivocal answer whether the patient suffers from IBD or other intestinal damage occurs. We present a case of perforation of the cecum caused by a chicken bone under the guise of Crohn's disease.

Case report

A 23-year-old man was admitted in February 2018 with typical clinical features of Crohn's disease with ileocecal lesion. Colonoscopy data showed 'knife-cut' ulcerative defects were revealed in the ileocecal junction; biopsy revealed focal infiltration of neutrophils and deformity of crypts. Test for Cl. Difficile toxins was negative. Despite the treatment with mesalazine (4g per day), budesonide (9mg per day), azathioprine (100mg per day), remission was not achieved. In September 2018, an ileocecal abscess with a size up to 7cm was detected. Due to deterioration of the patient's condition, we performed resection of the ileocecal junction with formation of ileotransverse anastomosis. Intraoperatively a large conglomerate was found; no Crohn's disease changes in the mesentery were

Figure 1: Removed part of ileum.

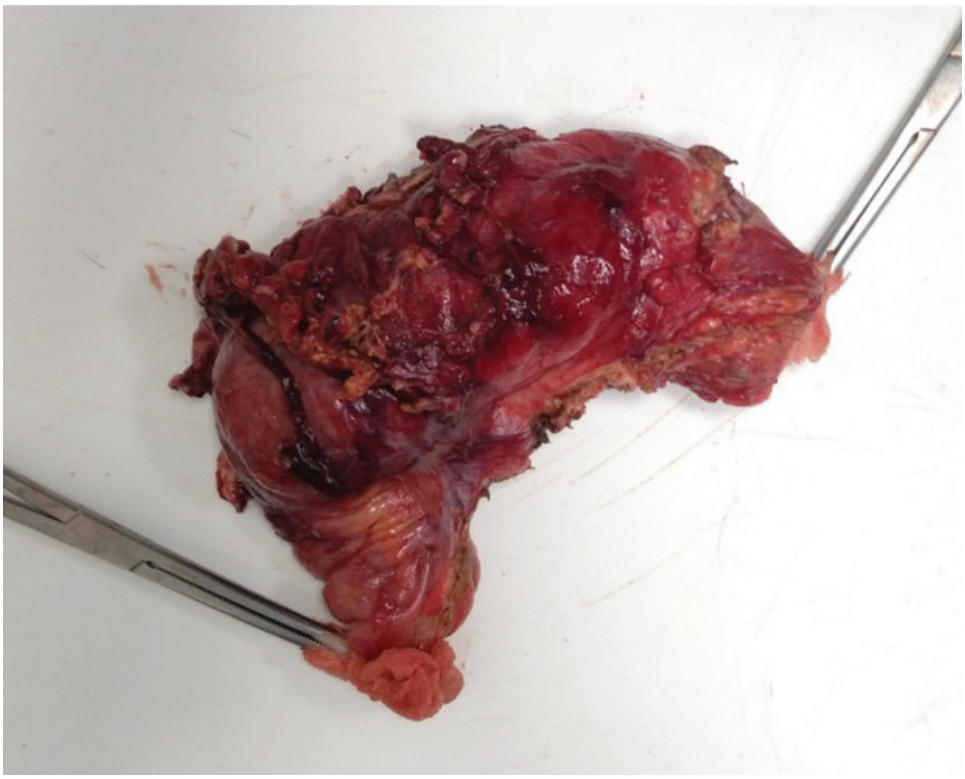
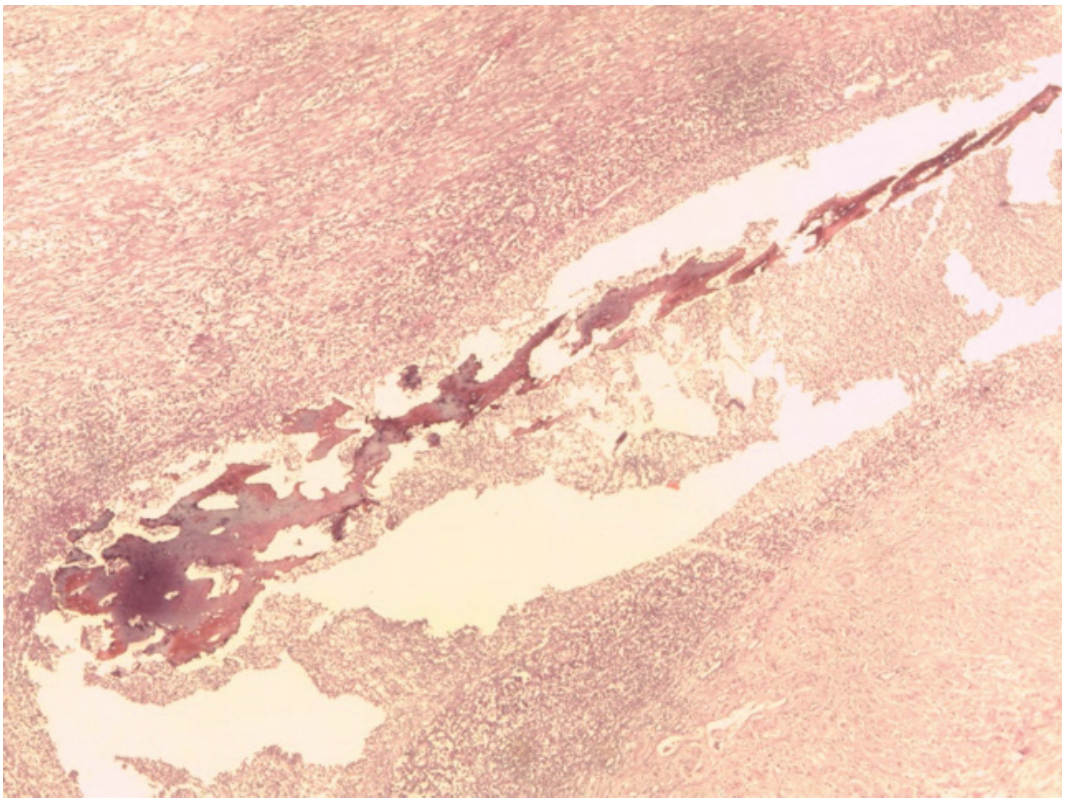


Figure 2: Chicken bone.



noted. Histological examination revealed a chicken bone that had perforated the cecum wall against the background of slit-like ulcers and crypt abscesses. Treatment of supposed Crohn's disease was stopped. Control colonoscopy and biopsy showed no signs of Crohn's disease with nine months after surgery.

Discussion

More than 300 cases of intestinal perforation caused by foreign bodies have been described in the literature, with fish bones, chicken bones, dentures, toothpicks and cocktail sticks being the most common objects.[1] Foreign-object-related perforations are usually found at the site of sharp bend and subsequent narrowing, and the most common localities of perforation in these cases are terminal ileum and the cecum.[2,3]

Typically, perforation occurs with peritonitis. In rare cases, an inflammatory infiltrate is formed around the foreign body, which simulates a malignant process. Perforation of the intestine by foreign bodies is found as an exceptional case. Usually these objects pass through the gastrointestinal tract without obstruction. There are two factors that allow foreign bodies to pass freely through the gastrointestinal tract. Foreign bodies usually pass along the central axis of the intestinal lumen. In the colon, foreign objects are usually located in the centre of the faeces, which additionally protects the intestinal wall from damage. In addition to anatomical and physiological 'obstacles', pathological contractions are also important—for example, strictures in Crohn's disease, fibrous strictures and exophytic or endophytic tumours of the gastrointestinal tract. Only few cases of perforation of the colon under such conditions are described in literature.[4–7]

According to modern concepts of Crohn's disease and intestinal anatomy, the mesentery plays an important role in the pathogenesis and development of the disease.[8] During surgery, the resection volume was selected in proportion to Crohn's disease (resection of the affected intestine with the mesentery), which reduces the possibility of recurrence.[9]

Conclusion

Thus, it can be assumed that the patient has Crohn's disease, and destructive changes in the intestinal wall (deep slit-like ulcers and stenosis of the affected intestinal wall due to oedema and inflammatory infiltration) led to perforation of the wall by a chicken bone. On the other hand, the aforementioned changes in the intestinal wall could develop against the background of perforation, since during the surgery no changes in the mesentery were found, and patient has no signs of recurrence.

Competing interests:
Nil.

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Response to 'The value of frenotomy for ankyloglossia from a parental perspective'

Rona Carroll, Whitney Davis, Katie Fourie, Nadya York, Steve Adams, Sophie Mace, Heather Johnston

I refer to the recent article entitled "The value of frenotomy for ankyloglossia from a parental perspective" by S Illing, et al published in the *New Zealand Medical Journal* (16 August 2019, Vol 132 No 1500).[1] The authors report primarily on the parental perspective after frenotomy at their practice, but include several other conclusions that are not justified based on the study design. I am writing to express my concern that this was published by the *Journal*.

This study as published has several methodological flaws. The authors did not include a control group and it is therefore inappropriate to conclude that the frenotomy procedure resulted in any improvement in breastfeeding. The authors state it would have been too difficult to include a control group. I disagree, as many parents are likely to accept an alternative approach in order to avoid an invasive procedure. In addition, most of the reasons listed for attending for assessment (Table 3) are common breastfeeding problems which can usually be resolved with input from a lactation consultant (LC). Were alternative approaches to frenotomy discussed as a part of informed consent to participate in this study, which would certainly be required ethically?

The paper does not detail if any breastfeeding support was given when infants were seen by the LC. It is good practice to offer these parents breastfeeding support, rather than an immediate surgical procedure, especially as more than half of referrals did not come from an LC. If breastfeeding support was given, what did this involve—how many appointments and over what time period? Did they observe and assess every baby breastfeeding before a procedure was offered? Furthermore, the authors do not report how many parents attended their clinic for breastfeeding support and were not offered the frenotomy procedure, and if any such clients exist, what were their outcomes.

The paper mentions that a statistician and a paediatrician were involved in the study through designing the data collection forms, but it appears they are not listed as authors or identified in the manuscript. I note that their 'tongue tie questionnaire' (Appendix A) has a section documenting lip frenulum examination. The study does not contain information about what was found on the lip examination. It is normal to find a lip frenulum in an infant[2] and there is insufficient evidence to support the surgical release of the labial frenum in infants to assist with breastfeeding difficulties.[3] Their lip frenulum assessment tool appears to be very subjective, and an unnecessary examination given the lack of evidence to intervene.

The first line of the conclusion states that "Frenotomy for infants with ankyloglossia and related feeding issues appears to be a safe and effective practice". This can in no way be concluded from the study design. This is a consumer satisfaction survey at best that can report simply on whether parents who paid for a frenotomy procedure were glad they had done so. The outcome that "98% of parents reported that if they were in similar circumstances again would choose a frenotomy" does not equate to the procedure being a success, particularly as the intervention has no comparator in this study. These are parents who are desperately seeking help, are paying money, and have often travelled a long way. The self-reported reduction in breast pain is very subjective and subject to bias and memory recall. An objective measurement of feeding time should have been used

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had the authors wished to report on this outcome. Self-reported feeding time typically reduces as the baby gets older, but the age of the baby in relation to feeding time wasn't reported, and neither was length of time post-procedure. Even if the design was appropriate to report this outcome, the authors need to report whether this finding was statistically significant.

Finally, the authors declared no competing interests are listed but receive financial benefit from patients seeking frenotomy at their practice. This is clearly a conflict of interest which of course doesn't preclude research in this area, but should be stated as such.

In summary, I am surprised that the *Journal* considered this manuscript appropriate for publication and am concerned that the conclusions, reported widely in the media since, are misleading. The above multiple serious flaws to the study as published undermine the validity of all but very superficial conclusions around customer satisfaction.

Competing interests:
Nil.

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Benefits and harms of spinal manipulative therapy for the treatment of chronic low back pain

This meta-analysis involved reviewing information from 47 randomised controlled trials involving more than 9,000 patients. Studies exclusively dealing with sciatica were excluded.

Spinal manipulative therapy (SMT) was defined as any hands-on treatment of the spine including manipulation and mobilisation. Recommended control therapies included exercise and drug treatments (eg, non-steroidal anti-inflammatory agents or analgesics).

The conclusions reached were that SMT has similar effects to recommended therapies, although it seems to be better for short-term improvement in function. Serious adverse effects appear to be rare and include case reports of cauda equina syndrome, fractures and neurological or vascular compromise. The researchers recommend that clinicians should inform patients of these potential risks.

***BMJ* 2019; 364:1689**

Drug-eluting or bare-metal stents for percutaneous coronary intervention

First-generation drug-eluting stents (DES) has been shown to reduce the need for repeat revascularisation compared with bare-metal stents (BMS). In this report the authors have meta-analysed the performance of new-generation DES. They defined new-generation as any DES subsequent to sirolimus or paclitaxel eluting stents.

New-generation DES have involved the use of glycoprotein receptor inhibitors or ticagrelor or prasugrel. Data from 26,616 patients in 20 randomised trials was evaluated.

The risk of the primary outcome (a composite of cardiac death or myocardial infarction) was reduced in the DES group compared with the BMS cohort ($P<0.001$). It was concluded that the use of BMS should no longer be considered the gold standard.

***Lancet* 2019; 393:2503–10**

C-reactive protein testing to guide antibiotic prescribing for COPD exacerbations

The Global Initiative guidelines on the management of COPD notes that patients with an exacerbation and a CRP level lower than 20mg/L are unlikely to be benefited by treatment with antibiotics. Those with purulent sputum and a level of CRP between 20 and 40mg/L are likely to benefit and those with levels of 40mg/L or more will probably benefit.

In this study 653 appropriate patients with an exacerbation of their COPD were randomised to receive usual care or usual care plus antibiotics on the basis of their CRP result.

It was concluded that CRP guided prescription of antibiotics for such patients resulted in a lower percentage of antibiotic use (57% vs 77.4%) with no evidence of harm.

N Engl J Med 2019; 381:111–20

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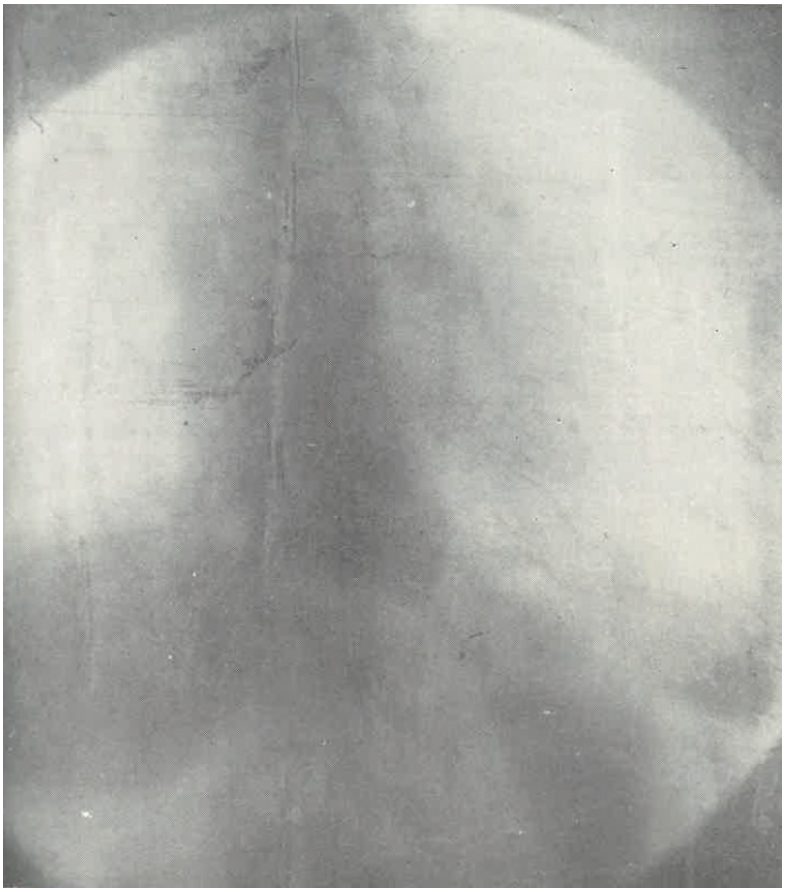
Dilatation of the Oesophagus Without Organic Obstruction

By W. M. YOUNG, M.D., F.R.C.S.E.



This condition is much more common than is generally supposed, and on that account I am bringing this case under your notice.

The patient is a domestic servant, aged 27. I was called in to see her because of persistent vomiting after meals, and of cough followed by vomiting on lying down, especially at night. The history is that about three years ago she began to have difficulty in swallowing, and regurgitation of food. The condition had gradually become worse, and for the past six months she frequently vomited after meals, and had developed the cough and vomiting on lying down. Lately she had vomited after every meal, and was getting thinner. Thinking the affection was in the throat she consulted Dr. Harty, who had a skiagram of the oesophagus taken. The photograph showed an extensive fusiform dilatation of the oesophagus. I sent her into hospital for further observation and treatment.

She looked fairly well nourished and is not of the neurotic type. Apart from the oesophageal condition we could find no other abnormality. Whilst in bed in hospital and on soft food there was no vomiting, but when put on solid food vomiting returned.

A large sized solid gum-elastic bougie passed down into the stomach meeting with little resistance; a soft rubber stomach tube also appeared to pass into the stomach readily. Another skiagram by Dr. Cameron taken after a bismuth meal showed a similar picture to the previous one. Dr. Harty was good enough to make an oesophagoscopic examination under an anaesthetic. With the patient recumbent and the head hanging over the edge of the table the oesophagoscope was introduced into the oesophagus and immediately evacuated a large amount of food. The oesophagus was examined down to its lowest portion, but it nowhere showed any dilatation or abnormality other than congestion.

It is very evident that the X-rays are essential for diagnosis in these cases.

We are treating this case by daily washing out the stomach and occasionally passing a bougie. Her condition has much improved, but her symptoms occasionally recur and she cannot yet swallow ordinary diet.

I should have mentioned that food regurgitated was alkaline in re-action, but food removed by the stomach tube was acid, showing that the tube actually passed into the stomach.

In Mayo Clinics for 1912, is published a paper by Dr. Plummer entitled "Diffuse Dilatation of the Oesophagus without Anatomic Lesion," and in the Proceedings of the Royal Medical Society for March, of this year, is published a paper with a similar title by Dr. Wm. Hill, and with it is published the discussion which followed.

Dr. Plummer records 91 cases from his clinic, 38 of which he had previously recorded as cases of cardiospasm. He classifies 130 cases of those two conditions thus:—

1. Diffuse dilatation of the oesophagus without anatomic stenosis, 91 cases. No gross lesions were found in this group and only five of the patients were of a neurotic type.
2. Severe cardiospasm without dilatation of the oesophagus—2 cases. Both patients had periodic attacks continuing from 3 to 14 days, during which they were not able to swallow either liquid or solid food.
3. Cardiospasm without diffuse dilatation, but with gross lesions in the stomach—12 cases. Of these cases 2 patients had ulcer, 2 syphilis, 3 carcinoma, and 3 suspected ulcer.
4. Mild cardiospasm without diffuse dilatation or gastric ulcer—24 cases. Almost without exception these patients were of a neurotic type, and many were distinctly hysterical.

Aetiology.—Whether the dilatation of the oesophagus is a primary condition resulting from a paralysis of the oesophageal muscle, or whether it is secondary resulting from a "functional stenosis" of the oesophagus, is a much debated point. Dr. Hill takes the latter view and maintains that the obstruction is not at the cardiac orifice of the stomach, but at the hiatus of the diaphragm, through which the oesophagus passes, and thinks it may be due to a spasm of the diaphragm. The dilatation (oesophagectasia) has been attributed to inco-ordination between the vagus and the sympathetic nerves, and Dr. Shattock has said that it was due to "an inco-ordination of the nervous impulses transmitted by the vagus during deglutition, which impulses should normally cause contraction of the tube above and an active dilatation of the cardia."

In this case that I record, not only did a large gum-elastic bougie pass readily into the stomach, but also did a soft rubber stomach tube. This supports the inco-ordination theory.

It is quite possible that in some cases there is a dilatation without stenosis. Neither sex nor age seems to be a determining factor in the condition. A few cases have been observed in young children.

Symptoms.—These may simulate the results of organic stenosis. Difficulty in swallowing and vomiting immediately after taking food are common symptoms. The conditions may give rise to waterbrash and rumination. In fact this is probably the condition which accounts for many of the reported causes of human ruminants. Loss of weight is not usually marked, but some cases have succumbed to asthenia from starvation. Cough on lying down is a symptom sometimes noted.

Treatment.—Gastrostomy with dilatation of the oesophagus from below has been tried, but sometimes fatally, and is not to be recommended.

Hill follows Plummer in recommending dilatation from above using distensible bags, distended either with water or mercury. Plummer used distension in 91 cases, of which 73 were completely relieved, 4 had died, and 3 were not traced. One died of rupture of the oesophagus due to too high pressure having been used.

Repeated washing out of the oesophagus and stomach and the mere passing of a bougie have been successful in some cases, and are to be recommended in all cases before attempting severer methods. Drugs, apparently, have little curative effects in this condition, nor has much success been achieved by electrical treatment.

Pathology.—Post mortem findings reveal no stenosis and sometimes no thickening of any part of the oesophagus; in some cases the wall of the dilated portion of the oesophagus has been recorded as being a little thinner than normal, but usually it is of normal thickness.

It seems to me that the passing of bougies and the stomach tube has the effect of re-educating the muscles of the oesophagus and restoring co-ordination.

I should like to hear what experience of this condition other members have had.

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Notice of retraction

The NZMJ retracts the following article

Are over-the-counter fish oil supplements safe, effective and accurate with labelling? Analysis of 10 New Zealand fish oil supplements Julia J Rucklidge, Shelby Hantz, Ian C Shaw NZMJ 20 September 2019, Vol 132 No 1502 ISSN 1175-8716

Errors are a part of science and publishing and require publication of a correction when they are detected. The ICMJE guidelines states that errors serious enough to invalidate a paper's results and conclusions may require retraction. The editor has received the notice below from the authors of the above manuscript.

We request retraction of our paper Are Over the Counter Fish Oil Supplements Safe, Effective and Accurate with Labelling – Analysis of 10 New Zealand Fish Oil Supplements *because we made errors in the calculation of the amounts of EPA and DHA in five of the fish oil supplement capsules which means that we have underestimated the doses. All are now within 15% of label value. This, in turn, affects our assessment of compliance with health claims; however, they remain variable. Our assessment of mercury risk is unchanged.*

We apologise for this error.

Julia Rucklidge, Shelby Hantz and Ian Shaw

The editor has reviewed the information available and this appears to be an honest error that has led to a major change in the direction and significance of the results, interpretations and conclusions.

The manuscript has therefore been retracted and appropriate notifications made.

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