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A case of skeletal fluorosis?

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"It's hard to ask": examining the factors influencing decision-making among end-stage renal disease patients considering approaching family and friends for a kidney

Merryn A Jones, Jon Cornwall

Patients who are eligible for living kidney donation find it hard to ask potential living donors for a kidney, and at present they feel relatively unsupported in this difficult task. They would like more targeted assistance, including psychological and social support, to help them when they are looking to recruit donors. A screening tool should be developed that assesses willingness and motivation to pursue LKD, along with assessing health literacy, self-efficacy and emotional wellbeing. The results of the assessment would enable tailored support strategies to be implemented according to unmet needs, leading to a potential increase in the rate of organ donation and transplant.

Early onset dementia in New Zealand Pacific boxers: a case series

Vahid Payman, Susan Yates, Sarah Cullum

We found an unusually large number of Samoan and Tongan former boxers in South Auckland who were suffering from early onset (40 and 50 years of age) dementia. When we looked into their histories, we found that most of had drunk heavily in their youth and also had other risk factors for dementia such as diabetes, high blood pressure or high cholesterol. We think that a combination of head injuries from boxing as well as these other risk factors puts young Pacific boxers at increased risk of developing early onset dementia. Sports physicians should warn young Pacific boxers about this risk.

The Dunedin Dementia Risk Awareness Project: a convenience sample of general practitioners

Yoram Barak, Charlene Rapsey, Dana Fridman, Kate Scott

We created a unique test of brain health knowledge. GPs in Dunedin were tested and are very knowledgeable about brain health. This makes GPs uniquely situated to help initiate dementia prevention for older adults.

Co-prescribing of contraindicated and use-with-caution drugs in a national cohort of new users of simvastatin: how well are prescribing guidelines followed?

Joshua Quon, Lianne Parkin, Katrina Sharples, David Barson

Statins (cholesterol-lowering medicines such as simvastatin) play a key role in the prevention of major cardiovascular events (heart attacks and strokes) and they are widely used in New Zealand. Some medicines inhibit the activity of the enzyme (CYP3A4) that metabolises simvastatin and this can lead to high levels of simvastatin in the blood, which in turn increases the risk of myopathy and rhabdomyolysis (muscle-related side effects). Prescribing guidelines state that some CYP3A4 inhibitor medicines should not be prescribed to people taking simvastatin ('contraindicated medicines') and some should only be used with caution and careful management of simvastatin dose ('use-with-caution medicines'). Overseas studies have reported concerning levels of use of CYP3A4 inhibitors in people taking certain statins, but the extent of any such co-prescribing in New Zealand was not known. We undertook a national study based on anonymised health and pharmaceutical dispensing data and found that the prescription of contraindicated and use-with-caution medicines to New Zealand patients taking simvastatin was not uncommon.

Off label or on trend: a review of the use of quetiapine in New Zealand

Mark Huthwaite, Marilyn Tucker, Lynn McBain, Sarah Romans

This paper reviews the use of quetiapine, a drug originally designed for the treatment of psychotic disorders and confirms previous New Zealand studies that quetiapine is largely being used 'off-label' (ie, not for what it is currently approved for) and that there is a growing trend for it to be prescribed to exploit its sedating effects and mild calming effects in the lower dose range. While it is commonly accepted that prescribing 'off-label' is at the prescriber's discretion, and not necessarily a "bad thing to do", the authors conclude that when prescribing quetiapine for a non-approved condition, or to a specific clinical population (the elderly and the young), the thoughtful prescriber will carefully document not only the clinical rationale for this prescribing but also that they have discussed this with their patient. The authors also suggest that the respective medical colleges and other representative bodies may wish to develop guidelines for the non-approved prescribing of quetiapine to allow prescribers to prescribe in accordance with accepted practice and current best practice guidelines.

Outcomes following therapeutic lymphadenectomy for Stage III malignant melanoma in a single unit

Rahul Jayakar, Emily Yassaie, Christopher Adams

Operations for melanoma that has spread to lymph nodes have a high risk of developing complications. The number of lymph nodes removed during these operations provides important information in assessing the adequacy of treatment and predicting outcomes. We support the development of national standards for treatment of melanoma in New Zealand and have suggested key performance indicators with respect to recovery of lymph nodes from different parts of the body.

Confidence in the safety of standard childhood vaccinations among New Zealand health professionals

Carol Lee, Isabelle Duck, Chris G Sibley

Using data from the 2013/14 New Zealand Attitudes and Values Study, the present study investigated the level of confidence in standard childhood vaccinations among New Zealand health professionals. Most health professionals showed higher levels of vaccine confidence, with 96.7% of those describing their occupation as GP or simply 'doctor' (GPs/doctor) and 90.7% of pharmacists expressing strong vaccine confidence. However, there were important disparities between some other classes of health professionals, with only 65.1% of midwives and 13.6% of practitioners of alternative medicine expressing high vaccine confidence. The consensus of belief in the vaccine safety among GPs/doctors is an encouraging finding, but the low level of confidence among midwives is a matter of concern that may have negative influence on parental vaccination attitudes.

Live kidney donation: managing the "tyranny of the gift"

Justin Roake, John Morton

The benefits of kidney transplantation from living donors are substantial for the recipient, for society and arguably for the donor. Recipients of live donor transplantation have a better chance of survival and of good kidney function than after deceased donor transplantation, and also a realistic prospect of preemptive transplantation before the need for dialysis. Society benefits because transplantation is cheaper than dialysis and living donation potentially frees deceased donor kidneys for recipients without realistic prospects of finding a living donor. Donors report that the act of giving enriches their lives and improves their self-esteem.

Initially, live donor transplantation was exclusively between blood relatives, and the health professionals involved often felt ambivalent about encouraging gifts of organs by living donors and about their own role in the process. However, as the risk of graft failure from rejection or technical complications and the risks of donor surgery have reduced, the practice has become more widely accepted and extended to donation by emotional relatives, especially spouses, and subsequently to the acceptance of well-motivated strangers—also known as altruistic or non-directed donors. Live donor transplants are now well established in New Zealand and account for nearly half of all kidney transplants.[1] This is partly because of low rates of deceased-donor transplantation in New Zealand in comparison to other developed countries but also because of active promotion of living donation by transplanting centres as the best option for prospective recipients. Live donation is now accepted to the extent that the Ministry of Health is supporting a nationally coordinated programme to promote living donor transplantation and increase the number of transplants. This is an important initiative because the demand for kidney transplantation far exceeds the supply of donated organs.

Living donor transplantation is predicated on the simple concept of a gift freely given without coercion or any thought for reparation. However, this is too simplistic and it has long been recognised that the transaction between donor and recipient takes place within a complex network of interpersonal relationships including families and health professionals and that "a complex exchange occurs through which considerably more than the organ is transferred".[2] The gift of organs for transplantation occurs within a paradigm of 'symmetrical and reciprocal' obligations; to offer and give; to receive and accept; to seek and find an appropriate way to repay. Failure to meet any of these obligations can lead to strains affecting the donor, the recipient and their associates.[3] We know for example that prospective donors and their families feel strong internal and external pressure to donate. Often it is the simple fact that live donor transplantation offers the recipient the best chance of normal or near normal life that creates this powerful pressure. A common manifestation of this is an almost instantaneous decision to donate without any actual request or process of informed consent. Perhaps more troubling is that many recipients describe a sense of indebtedness and obligation to repay their donors where there can be no reciprocity. Fox[2,3] used 'tyranny of the gift' to describe the sense of debt that recipients feel and noted that this may impact on the relationship between donor and recipient in unforeseen ways. The potential for harm suggests that the engagement between donor and recipient requires careful management from the earliest stages.

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In relation to organ donation, the way in which information is presented or requests are made can be major determinants of the outcome. For instance we know from studies of requests for organs from deceased donors that factors such as the timing of the request, the specific words that are used, and who makes the request can be critical determinants of whether consent is given.[4,5]. Although the circumstances in living donation are very different, it seems likely that the specifics of how and when information is presented, the information itself and whether a direct request is made may impact directly on the outcomes.

Obviously potential recipients may not be cognisant of these complexities but it is not surprising that they find it difficult to raise the subject of their need for a transplant with their family and friends as described in the article in this edition titled *It's hard to ask*.[6] We see that the themes emerging from this research in New Zealand echo those identified by Fox.[3] The 'difficulty' that potential recipients identify may reflect a deep sense that in some way this type of request is inapt—the 'gift of life' is too great and cannot be repaid. We also recognise that in New Zealand there are unique cultural and ethnic factors that come into play.

Given our knowledge of the complexity involved in approaching family or friends on the subject of donation it seems inappropriate to leave this to potential recipients without providing substantial guidance and resources. We, the authors, believe that it is unwise, unreasonable and possibly unethical for us as professionals to expect patients to request donation from relatives or friends although we accept that patients have freedom to make such requests. In contrast we think it is acceptable, and to be encouraged, that relevant, factually accurate information is provided to family and friends and that genuine offers are accepted. We acknowledge that this is a rather nuanced argument and that patients and professionals alike may require education to understand the importance of the distinction. It is concerning that in the drive to do the best for potential recipients and achieve high rates of transplantation we, as a profession, have projected 'a need to ask' rather than to provide information and receive offers. This is conveyed by our words and actions. Words are powerful and need to be chosen carefully—for example, is it right to talk about 'recruitment' of living donors?

New Zealand's transplanting centres provide ample, good quality and appropriate information on the processes and protocols involved in organ donation and transplantation including a discussion on the balance of risks and benefits as part of obtaining informed consent. Additionally, potential donors are required to have a psychological assessment and counseling, but there is no consistent approach delivering culturally safe practices, counseling and support to potential recipients as they begin to engage with their family and friends on the delicate subject of donation. In 2014, renal transplantation in New Zealand became a nationally organised service. This provides an opportunity for the National Renal Transplant Leadership Team to respond to the concerns identified above and develop a nationally consistent framework and resources in support of potential recipients and the health professionals involved in their care.

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Nil.

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REFERENCES:

1. Aotearoa New Zealand ANZDATA Working Group. 2018
2. Fox RC, Swazey JP. 1978. The courage to fail. A Social View of Organ Transplants and Dialysis (2nd Ed). Chicago: University of Chicago Press.
3. Fox RC, Swazey JP. 1992. Spare Parts. Organ Replacement in American Society. New York: Oxford University Press. 31–42.
4. Roake JA, Riminton DS, Morton JB. 1988. Cadaver kidney retrieval for transplantation in Canterbury and Westland: 1972–1987. NZ Med J 101(855):632–3.
5. Simpkin AL, Robertson LC, Barber VS, Young JD. 2009. Modifiable factors influencing relatives' decision to offer organ donation: systematic review. BMJ 338:b991. doi: 10.1136/bmj.b991.
6. Cornwall J, Jones M. (2018) "It's hard to ask": examining the factors influencing decision-making among end-stage renal disease patients considering approaching family and friends for a kidney. NZ Med J 2018; 131(1474):10–19.

"It's hard to ask": examining the factors influencing decision-making among end-stage renal disease patients considering approaching family and friends for a kidney

Merryn A Jones, Jon Cornwall

ABSTRACT

AIM: People needing kidney transplants in New Zealand can receive organs from deceased donors or from a living kidney donor. This project explored issues surrounding donor recruitment, examining the lived experience of end-stage renal disease (ESRD) patients in order to facilitate improved donor recruitment for ESRD patients.

METHOD: A qualitative study comprising interviews of ESRD patients in Hawke's Bay, focusing on the factors surrounding approaching family and friends for a kidney. Purposeful sampling and thematic analysis of data was utilised.

RESULTS: Fifteen participants were interviewed (Five female; mean age 49.8yrs). Most stated it was hard to ask for a kidney; almost half had never approached anyone. For many, approaching potential donors was a barrier. Many Māori had limited recruitment opportunities due to comorbidities within extended whanau, making the decision of *who* to approach difficult. Other barriers included concern for donor health, poor health literacy and poor self-efficacy.

CONCLUSION: Recipients desired more support to facilitate approaching donors, with cultural differences observed between Māori and non-Māori in recruitment expectations. Tailored support could be enabled with development of a screening tool to assess willingness and motivation to accept donation, cultural needs, self-efficacy, communication skills and health literacy. Psychosocial support could help address barriers such as reciprocity concerns.

Kidney transplant is the best option for the long-term health of patients with end-stage renal disease (ESRD). Kidneys may be transplanted either from a deceased donor or a living donor, with transplant from a living kidney donor (related, non-related, altruistic or kidney exchange) being the best option. Living kidney donation (LKD) yields improved graft, and patient survival compared with deceased donation is more likely to pre-empt the need for dialysis, and means that other patients without a suitable living donor have a better chance of acquiring a kidney from the deceased donor list.[1] Patients who are listed on the deceased donor list (DDL), as well as having family or friends who can donate a living kidney, have two opportunities to receive kidneys. However, for those who are not eligible for inclusion on the DDL, their only option is to find a donor among their network of family and friends.

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There are many barriers to transplant, including financial hardship, social responsibilities, geographical isolation, poor health literacy and lack of suitable donors,[2,3] and the likelihood of successful living kidney transplant for some individuals may therefore be compromised.[4–6] One barrier that is sometimes voiced by patients with ESRD is that it is hard to approach family and friends to donate a kidney.[7–9] Evidence from DDL patients within New Zealand suggests this is also the case;[2] it remains unknown whether non-DDL listed patients experiences and perceptions of the 'donor conversation' are similar to those of DDL patients.

In New Zealand, patients requiring a kidney are encouraged to inform friends and family of their need for a kidney, though it is not suggested they ask directly for one. Anecdotally, ESRD patients often make assumptions about who would, or would not, be a suitable donor within their networks of family and friends.[10] Patients may approach some members of their family and not others, based on preconceptions of what makes a successful donor. Alternatively, patients may not approach others at all, preferring to wait for family or friends to offer.[11] Currently, there is a lack of information on the motivations and experiences of New Zealand ESRD patients who have experienced approaching others for a kidney. In particular, information on why some ESRD patients do not approach friends or family for a kidney, or why they might ask some family members and not others. An understanding of whom patients choose to approach, or *not approach*, would enable New Zealand health services to tailor support to patients who are eligible for transplant; this is important when the Ministry of Health is actively seeking to increase donor rates,[12] particularly among Māori and Pasifika patients who suffer health inequity in ESRD outcomes.[13] Within New Zealand, there is marginalisation of Māori within the New Zealand healthcare system, which results in inequity of care, delayed specialist care and lower life expectancy that cannot be explained by conventional individual and community risk factors,[14–17] and further identification of factors contributing to this position are required. This study therefore aimed to examine the factors influencing decision-making among a group of New Zealand ESRD patients considering approaching family and friends for a kidney, in order to gather information that could facilitate development of supports for recipients to identify and successfully recruit potential donors.

Methods

Ethical approvals for the study were given by Health and Disability Ethics Committee (HDEC), HBDHB Research Committee and HBDHB Māori Health Service, and the Victoria University of Wellington Human Ethics Committee. This project utilised a qualitative descriptive approach to analyse interview data from patients with ESRD, examining the lived experience of patients with ESRD who are encouraged to find living kidney donors from their social networks and the factors that influence their decision-making. Participants were recruited from patients with ESRD through the Hawke's Bay District Health Board (HBDHB) and were identified as being on the deceased donor list (DDL), or had family or friends being worked up for living kidney donation (LKD), or both. Participants were interviewed one-on-one, with interviews examining decision-making surrounding donor recruitment, and explored questions such as: With whom did they discuss their need for a kidney, and why? Who did they not approach, and why? How did they approach the request, and what were their reasons for approaching in this way? Had they received offers to donate and how did this feel? Could they identify additional strategies which might have been useful to them, but were either not considered or unavailable? What advice would they give to others in a similar position?

Interviews were transcribed and thematically analysed using NVivo Pro software (Version 11, QRS International, Melbourne, Australia). Various methods can be used for conducting a thematic analysis;[18] in this instance a cross-case analysis was adopted to allow insight into the motivations surrounding asking or not asking for a kidney, while not ignoring the nuances of highly individualised responses.[19] This method also provides an analytical strategy that focuses on identifying underlying themes across idiographic explanations,

which fitted well with the project's aims of identifying the range and type of motivations articulated by participants.[20] Core themes of each interview were first identified during a preliminary line-by-line examination of the transcribed text, and individual motivations were identified. Themes of motivations surrounding asking or not asking for a kidney were coded, along with a detailed explanation of these motivations. Individual motivations were aggregated on the basis of what was primarily emphasised or foregrounded in the interviews.

Results

A total of 15 participants (five female) were interviewed, with ages ranging from 23 to 68 years (mean 49.8); mean interview length was 23 minutes (range 11–45 minutes). This gender proportion was consistent with the eligible population listed on the DDL for the HBDHB. Six participants identified as Māori, three identified as Māori/New Zealand European, five identified as New Zealand European, and one identified as Other European. In 2016, the HBDHB dialysis unit population identified their ethnicity as 63% Māori, 28% New Zealand European, 7% Pasifika and 2% other.

Five participants were pre-dialysis patients who were currently listed on the DDL or had living donors being worked up. Ten patients were already on dialysis, seven of these on haemodialysis and three on peritoneal dialysis. Eight patients were listed on the DDL alone with no living donors being worked up, while three patients were DDL listed and had living donors being worked up. Four patients were not DDL listed, but had living donors being worked up. From the interviews, five major themes arose, with subthemes also identified. These major themes were: will ask; won't ask; offers; barriers to asking; advice to others (Table 1).

Will ask

'Will ask' encompassed subthemes of direct recruitment and indirect recruitment, reflecting the approach that the participants used to ask for a kidney. Most participants struggled with communicating need; many participants refrained from approaching friends and family at all, and even those who were practised at discussing their need for a kidney still admitted it was difficult for them to approach others, stating that "it's hard to ask". Most participants who approached friends and family favoured a direct approach. However, those who found it too difficult to approach people directly preferred to share their story about their illness rather than ask for a kidney in the hope that sharing their story might engender offers to donate; a small number of participants or their families used social media to do this indirectly.

Won't ask

'Won't ask' contained subthemes such as 'won't ask and won't accept an offer' and 'won't ask, but will accept an offer'. Many Māori had limited recruitment opportunities due to comorbidities within the extended whanau group. It was difficult for many Māori participants to identify any suitable candidates to approach. Several participants stated that they would never ask a loved one for a kidney; however, some agreed that they would accept an offer of a kidney donation. Other participants, mostly Māori, had turned down all offers to donate, preferring to wait until a deceased kidney became available. Several participants expressed a burden of responsibility when they talked about caring for a transplanted kidney from a living donor, but that the burden did not exist with a deceased kidney because the person donating was already dead. Reciprocity is an important concern for many Māori, but it was also identified as an issue for several non-Māori participants. The donation of a living kidney from a family member or friend was, for some recipients, too big to be considered a gift, and was difficult to accept. Two participants talked about the fact that a living kidney could not be given back; it was not like a favour that can be returned at some point.

Offers

'Offers' explored participants' experience of receiving offers, or that of waiting for an offer. Almost half the participants stated they had not approached friends or family for a kidney, with some of those who had never approached friends or family receiving offers that they had declined. Often the offers were deemed inappropriate, from persons who might not have good health, or had weight or lifestyle factors that might rule them out as donors. Several

Table 1: Thematic analysis of interview data.

Theme	Sub-theme	Topics
Will ask	Direct recruitment	• Asking friends and family for a kidney • "It's hard to ask" • Anticipating rejection • Self-efficacy
	Indirect recruitment	• Sharing their story • Using social media • Family or friends recruiting on behalf
Won't ask	Won't ask and won't accept an offer	
	Won't accept offers	• Cultural or traditional values • Philosophical beliefs: Acceptance of how things are; Not wanting loved ones to donate; The anonymity of a deceased kidney
	Won't ask but will accept an offer	
Offers	Waiting for offers from family or friends	
	Receiving offers	
	What it feels like to have people offer	
Barriers to asking	Managing risks	• Donor health risks • Financial impact on donor • Relationships
	"I don't look sick"	
	Predetermining suitability	
	Limited recruitment opportunities	• Poor family health • Small social circle
	Waiting for a deceased kidney	• Availability • Legislation
	Misinformation	
Advice to others	Effective recruitment	
	Health literacy	
	Resources	
	Psychosocial support	
	Media focus	
	Raising awareness	
	Shock tactics	
	Future technologies	

participants appeared physically uncomfortable when stating that they had no family or friends who had offered.

Over half the participants talked about their experience of receiving offers, stating family or friends had come forward and freely offered a kidney. Several participants said they didn't get to ask before offers were made. For most, having offers come from family and friends provided a sense of feeling loved. However, while offers were gratefully received, receiving offers could also cause concern; one participant expressed worry that it appeared she was valuing some family member's lives over others if she accepted a donation from a daughter but not a granddaughter, while another expressed sadness when considering the donor was offering a part of themselves in order to "fix" her. Most participants expressed concern about the perceived risks to loved ones.

Barriers to asking

Barriers to asking grouped subthemes such as limited recruitment opportunities, managing risks and waiting for a deceased donation. Few understood that donor workup was designed to screen the donor to ensure they would be considered safe to donate and live with one kidney, indicating poor health literacy creates a barrier to initiating a donor conversation for some participants: only two of the 15 participants knew that donating a kidney was not likely to cause long-term harm to the donor. Other barriers included limited recruitment opportunities, how to communicate the need for a kidney when the participant looked well, factors relating to legislation (eg, limited availability of organs from deceased persons), and management of risks associated with having poor health.

Advice to others

'Advice to others' contained recipients' responses to what advice they might give to someone in their position, or what they might have done differently. Many participants felt understanding the transplant process, and what makes for a suitable donor, was important information to have *before* approaching potential donors, so they could be prepared to answer questions friends and family might have. Several participants expressed reticence with following up potential donors, as follow up contact could be perceived as putting pressure on potential donors. Several also expressed regret that they had not been aware of how to slow progression of their chronic kidney disease (CKD) to delay dialysis.

Discussion

This is the first New Zealand study examining the decision-making of patients with ESRD and the reasons they choose to approach, or not approach, potential living kidney donors. In New Zealand, patients with ESRD who are transplant-eligible are encouraged to discuss their treatment options with family and friends to see if any offers to donate a kidney are forthcoming. Many patients perceive this approach, albeit indirect, as "asking" for a kidney. Data highlighted the difficulty many participants face when considering who, how and when to initiate conversations with potential donors, and also illuminated the impact of family comorbidities on the donor conversation for some Māori individuals. Further, many Māori participants preferred to wait for a deceased kidney to become available in preference to approaching whanau, or believed that the DDL was their only option for transplant. Findings illuminate the complexity of this interaction for all participants, with information highlighting potential avenues for support for ESRD patients who are looking to recruit a living donor. Cultural, ethnic, psychosocial and economic factors also influence patient willingness to approach potential donors,[5,21–24] and all participants experienced one or more of these barriers. Suggestions are made as to how to address some of the identified issues.

Cultural influences on decision making

Māori face significant disparities in both healthcare[14–17] and LKD transplant, with low likelihood of receiving pre-emptive kidney transplantation.[13] Several Māori participants stressed there was a need to involve whanau in decision-making when it comes to treatment options; this is congruent with New Zealand research on DDL patients and requires consideration in donation operational procedures to allow appropriate consultation with whanau

when donation is being considered between family members.[13,25] Most Māori participants in this study were from large families and had relatives who were well intentioned, but because comorbidities are often prevalent in Māori health, they struggled to identify suitable donors. More research into streamlining care pathways for Māori ESRD patients is required, and should also involve other at-risk New Zealand groups such as the Pasifika ESRD community to facilitate communication and identify appropriate care pathways.

Donor conversations

All participants described difficulty with approaching friends and family for a kidney, many stating that "it's hard to ask", and that donor conversations, or being offered a kidney donation, was a highly emotional experience. For many, initiating a donor conversation was a barrier in itself: almost half had never asked anyone to donate due to concerns for donor health and well-being, limited recruitment opportunities or because of poor communication skills, self-efficacy or health literacy. Several participants had poor health literacy,[7,26] which has an impact on decision-making and informed choice, identification of available treatment options or of suitable potential donors, and problem-solving. In communities where living kidney transplant uptake is low,[4,22,23] a correlation between improving health literacy and improved transplant uptake has been demonstrated,[22,23] and our data reinforces the necessity to address health literacy with potential recipients in New Zealand. Additionally, there is growing support for recruitment of a patient advocate within the patient's network of family and friends, who would act on behalf of the transplant candidate to initiate important donor conversations.[10]

Many participants stated a preference to wait for offers rather than ask family or friends to consider donating, to avoid pressuring potential donors who may be reluctant to donate; others thought that asking may affect personal relationships. This highlights the difference for patients between facilitating conversations about donation, and about asking directly for one which may be perceived to carry an element of risk for some persons. Many factors contribute to a reluctance to initiate a donor conversation or accept an offer of a kidney, including lack of confidence, poor self-efficacy, inability or non-willingness to communicate need, fear that their request for a kidney may be declined, or worry that the donor might need to give their kidney to a more 'deserving' family member in the future.[4,9,27] Additionally, patients fear post-transplant rejection of a donated kidney, or are concerned about donor health risks.[2,9,28–31] They may also feel an obligation for a 'gift' that could not be reciprocated, or guilt should the kidney be rejected.[9,32,33] Findings suggest these factors and concerns need to be addressed in New Zealand ESRD patients prior to initiating donor conversations, perhaps through providing communication skills training in conjunction with health literacy and support to develop an appreciation of the various ways in which donor conversations can safely occur.

Suggested support strategies for ESRD patients looking to acquire a kidney

Support was a key theme identified by many participants, with almost all desiring more support to facilitate approaching potential donors. The type of support requested was multifactorial, and several support strategies have been proposed to address concerns arising from the data (Table 2). Findings suggest psychological support, counselling, cultural or spiritual support should be made available to all recipients, ideally before the patient has approached any potential donor, in order to address concerns such as self-efficacy, reciprocity and relationship management. This support could also address negative quality of life, depression or distress that may arise as the result of being diagnosed with a chronic, life-limiting disease.

Educational support is required to ensure adequate health literacy and facilitate early clinical engagement. Participants who had a good understanding of their renal disease and treatment options were more likely to be proactive in their health management and in trying to recruit donors. Participants also felt that having accurate information about the transplant process *before* they approached potential donors was paramount; it is therefore important clinicians

Table 2: Aims, potential support strategies and possible outcomes for patients who will be asking family and friends for a kidney.

Aim	Potential support strategy	Outcome
Support for emotional wellbeing	Availability of psychology support to all recipients (as required) prior to approaching donors	Patients feel better supported to approach donors, removing some of the "hard to ask" barriers Renal services are adequately resourced with qualified psychologists to meet the need of potential transplant candidates
Identification of barriers	Develop a screening tool to assess willingness and motivation to pursue LKD as well as identify health literacy, communication, social or self-efficacy barriers; support is tailored to meet unmet needs	Potential for ongoing psychosocial support, counselling, cultural and spiritual support Development of an action plan to support patient's health literacy, communication skills, confidence or approach to donors and help navigate transplant process
Cultural competency	Involve whanau in CKD treatment decision-making where possible or where indicated by patient or screening tool results	Transplant candidates and their whanau are provided with education and support about the treatment options and the transplant process in order to make informed decisions
Consistent transplant messages	Revisit transplant conversation regularly; ensure transplant pathway is noted on all GP letters; have consistent messages re: transplant	Transplant candidates and their health providers have consistent information about the transplant pathway and expected outcomes
Peer support	Peer support available to recipients to help with decision-making and provide non-clinical emotional and practical support and information	Transplant candidates have the opportunity to discuss any concerns or questions with someone who has a lived experience of transplant
Indirect donor recruitment support	Development of sample social media templates in a variety of languages, with ability to be customised	Patients and their networks are supported to initiate indirect recruitment with tools that offer accurate information and direct the reader to transplant coordinators

regularly revisit the transplant conversation, as attitudes towards transplant, viewpoints and circumstances change over time.[2] Such conversations and information must be congruent between transplanting centres, renal service staff, general practitioners and community health workers, in order to deliver similar messages to the patient and increase the likelihood of transplant;[2,31] Walker et al (2017) found that delayed diagnosis created marginalisation among many Māori patients with CKD, which created a missed opportunity to engage preventive care,[13] reinforcing the likely benefit of effective patient-clinician communication and the necessity to tailor support specifically for Māori and other disproportionately disadvantaged groups in order to address existing health inequities.

To provide tailored support for New Zealand ESRD patients, development of a screening tool is suggested to assess transplant willingness and motivation, health literacy, communication skills and emotional wellbeing. Further New Zealand-centred research is also required to determine how such a tool may best serve New Zealand's unique cultural and ethnic profile, including Māori or Pasifika ESRD patients who are currently disadvantaged in health provision within New Zealand.[15–17] Further, peer engagement between recipients has not previously been explored for New Zealand ESRD patients, and this could be considered to support recipient's concerns, allay specific anxieties, build confidence or reassure the recipient as they make treatment decisions. This is especially necessary to determine how to best serve New Zealand's various cultures, including Māori communities, where this and previous studies have identified whanau interaction is important in the decision-making process.[33,34] Finally, some participants were turning to social media sites such as Facebook to recruit donors, and development of social media templates for ESRD patients to utilise could facilitate awareness of the need for organs or encourage families to discuss organ donation, which can assist in raising donor rates.[35]

Limitations

There were some limitations to this small study. A modest number of participants were interviewed (n=15), however there was good thematic saturation in the data gathered, which supports the validity of the findings. Participants were all ESRD patients registered with the HBDHB Renal Service and eligible for transplant, and therefore were a homogenous group that reflected the renal population awaiting transplant in one geographical region of New Zealand. This could introduce potential selection bias, however the data is potentially generalisable to other New Zealand regions, such as Northland, who have a demographically similar renal population to Hawke's Bay.

Conclusion

This is the first New Zealand study to examine ESRD patients' experience of the donor conversation. It highlights the many difficulties facing ESRD patients who are looking to acquire a donor kidney, including that "it's hard to ask", and raises the question of whether donors feel an expectation to ask for a kidney, as opposed to facilitating donor conversations about need. Despite the small sample size, some differences were noted between Māori and non-Māori ESRD patients who are looking to recruit donors. Findings show that for some Māori, LKD may not be a feasible transplant option, even if the patient is a suitable transplant candidate. Many factors identified were similar to those seen in international research of ESRD patient populations, such as low uptake of LKD in some indigenous communities where poor health literacy or limited recruitment opportunities are present. It is suggested that a New Zealand-specific screening tool be developed to assess willingness and motivation to proceed with transplant, along with an assessment of cultural needs, health literacy, ability to communicate need and emotional wellbeing. Champions from within the patient's network of family and friends can play an important role in initiating donor conversations for those transplant candidates who struggle to advocate for themselves, and further support could be provided to develop initiatives in this area. Psychological support should also be made available to all potential recipients to negate effects of stress and its impact on personal relationships that both the situation and conversations around donation frequently impart.

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REFERENCES:

1. Davison S, Kromm S, Currie G. Patient and health professional preferences for organ allocation and procurement, end-of-life care and organization of care for patients with chronic kidney disease using a discrete choice experiment. Nephrol Dial Transpl. 2010; 25:2334–41.
2. Martin P. Increasing the rate of living donor kidney transplantation in New Zealand: developing an evidence base. (PhD, The University of Victoria, Wellington, New Zealand). 2013. Retrieved from http://researcharchive.vuw.ac.nz/xmlui/bitstream/handle/10063/2932/thesis.pdf?sequence=2
3. McGrath P, Holewa H. It's a regional thing: financial impact of renal transplantation on live donors. Rural Remote Health. 2012; 12(4):1–10.
4. Rodrigue J, Paek M, Egbuna O, et al. Readiness of wait-listed black patients to pursue live donor kidney transplant. Prog Transplant. 2014; 24(4):355–61.
5. Waterman A, Rodrigue J, Purnell T, et al. Addressing racial/ethnic disparities in live donor kidney transplantation: priorities for research and intervention. Semin Nephrol. 2010; 30(1):90–102.
6. Weng F, Reese P, Mulgaonkar S, Patel A. Barriers to living donor kidney transplantation among black or older transplant candidates. Clin J of Am Soc Nephro. 2010; 5(12):2338–47.
7. Barnieh L, McLaughlin K, Manns BJ, et al. Barriers to living kidney donation identified by eligible candidates with end-stage renal disease. Nephrol Dial Transpl. 2011; 26(2):732–8.
8. Reese P, Shea J, Berns J, et al. Recruitment of live donors by candidates for kidney transplantation. Clin J Am Soc Nephro. 2008; 3(4):1152–9.
9. Pradel F, Mullins C, Bartlett S. Exploring donors' and recipients' attitudes about living donor kidney transplantation. Prog Transplant. 2003; 13(3):203–10.
10. Garonzik-Wang J, Berger J, Ros R, et al. Live donor champion: finding live kidney donors by separating the advocate from the patient. Transplantation 2012; 93(11):1147–50.
11. Kranenburg L, Zuidema W, Weimar W, et al. Psychological barriers for living kidney donation: how to inform the potential donors? Transplantation. 2007; 84:965–71.
12. Ministry of Health. Live Kidney Donation Aotearoa: Give a kidney – Change a life. Wellington, New Zealand: 2013. Retrieved from http://kidneydonor.org.nz/about-us
13. Walker R, Walker S, Morton R, et al. Māori patients' experiences and perspectives of chronic kidney disease: a New Zealand qualitative interview study. BMJ Open. 2017; 7:e013829. doi: 10.1136/bmjopen-2016-013829.
14. Reid P, Robson B, Jones CP. Disparities in health: common myths and uncommon truths. Pac Health Dialog 2000; 7:38–47.

15. Kerr S, Penney L, Moewaka Barnes H, et al. Kaupapa Maori action research to improve heart disease services in Aotearoa, New Zealand. Ethn Health 2010; 15–31.
16. Wilson D, Barton P. Indigenous hospital experiences: a New Zealand case study. J Clin Nurs 2012; 21:2316–26.
17. Elers P. Maori health: issues relating to health care services. Te Kaharoa 2014; 7:163–72.
18. Braun V, Clarke V. 2006. Using thematic analysis in psychology. Qual Res Psychol 3:77–101.
19. Guest G, MacQueen KM, Namey EE. 2012. Applied thematic analysis. Thousand Oaks, CA: Sage.
20. Babbie E. 2014. The Practice of Social Research. 14th Edition. Boston: Cengage Learning.
21. Skelton S, Waterman A, Davis L. Applying best practices to designing patient education for patients with end-stage renal disease pursuing kidney transplant. Prog Transplant. 2015; 25(1):77–84.
22. Tamura M, Li S, Chen S-C, et al. Educational programs improve the preparation for dialysis and survival of patients with chronic kidney disease. Kidney Int. 2014; 85(3):686–92.
23. Kucirka L, Grams M, Balhara K, et al. Disparities in provision of transplant information affect access to kidney transplantation. Am J Transplant. 2012; 12:351–7.
24. Hanson C, Chadban S, Chapman J, et al. The expectations and attitudes of patients with chronic kidney disease toward living kidney donor transplantation. Transplantation 2015; 99(3):540–54.
25. Durie M. Providing health services to indigenous peoples. Brit Med J. 2003; 327:408–9.
26. Dageforde L, Petersen A, Feurer I, et al. Health literacy of living kidney donors and kidney transplant recipients. Transplantation. 2014; 98(1):88–93.
27. Hanson C, Chadban S, Chapman J, et al. The expectations and attitudes of patients with chronic kidney disease toward living kidney donor transplantation. Transplantation. 2015; 99(3):540–54.
28. de Groot I, Schipper K, van Dijk S, et al. Decision making around living and deceased donor kidney transplantation: a qualitative study exploring the importance of expected relationship changes. BMC Nephrol. 2012; 13:103–14.
29. Siegel J, Alvaro E, Hohman Z, Maurer, D. “Can you spare an organ?”: exploring Hispanic Americans’ willingness to discuss living organ donation with loved ones. Health Commun. 2011; 26(8):754–64.
30. Gordon E. “They don’t have to suffer for me”: why dialysis patients refuse offers of living donor kidneys. Med Anthropol Q. 2001; 15(2):245–67.
31. Zimmerman D, Albert A, Llewellyn-Thomas H, Hawker G. The influence of socio-demographic factors, treatment perceptions and attitudes to living donation on willingness to consider living kidney donor among kidney transplant candidates. Nephrol Dial Transpl. 2006; 21:2569–76.
32. Kranenburg L, Zuidema W, Weimar W, et al. Postmortal or living related donor: preferences of kidney patients. Transpl Int. 2005; 18:519–23.
33. Ghahramani N. Potential impact of peer mentoring on treatment choice in patients with chronic kidney disease: a review. Arch Iran Med. 2015; 18(4):239–42.
34. Hughes J, Wood E, Smith G. Exploring kidney patients’ experiences of receiving individual peer support. Health Expect. 2009; 12(4):396–406.
35. Australian Government Organ & Tissue Authority. Retrieved from http://www.donatelife.gov.au/sites/default/files/OTA_Fact_Sheets_-_International_approaches_to_organ_donation_reform_November_2013.pdf

Early onset dementia in New Zealand Pacific boxers: a case series

Vahid Payman, Susan Yates, Sarah Cullum

ABSTRACT

AIM: To describe the biopsychosocial characteristics of a series of Pacific men living in South Auckland with a history of boxing presenting with early onset dementia. We discuss the history of boxing in Pacific people and the possibility of increased risk of early onset dementia in New Zealand Pacific men compared to their European counterparts.

METHOD: We reviewed the files of Pacific men with a history of amateur or professional boxing who presented to our memory and older adult mental health services with early onset dementia over a 45-month period. We gathered relevant information to construct a biopsychosocial paradigm as possible explanation of this phenomenon.

RESULTS: We identified a series of eight New Zealand Pacific men with early onset dementia and with a history of boxing. Alcohol was a contributing factor in seven of the eight cases, and vascular risk factors in five.

CONCLUSION: Historical, cultural and socio-economic factors underpin the attraction of some Pacific men to boxing as a sport. Given that New Zealand Pacific peoples may have an earlier onset of dementia than their European counterparts, further research is required to establish whether boxing is a contributory factor. Sports physicians should advise young New Zealand Pacific boxers about the long-term risks associated with their sport.

We present a case series of eight former amateur or professional boxers, all of Pacific background and all living in South Auckland, New Zealand, seven of whom present with early onset dementia (onset prior to age 65) and one with onset of dementia at age 71. The series is interesting and unusual for various reasons: first, it represents an unusually large number of people with early onset dementia from a single ethnic grouping; second, it identifies a unique subcultural typology involving issues of history, identity and masculinity; third, it casts some light on the growing understanding of the probable multi-factorial nature of early onset dementia in boxers; and fourth, it suggests that a large scale dementia prevalence study is needed in New Zealand to determine whether New Zealand Pacific people present with earlier onset dementia compared to their European counterparts.

The eight cases described below had all been referred either to the Memory Team or the Mental Health Service for Older People at Middlemore Hospital in South Auckland during the 45-month period between 23 December 2011 and 3 September 2015. Middlemore Hospital is a large teaching hospital that is governed by Counties Manukau District Health Board (CMDHB), which serves the people of seven localities in South Auckland: Mangere, Otara, Papatoetoe, Howick, Manurewa, Papakura and Franklin. Based on a 2011 census, the total estimated population of these seven localities is 500,000, of which 49% were male.[1] Just under 49,000, or 10%, of the population is over 65 years of age, compared to the New Zealand average of 13%. The ethnic

breakdown is as follows: Māori 84,000 (17%), Pacific people 111,500 (22%), Indian 41,800 (8%), other Asian, predominantly Chinese, 59,400 (12%), and 'other', predominantly white New Zealanders of European ancestry, 204,200 (41%). CMDHB has almost twice as many Pacific people than any other DHB in the country, and their numbers are projected to increase by 66% in the period 2006–2026, compared to 40% for all other ethnicities. Pacific people represent 16% of the population aged between 45 and 64 in Counties Manukau. This compares with New Zealand European (50%), Asian (23%) and Maori (12%). At CMDHB, dementia is mostly diagnosed by the Memory Team: between 2013 and 2016 the ethnicities of those who received a new diagnosis were New Zealand European (39%), Pacific (35%), Māori (12%), non- New Zealand European (11%) and Asian (3%) (Cullum S, 2018 personal communication).

Method

The files of nine men were reviewed. These nine men had presented with early onset dementia to either the Memory Team or the Mental Health Services for Older People. We collected data on the following variables: current age, ethnicity, marital status, boxing history (including, where available, number of fights, number of concussions and number of episodes of loss of consciousness), schooling, employment, medical history, family history, age of onset of cognitive decline, mental state examination, neuro-psychological assessment and brain imaging results.

Consent for release of medical information and its publication was sought from next of kin. Eight of nine next of kin consented.

Results

We have separated the cases' age and ethnicities from their histories in order to reduce the chance of identification. The age of onset of cognitive decline ranged from age 46 to age 71: Four cases were aged between 45 and 55, four were aged between 56–65, and one was over 65. Of the eight cases, six were Samoan and two were Tongan.

Case 1

A married man who was a professional boxer in his Pacific country of origin for 15 years. He had been knocked out several times and had suffered numerous concussions, but had never been hospitalised from his boxing. His schooling was limited and he moved to New Zealand after his retirement. He drank alcohol excessively and had police charges of dangerous driving and domestic assault. Six years after retirement, he was noted to have delusions of infidelity, was convinced that his daughter's boyfriend was having an affair with his wife and threatened to kill them with a machete. He also had auditory hallucinations of Satan, and accompanying religious and grandiose delusions. He was treated with Olanzapine. Two years later, his Rowland Universal Dementia Assessment Scale (RUDAS) score was 16/30, indicating moderately severe cognitive impairment.[2] One year later, neuropsychological assessment showed global severe cognitive impairment, and two years later, he was noted to have ataxia, tremor and lack of spontaneous speech.

Case 2

A married man whose boxing career started in childhood in his country of origin and lasted 11 years. He also played rugby and was knocked out twice, and drank heavily in his youth. He worked as a storeman. He presented with cognitive impairment: Addenbrooke's Cognitive Examination (ACE) score at presentation was 53/100 and Mini Mental State Examination (MMSE) score was 15/30.[3,4] He was commenced on donepezil. Five years after presentation, he developed delusions that his son in law was stealing his clothes and he was treated with Risperidone. He subsequently developed delusions of infidelity towards his wife and threatened her with a knife. He became increasingly dependent on his wife for his activities of daily living, and eight years after presentation was placed in a rest home.

Case 3

A married man who had boxed for four years and sustained multiple concussions. He had limited primary schooling and worked in a factory. He drank heavily

Table 1: Characteristics of eight Pacific boxers with early onset dementia.

Case number	1	2	3	4	5	6	7	8
Alcohol	+++	+++	+++	-	+++	+++	+++	++
Vascular risks	-	-	+++	-	+++	++	++	+
LOC by knockout	>1	>1		1		-		-
Education*	+		+		++	+	+	+
Family history			+		+	-		
Delusions infidelity	+	+		-	+	-		-

*education: + indicates primary education only; ++ indicates secondary education
(empty cells indicate information not collected or unavailable).

throughout his life and had a history of type 2 diabetes mellitus, hypertension and hyperlipidaemia. A younger brother also suffered from dementia. Two years prior to presentation, he developed REM sleep disturbances and his driving deteriorated. At presentation, his RUDAS score was 8/30. Subsequently, a knife was found in his bed and he had made threats to kill his wife. He was placed in a dementia unit, where he subsequently assaulted other residents. He was treated with Risperidone, Donepezil, and Escitalopram.

Case 4

A married man who was a professional heavyweight boxer for more than 20 years. He was knocked out once during his career. He was a non-drinker and non-smoker. At least a decade prior to presentation, he began to decline cognitively. At presentation, his ACE score was 39/100 and MMSE was 19/30.

Case 5

A married man who was a professional boxer in his youth. His mother suffered from dementia and his father from alcoholic dementia. He completed secondary school and worked in an administrative position. His medical history included impaired glucose tolerance and hypertension, and he was a heavy smoker and drinker. At presentation, his RUDAS score was 18/30 and Frontal Assessment Battery (FAB) score was 8/18.[5] He also had delusions of infidelity.

Case 6

A married man who was initially an amateur boxer and then a professional boxer for over 11 years. He suffered no knockouts. He left school at the age of 14 and worked as a labourer. He was a heavy drinker and non-smoker, and had a medical history of type 2 diabetes mellitus and hyperlipidaemia. There was no family history of dementia. At presentation, his ACE score was 51/100. He also had persecutory delusions.

Case 7

A married man who was an amateur boxer and who also got involved in public bar fights when drunk. He attended primary school for five years and worked as a labourer. He was a heavy drinker and smoker, and had a medical history of hypertension. At presentation, he scored 12/30 on the Montreal Cognitive Assessment.[6]

Case 8

A married man who was an amateur and then professional boxer. He "took many punches to the head" and retired in his fourth decade due to frequent headaches. There was no history of knockouts. He left school at age 15 and worked in a factory. He was a moderate to heavy drinker, non-smoker, and had a medical history of hypertension. At presentation, his RUDAS score was 20/30 and FAB score 11/18.

The salient characteristics of these eight cases are summarised in Table 1.

A ninth case, from whom we were unable to obtain consent for release of his medical and psychiatric history, presented with features similar to the above cases.

Seven of the eight cases had neuroimaging (CT scan) performed and the results are summarised in Table 2.

Table 2: Brain CT scan characteristics of seven Pacific boxers with early onset dementia.

Case	1	2	3	4	5	7	8
Infarcts	-	-	Right parietal cortex	-	-	-	-
SVID	++	-	-	-	+	-	-
Cerebral atrophy	Temporal ++ Frontal +	Diffuse ++	Frontal +	Diffuse +	Temporal + Frontal +	Diffuse +	Diffuse +
Cerebellar atrophy	+/++	-	-	-	-	-	-
CTE changes	VD++ CT+ CSP	VD+	VD+	CSP	VD+	-	CSP

+ = mild; ++ = moderate; +++ = severe; SVID = small vessel ischaemic disease; VD = ventricular dilatation; CT = callosal thinning; CSP = cavum septum pellucidum.

Discussion

Anthropological evidence from prehistoric Tongan burial mounds suggests that ritualised violence, in the form of fist-fighting, performed an important ceremonial function and also helped to "maintain important kinship relations by relieving stress and aggression".[8] Indeed, when Captain James Cook arrived in Tonga in 1777, he was royally entertained with boxing and wrestling exhibitions, involving both men and women. David Samwell, who was surgeon on the boat *Discovery*, which accompanied Cook's boat *Resolution* on the third voyage, described in excellent detail the manner in which the Tongans boxed and notes how *"these Exercises are held in great Esteem among them, the Children are brought up in the Practice of them from their Infancy, especially the Sons of the Chiefs..."*[9]

Following the post-war wave of Pacific immigration to New Zealand, Samoan and Tongan boxers dominated the local boxing scene, winning many national titles during the 1950s and 1960s, and acting as role models for the cohort of cases described in our series. Their dominance continues to this day: between 2009 and 2013, four out of five New Zealand amateur title holders in the heavyweight and super heavyweight divisions were of Pacific descent;[10] at the 2007 Pacific Games held in Apia, 6 out of 11 gold medals in men's boxing were won by Samoans.[11]

These snapshots over the course of centuries suggest that boxing may have been and may continue to be an important part of some Pacific subcultures and male identity development. A Pacific man, known to the authors of this paper, reports that, on returning as a child to his mother's village in the islands, he was invited to box against the leading boy of the village before he could be accepted into the local peer group. Instead, he decided to take flight rather than submit his developing brain to the onslaughts of his older opponent (anonymous, 2015 personal communication). It could be argued that this is nothing unusual, and that boys everywhere use fighting to establish pecking orders and resolve disputes. This has been referred to as the 'predacious interval' in male development.[12] The length of the predacious interval, however, is culturally determined, extending it or channeling it into acceptable forms, such as boxing. It is interesting to note that the COMPASS study (Combating Obesity in Māori and Pasifika Adolescent School-Children Study) included non-contact boxing training as its culturally-appropriate exercise paradigm.[13] It is, of course, important to avoid the assumption that Pacific culture is a unitary concept. Indeed, the cases in this series are from Samoa and Tonga only, which suggests that the term 'Pacific' or 'Pasifika' may be too broad and homogenous a label for the cultural phenomenon we are describing.

In addition to cultural-historical factors, there are social and economic factors that determine a particular sport's attraction to young people. Boxing subcultures flourish in urban centers in which ethnic minorities are over-represented. Boxers often tend to be the children of first generation immigrants, who have not yet established themselves financially in a new country. As successive waves of immigrants entered the US, for example, boxers often came from those ethnic groups at the bottom of the socio-economic ladder.[14] As these ethnic groups improved their lot in life, the attraction to a sport like boxing diminished. Seven of the cases reported in our series lived in either Otara or Mangere, which are the two localities in Counties Manukau with the lowest incomes. The percentage of adults in these two localities with incomes less than $20,000 per annum are 52% and 49% respectively.[1]

The idea of boxing one's way out of poverty might, however, be an oversimplification of the sport's attraction to young men. The disciplining rhythms of training provide young men with a sense of purpose and work-ethic, and an acceptable avenue for asserting one's emerging masculinity. Joining a boxing club provides a safer option than joining a gang. Many young men are also attracted to the sport in their early teens simply to have a good time, to become fit, to travel to tournaments and hopefully win titles.[15] They do not necessarily see it as a profession and it is only those with talent who are later groomed for more serious careers.

The neuropsychiatric consequences of boxing have been well known in the medical literature since descriptions of the 'punch-drunk' syndrome by the pathologist Harrison S. Martland in 1928 and 'dementia pugilistica' by Millspaugh in 1937.[16] These consequences occur in 10–20% of professional boxers and consist of motor symptoms, such as Parkinsonism, dysarthria, ataxia and spasticity; cognitive symptoms, such as amnesia; and emotional or behavioural symptoms, such as depression, irritability, aggression and addiction. Risk factors for dementia pugilistica include older age, longer duration of career, number of fights, frequent knockouts, lengthy sparring sessions, "good staying power" and carriers of the apolipoprotein E4 (APOE4) genotype.[16] Amateur boxers fighting under Olympic-style rules, which provide stricter protective measures, are at less risk than professional boxers.

With the more recent observations that similar consequences can be seen in athletes from other body contact sports, such as football, ice hockey and wrestling, the term Chronic Traumatic Encephalopathy (CTE) is now used to encompass the syndrome and the pathological changes seen in athletes who have suffered repetitive traumatic brain injuries. Until recently, boxers suffering from the clinical changes seen in CTE were diagnosed with Alzheimer's disease, but it is becoming clearer that the brain in CTE has pathological changes which are distinct from, though overlapping to some extent with, Alzheimer's disease. These changes are well described elsewhere[15] and include atrophy, especially of the frontal, temporal and cerebellar lobes, cavum septum pellucidum, ventricular dilatation and callosal thinning. Cavum septum pellucidum can be a normal variant and is seen reasonably frequently in asymptomatic subjects with normal scans. In our series, 3/7 had focal atrophy, 3/7 had cavum septum pellucidum, 4/7 had ventricular dilatation and 1/7 had callosal thinning.

In the cases that we describe above, it is more than likely that the cause of the early onset dementia was mixed. Seven of the eight cases described drank alcohol heavily and five had one or more vascular risk factors. On neuroimaging, seven cases had changes consistent with CTE, five had cerebellar atrophy or focal frontal atrophy possibly secondary to alcohol and three had ischaemic changes. This combination of alcohol, cerebrovascular risk factors and boxing-related repetitive head injury has been noted elsewhere in the boxing-dementia literature,[17] and describes a stereotypic constellation of behavioral and lifestyle choices in subcultural groups, placing them at higher risk of early onset dementia. A prospective study following Pacific boxers and matched controls over a 30-year period, starting at the beginning of their boxing careers and continuing through to middle age, would be useful to establish a causal link between boxing and early onset dementia.

Three of our eight patients suffered from delusions of infidelity. All three of these also drank heavily, a well-known risk factor

for pathological jealousy. Our findings replicate those of Johnson, who found that 5 of 17 ex-boxers in his case series had delusions of infidelity.[18]

Pacific peoples living in New Zealand are at risk of early onset dementia for a number of reasons. In the period between 1982 and 2002, stroke incidence increased in New Zealand Pacific peoples by 21%.[19] This compared with a decline by 19% in stroke incidence among New Zealand Europeans during the same period. New Zealand Pacific peoples have a mean age of onset of stroke of 65 years compared to 76 years in New Zealand Europeans, and they also have higher prevalence rates and earlier onset of diabetes, poorer glycaemic control and higher rates of diabetes-related complications.[20] In addition, 62% of New Zealand Pacific peoples are obese and 26% smoke.[21] Other risk factors for dementia, such as hazardous drinking patterns, lower levels of education and depression, also occur at higher rates in Pacific New Zealanders than in their European counterparts.[22–24]

For the reasons above, it is reasonable to hypothesise that New Zealand Pacific peoples might have earlier onset of dementia compared to New Zealand Europeans. Currently, there is no dementia prevalence data in New Zealand to confirm this. There are also no genetic data concerning APOE4 status among Pacific populations.

Boxers of Pacific origin living in New Zealand may therefore be at additional risk of developing early onset dementia. It would be important for such individuals to be fully informed about such risk before embarking on a boxing career. It would also be wise for such individuals to ascertain their APOE4 status at the beginning of their careers, as heterozygosity and homozygosity for this isoform increases the risk of developing Alzheimer's disease by factors of 3 and 12 respectively.[25]

To conclude, this study highlights a series of Samoan and Tongan men in South Auckland with a history of amateur or professional boxing who have presented to our service with early onset dementia. A history of boxing is superimposed on other risk factors, such as alcohol and vascular disease, suggesting a multifactorial cause for their dementia. Historical, cultural and socio-economic factors appear to underlie the attraction of some Pacific men to boxing as a sport. We encourage sports physicians to inform young New Zealand Pacific boxers of the long-term risks associated with their sport.

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REFERENCES:

1. Counties Manukau DHB (2011). Residential Locality Profiles for Counties Manukau DHB, CMDHB Overview.
2. Storey JE, Rowland JTJ, Conforti DA, et al. The Rowland Universal Dementia Assessment Scale (RUDAS): a multicultural cognitive assessment scale. Int Psychogeriatr. 2004; 16:13–31.
3. Mioshi E, Dawson K, Mitchell J, et al. The Addenbrooke's Cognitive Examination Revised (ACE-R): a brief cognitive test battery for dementia screening. Intl J Geriatr Psychiatry. 2006; 21:1078–1085.
4. Folstein MF, Folstein SE, McHugh PR. "Mini-mental state." A practical method for grading the cognitive state of patients for the clinician. J Psychiatr Res. 1975; 12:189–198.
5. Dubois B, Slachevsky A, Litvan I, et al. A frontal assessment battery at bedside. Neurology. 2000; 55:1621–1626.
6. Nasreddine ZS, Phillips NA, Bedirian V. The Montreal Cognitive Assessment, MoCA: A Brief Screening Tool for Mild Cognitive Impairment. J Am Geriatr Soc. 2005; 53:695–699.
7. Mallon S. Punching Above Their Weight: A Hard Hitting History of Polynesian Fighters from New Zealand. 2015. Available at: http://fightland.vice.com/blog/punching-above-their-weight-a-hard-hitting-history-of-polynesian-fighters-from-new-zealand. Accessed 8 September 2015.
8. Scott RM, Buckley HR. Exploring Prehistoric Violence in Tonga: Understanding Skeletal Trauma from a Biocultural Perspective. Current Anthropology. 2014; 55:335–347.
9. Samwell D. Some Account of a Voyage to South Sea's. In: The Journals of Captain James Cook, The Voyage Of The Resolution and Discovery, 1776–1780 Part Two. Beaglehole JC (ed) London, Cambridge University Press For The Hakluyt Society, 1967
10. Boxing New Zealand. New Zealand Amateur Champions. Available at: www.boxingnz.org.nz/default.aspx?page=champions&cat=2 Accessed 22 February 2016.
11. Wikipedia. Boxing at the Pacific Games. Available at: http://en.wikipedia.org/wiki/Boxing_at_the_Pacific_Games Accessed 11 February 2016.
12. Veblen T. The theory of the leisure class. New York, Mentor, 1956.
13. Stoner L, Shultz SP, Lambrick DM, et al. The Combating Obesity in Māori and Pasifika Adolescent School-Children Study: COMPASS Methodology and Study Protocol. Int J Prev Med. 2013; 4:565–579.
14. Sugden J. Boxing and society, an international analysis. Manchester, Manchester University Press, 1996.
15. Smith DH, Johnson VE, Stewart W. Chronic neuropathologies of single and repetitive TBI: substrates of dementia? Nat Rev Neurol. 2013; 9:211–221.
16. Forstl H, Haass C, Hemmer B, et al. Boxing – Acute Complications and Late Sequelae. Dtsch Arztebl Int. 2010; 107:835–839.
17. Nowak LA, Smith GG, Reyes PF. Dementia in a retired world boxing champion: case report and literature review. Clin Neuropathol. 2008; 28:275–280.
18. Johnson J. Organic Psychosyndromes due to Boxing. Br J Psych. 1969; 115:45–53.
19. Feigin VL, McNaughton H, Dyall L. Burden of stroke in Māori and Pacific peoples of New Zealand. Intl J Stroke. 1969; 2:208–210.
20. Joshy G, Simmons D. Epidemiology of diabetes in New Zealand: revisit to a changing landscape. N Z Med J. 2006; 119:91–105.
21. Ministry of Health (2013) The Health of Pacific Adults and Children. Available at: http://www.health.govt.nz/system/files/documents/publications. Accessed November 2014.
22. Ministry of Health 2013 Hazardous drinking in 2011/12: findings from the NZ Health Survey. Available at: http://www.health.govt.nz/system/files/documents/publications/12-findings-from-the-new-zealand-health-survey.pdf. Accessed 26 November 2014.
23. Jatrana S, Blakely T. Ethnic inequalities in mortality among the elderly in New Zealand. Aust N Z J Public Health. 2008; 32:437–43.
24. Baxter J, Kokaua J, Wells J, et al. Ethnic comparisons of the 12 month prevalence of mental disorders and treatment contact in Te Rau Hinengaro: the New Zealand Mental Health Survey. Aust N Z J Psych. 2006; 40:905–913.
25. Schu MC, Sherva R, Farrer LA, et al. The Genetics of Alzheimer's Disease. In: Alzheimer's Disease – Modernizing Concept, Biological Diagnosis and Therapy. Advances in Biological Psychiatry. Hampel H & Carrillo MC (eds) Basel, Karger, 2012.

The Dunedin Dementia Risk Awareness Project: a convenience sample of general practitioners

Yoram Barak, Charlene Rapsey, Dana Fridman, Kate Scott

ABSTRACT

AIMS: Recent recommendations of US and UK governmental and academic agencies suggest that up to 35% of dementia cases are preventable. We aimed to appraise general practitioners' (GPs) awareness of risk and protective factors associated with dementia and their intentions to act within the context of the Health Beliefs Model.

METHODS: We canvassed degree of dementia awareness, using the modified Lifestyle for Brain Health (LIBRA) scale among a convenience sample of local GPs.

RESULTS: Thirty-five GPs, mean age 56.7 ± 6.8 years (range: 43–72) participated. There were 19 women and 16 men, all New Zealand European. Genetics was the most commonly cited risk for dementia and exercise the most commonly cited protective factor. More than 80% of participants correctly identified 8/12 LIBRA factors. Factors not identified were: renal dysfunction, obesity, Mediterranean diet and high cognitive activity. The majority of participants felt they were at risk of suffering from dementia, that lifestyle changes will help reduce their risk and wished to start these changes soon.

CONCLUSIONS: GPs are knowledgeable about dementia risk and protective factors. They reported optimism in their ability to modify their own risk factors through lifestyle interventions. This places GPs in a unique position to help disseminate this knowledge to their clients.

Dementia is a global public health priority.[1] The total number of people with dementia is predicted to increase due to an aging population and so will associated care costs.[2,3] Universal, selective and indicated preventive interventions are a mandated goal of primary prevention.[4,5] Interventions to prevent mental ill-health aim to counteract risk factors and reinforce protective factors along the lifespan in order to disrupt those processes that contribute to human mental dysfunction.

The risk factors that more narrowly focus on the older adults and the elderly include, among others: access to alcohol, isolation, lack of education, poor nutrition and poverty. Protective factors in the elderly include social support and community networks.[6,7] A recent review suggested that seven major modifiable risk factors (diabetes mellitus, midlife hypertension, midlife obesity, smoking, depression, and cognitive and physical inactivity) account for about 50% of all cases of Alzheimer's disease (AD) dementia.[8] This year, two important publications have "revolutionised" the way we think about preventing dementia. After a very pessimistic and negative view on dementia prevention published in 2010, the National Academies for Science Engineering and Medicine of the USA have changed their position. The recommendations are now as follows: "The systematic review identified no specific interventions that are supported by sufficient evidence to justify mounting an assertive public health campaign to encourage people to adopt them for the purpose of preventing cognitive decline and dementia. The systematic review did, however, find some degree of support for the benefit of three classes of intervention: cognitive training, blood pressure

management in people with hypertension and increased physical activity".[9] Closely following this important review undertaken by the NIH, the *Lancet* commissioned report on dementia prevention, intervention and care was published.[10] In this report, the emphasis on prevention is even more definite: "Be ambitious about prevention. We recommend active treatment of hypertension in middle aged (45–65 years) and older people (aged older than 65 years) without dementia to reduce dementia incidence. Interventions for other risk factors, including more childhood education, exercise, maintaining social engagement, reducing smoking, and management of hearing loss, depression, diabetes and obesity might have the potential to delay or prevent a third of dementia cases."

Several studies developed prediction models to calculate individual dementia risk. However, a limitation inherent in most models is that these risk indices comprise both modifiable and non-modifiable factors such as age, sex and apolipoprotein E genotype. Although including the latter might increase predictive accuracy, such factors are not amenable to change, cannot be targeted in routine care and do not indicate individual 'room for improvement'. Recently, Schiepers and colleagues (2018) reported on a new prediction model for dementia that differs from previous risk indices by focusing exclusively on modifiable risk factors, increasing its potential application in the development of tailored interventions and primary prevention.[11] This model (the Lifestyle for Brain Health [LIBRA] scale) was evaluated in a large population-based study containing extensive information about risk and protective factors for dementia and cognitive decline.[11]

A report issued by the CDC and the Alzheimer's Association recommended with high priority to "determine how diverse audiences think about cognitive health and its association with lifestyle factors."[12] In the present study we report results of a convenience sample of GPs who were evaluated as to their awareness and perceptions of brain health and self-efficacy in undertaking lifestyle changes to improve brain health.

Methods

The method we employed in the present study was based on the American Institute for Cancer Research (AICR) commissioned Cancer Risk Awareness Surveys aimed at gauging Americans' awareness of various lifestyle-related cancer risk factors.[13] Briefly, the AICR Cancer Risk Awareness Survey has been conducted periodically since 2001. A random sample of Americans aged 18 and older is telephoned on behalf of AICR by SSRS (www.ssrs.com). The survey provides important insights and trends into how Americans are able to separate clearly established cancer risks from factors about which there is no scientific consensus, but which many of the general public believe cause cancer. Respondents to the AICR survey are read the following question: "Which of the following do you believe has a significant effect on whether or not the average person develops cancer?" The risk factors are randomly ordered, and read to respondents one at a time; to each, respondents answer 'Yes', 'No' or 'Don't Know'.

We have modified the LIBRA scale (see Appendix 1) to conform to the AICR survey format, and added open-ended questions as to dementia risk and protective factors. Finally, we use five 'Yes/No' questions to gauge participants' health beliefs based on the health beliefs scale.[14]

Participants

This sample was selected for convenience. Prior to an academic update for GPs the questionnaire was distributed. All 35 attendees consented to participate. The meeting was part of a series of annual meetings for GPs that are recognised for Continuous Medical Education (CME) accreditation. The subject of the meeting was 'brain health'. GP participants all completed a hard copy survey at the CME meeting.

Procedures

Participants were asked a series of identical questions about dementia risk awareness, beginning with open-ended questions asking about their unprompted (recall) knowledge of dementia risk factors overall; "What do you believe are the three most important risk factors for dementia?"

and "What do you believe are the three most important protective factors for dementia?". Respondents were then prompted specifically about the modified LIBRA risk factors; "Which of the following do you believe has a significant effect on whether or not the average person develops dementia?" Finally, five questions assessing the participants Health Belief Model were asked.

This study used unprompted recall and prompted recognition to explore different levels of awareness. Unprompted recall retrieves knowledge that is readily accessible, and likely to be more influential in day-to-day behaviour choices than recognition, which requires a prompt to elicit the information.

See Appendix 2 for the pilot survey questionnaire.

Analyses

Respondent characteristics are described using appropriate summary statistics and the proportions affirming each belief will be presented.

Compliance with Ethical Standards

Ethical approval for the proposed survey was obtained from the University of Otago Ethics Committee and the Department of Psychological Medicine Ethics Committee.

The Human Ethics Committee's reference number for this study is D17/231.

Consent was given orally following detailed explanation of the study and prior to endorsing the survey questionnaire.

Results

Thirty-five GPs, mean age 56.7 ± 6.7 years (range: 43–72) participated in the present survey. There were 19 women and 16 men; all were New Zealand Europeans.

Their answers to the survey questions were as follows:

Risk and protective factors

Open ended

"What do you believe are the three factors that will **increase** the chances of a person experiencing memory problems in older age?"

- Genetics was most commonly emphasised followed by smoking and sedentary lifestyle.

"What do you believe are the three factors that will **reduce** the chances of a person experiencing memory problems in older age?"

- Exercise was most commonly emphasised followed by dietary changes and cognitive training.

Prompted

See Figure 1 for a graphic representation of the answers to the prompted factors.

In relation to established risk and protective factors as reflected in the LIBRA score,[11] more than 80% of participants correctly identified 8/12 LIBRA factors. Factors not identified were: renal dysfunction, obesity, Mediterranean diet and high cognitive activity.

Health beliefs

The majority of participants felt they were at risk of suffering from dementia, that this will change their lives significantly, that lifestyle changes will help reduce their risk, that they can make the necessary changes and wish to start these changes soon.

The answers to the questions reflecting health beliefs and readiness for change were as follows:

- "I am at risk to suffer from dementia in the future" Yes: 29, No: 6.
- "If I were to suffer from dementia my whole life would change" Yes: 31, No: 4.
- "Changing lifestyle behaviours (for example: diet, smoking, exercise) will reduce the risk of dementia" Yes: 34, No: 1.
- "Changing lifestyle will be too difficult" Yes: 5, No: 30.
- "I feel confident that I could make lifestyle changes to help prevent dementia" Yes: 28, No: 7.
- "I want to start lifestyle changes soon" Yes: 29, No: 6.

Discussion

In the present study, the majority of GPs correctly endorsed eight of the 12 LIBRA factors. Risk and protective factors not identified by the majority of GPs were obesity, renal dysfunction, the Mediterranean diet and high cognitive activity respectively.

This may be a reflection of cultural bias (the Mediterranean diet) or the fact that diet and cognitive activity are conceptualised as areas related to allied health professionals interests and expertise and not to the 'core' practice of general medicine. Obesity stands out as a factor that may need to be emphasised for GPs as an important risk for dementia. The conceptualisation of dementia as highly 'genetic' does not reflect the current scientific evidence and again may be an area in need of further education for GPs. Finally, although pessimism was reflected in the majority of GPs reporting they feel they are at risk of suffering from dementia, as a group they were optimistic, confident and ready to start lifestyle changes to decrease risk of dementia.

Health promotion is an important element of national health strategy, however attitudes among GPs are ambivalent. Many GPs state they lack the skills needed to deliver effective health promotion.[15] In a survey among UK general practices attitudes to health promotion were generally positive, but lack of training in lifestyle counselling was perceived to be a problem. Beliefs in the effectiveness of lifestyle counselling were associated with positive attitudes towards health promotion and better confidence in training. This is relevant to our findings as the majority of GPs reported feeling confident they can make the appropriate lifestyle changes for themselves. The attitudes of health professionals are crucial to the implementation of prevention strategies.[16] However, as no association between personal health behaviour and attitudes towards health promotion were observed[15] we need to be cautious in assuming the positive stance on health behaviours reported by GPs in the present study will indeed translate into prevention interventions for older adults.

Studies that have examined public knowledge about AD were mostly based on specific at-risk populations. This and other limitations make it difficult to assess the representativeness of reported results. The present study addresses this challenge by examining knowledge and beliefs about dementia risk and protective factors among a convenience sample of GPs. The support and advancement of preventive measures by GPs can make a significant difference on patients' decisions to engage in lifestyle changes.[17] Studies have identified patients' regular GPs as a strong influence especially given the complexity involved in making decisions about preventive interventions. GPs should be aware of their major influence on patients and regularly discuss health-related issues with older adults and their carers.[18]

The current study has several limitations. It is not a representative sample of GPs in New Zealand. However, all GPs are required to participate in CME and there is no reason to believe that the GPs attending this event would have more or less knowledge about risk and protective factors for dementia.

The growing attention to cognitive health promotion among older adults emphasises the importance of scrutinising public understanding of risk and protective factors for dementia. An increased understanding of public views about dementia is a priority. Health beliefs have long been recognised as an important factor in risk self-management. Perceived threat of disease—personal susceptibility—is associated with willingness to seek out preventive options whereas beliefs about causes influence self-management.[1] A large scale effort to reduce the number of people developing dementia was piloted by several NGOs in the UK as part of the NHS Health Check programme—a free health check-up for adults in England aged 40–74, designed to reduce their risk of stroke, kidney disease, heart disease, type 2 diabetes or dementia. Seventy-five percent of people participating in the NHS programme said advice on dementia risk reduction would encourage them to adopt a healthier lifestyle while 80 percent said the advice would have some impact on their behaviour.

The perception of old age differs in different societies and cultures: in Western societies, the loss of youth, multiple losses of functions and independence resulting in disability produce a social stigma.

Dementia is common among the elderly, regardless of ethnic background. In countries led by Western philosophical thought, the cognitive domain has been privileged over other mental domains.[20] Studies are currently dominated by biomedical models that consider dementing disorders solely as pathological entities caused by neuronal and neurotransmitters loss, and focus on the individual without regard to sociocultural context. The experience of dementia is not universal, but is profoundly shaped by the culture in which a person lives. Sociocultural conceptualisation of the symptoms of dementing diseases remains obscure among both patients and healthcare providers. The relevance of loneliness, exercise, nutrition, depression and a more holistic bio-psycho-social conceptualisation of dementia is called for. There is an urgent need to expand the conceptualisation of dementia beyond a genetic medical model GPs expressed in the present study.

In conclusion, prevention is viewed as a key issue for general practice, yet there is a lack of evidence regarding general practitioners' interventions in both middle-aged and elderly people. GPs should design and implement prevention services and programmes to promote healthy and active ageing. Empowering people to become fit and eat healthier is crucial if we are to reduce the number of people developing dementia.[21] GPs are uniquely placed to advance these messages as clearly demonstrated by their enthusiasm about changing their own lifestyle captured in the present study.

Appendix 1

LIBRA score

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Table 1: Algorithm for calculating individual Lifestyle for Brain Health (LIBRA) score.[a]

Modifiable risk factor	Relative risk (RR)	Ln (RR)/beta weight	Score	Available in MAAS
Low/moderate alcohol consumption	0.74	-0.30 (reference)	-1.0	+
Coronary heart disease	1.36	0.31	+1.0	+
Physical inactivity	1.39	0.33	+1.1	+
Renal dysfunction	1.39	0.33	+1.1	+
Diabetes	1.47	0.39	+1.3	+
High cholesterol	1.54	0.43	+1.4	+
Smoking	1.59	0.46	+1.5	+
Obesity	1.60	0.47	+1.6	+
Hypertension	1.61	0.48	+1.6	+
Mediterranean diet	0.60	0.51	+1.7	-
Depression	1.85	0.62	+2.1	+
High cognitive activity	0.38	-0.97	-3.2	+
Low unsaturated fat intake[b]	-	-	-	-

Appendix 2

The Dunedin Dementia Risk Awareness Survey

Age:

Gender:

Ethnicity:

Education:

What do you believe are the three most important risk factors for dementia?

-

-

-

What do you believe are the three most important protective factors for dementia?

-

-

-

Which of the following do you believe has a significant effect on whether or not the average person develops dementia?

- Low/moderate alcohol consumption
- Coronary heart disease
- Oral hygiene
- Physical inactivity
- Renal dysfunction
- Diabetes
- High cholesterol
- Curcumin
- Smoking
- Obesity
- Hypertension
- Mediterranean diet
- Depression
- Prescription drugs
- High cognitive activity
- Low unsaturated fat intake

Please answer 'Yes/No' for the following statements:

- "I am more than likely than the average person to suffer from dementia in the future"
- "If I were to suffer from dementia my whole life would change"
- "Changing lifestyle behaviours will reduce the risk of dementia"
- "Taking preventive measures will be too resource intensive"
- "I know how to initiate dementia prevention"
- "I want to start dementia prevention early"

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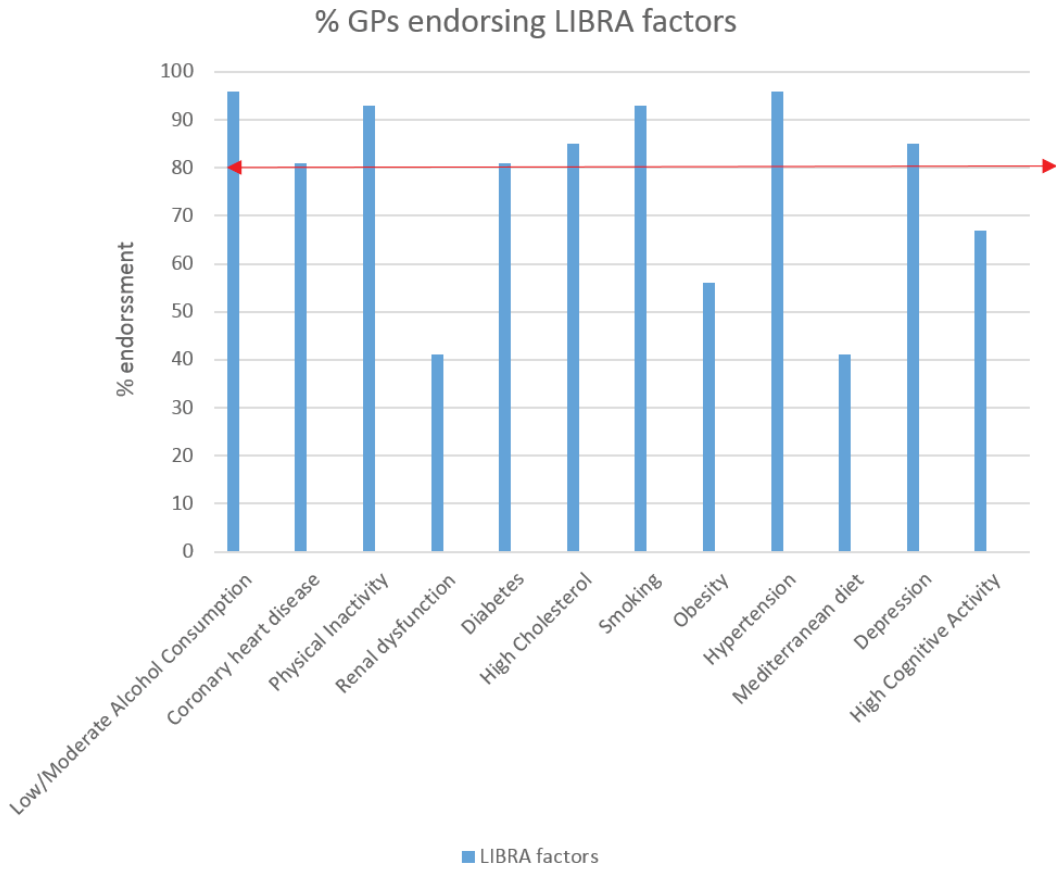
Figure 1: % GPs endorsing LIBRA factors.



Competing interests:
Nil.

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REFERENCES:

1. World Health Organization. 2012. Dementia: a public health priority. WHO Geneva.
2. Hebert LE, Weuve J, Scherr PA, Evans DA. 2013. Alzheimer disease in the United States (2010–2050) estimated using the 2010 census. Neurology 80:1778–1783.
3. Hurd MD, Martorell P, Delavande A, Mullen KJ, Langa KM. 2013. Monetary costs of dementia in the United States. N Engl J Med 368:1326–1334.
4. Gordon R. 1983. An operational classification of disease prevention. Pub Health Rep 98:107–109.
5. Gordon R. 1987. An operational classification of disease prevention. In: Steinberg JA, Silverman MM, eds. Preventing mental disorders: a research perspective. Rockville, MD, Department of Health and Human Services: 20–26.
6. Stevens N, van Tilburg T. 2000. Stimulating friendship in later life: A strategy for reducing loneliness among older women. Educat Gerontol 26:15–35.
7. Jané-Llopis E, Muñoz R, Patel V. 2005. Prevention of depression and depressive symptomatology. In: Hosman C, Jané-Llopis E, Saxena S, eds. Prevention of mental disorders: effective interventions and policy options. Oxford, Oxford University Press.
8. Barnes DE, Yaffe K. 2011. The projected effect of risk factor reduction on Alzheimer's disease prevalence. Lancet Neurol 10:819–828.
9. National Academies of Sciences, Engineering, and Medicine. 2017. Preventing Cognitive Decline and Dementia: A Way Forward. Washington, DC: The National Academies Press. doi: https://doi.org/10.17226/24782.
10. Livingston G, Sommerlad A, Orgeta V, et al. 2017. The Lancet Commissions: Dementia prevention, intervention and care. Lancet S0140-6736(17)31363-6.
11. Schiepers OJ, Köhler S, Deckers K, Irving K, O'Donnell CA, van den Akker M, Verhey FR, Vos SJ, de Vugt ME, van Boxtel MP. 2018. Lifestyle for Brain Health (LIBRA): a new model for dementia prevention. Int J Geriatr Psychiatr 33:167–175.
12. Alzheimer's Association. Brain Health [Internet]. 2014. Available at: http://www.alz.org/we_can_help_brain_health_maintain_your_brain.asp
13. AICR/WCRF. 2017. Food, Nutrition, Physical Activity, and the Prevention of Cancer: a Global Perspective and the Continuous Update Project (CUP) reports.
14. Champion VL. 1984. Instrument development for health belief model constructs. Adv Nursing Sci 6:73–85.
15. Peckham S, Hann A, Boyce T. 2011. Health promotion and ill-health prevention: the role of general practice. Qual Prim Care 19:317–323.
16. Steptoe A, Doherty S, Kendrick T, Rink E, Hilton S. 1999. Attitudes to cardiovascular health promotion among GPs and practice nurses. Fam Pract 16:158–163.
17. Bonner C, Jansen J, McKinn S, Irwig L, Doust J, Glasziou P, McCaffery K. 2015. How do general practitioners and patients make decisions about cardiovascular disease risk? Health Psychol 34:253–261.
18. Reeve E, Low LF, Hilmer SN. 2016. Beliefs and attitudes of older adults and carers about deprescribing of medications: a qualitative focus group study. Br J Gen Pract 66:552–560.
19. Janz NK, Becker MH. The Health Belief Model: A decade later. Health Educ Q 1984; 11:1–47.
20. Cipriani G, Borin G. Understanding dementia in the sociocultural context: a review. Int J Soc Psychiatry 2015; 61:198–204.
21. Alzheimer's Research UK. [Internet]. 2017. "Dementia education on risk inspires people in midlife to consider healthier lifestyles" August 15, 2017. https://medicalxpress.com/news/2017-08-dementia-people-midlife-healthier-lifestyles.html

Co-prescribing of contraindicated and use-with-caution drugs in a national cohort of new users of simvastatin: how well are prescribing guidelines followed?

Joshua Quon, Lianne Parkin, Katrina Sharples, David Barson

ABSTRACT

AIM: To describe the use of contraindicated and use-with-caution medicines among new users of simvastatin.

METHODS: We used information from Ministry of Health national datasets to establish a cohort of all patients aged ≥18 years who initiated simvastatin use between January 2006 and December 2013 (n=349,371). We estimated the cumulative incidences of the first dispensing of contraindicated and use-with-caution medicines during simvastatin use, and explored factors associated with co-prescription, using Kaplan-Meir and Cox regression methods, respectively.

RESULTS: Eleven percent and 16% of patients were dispensed a contraindicated and use-with-caution medicine, respectively, during the first two years of simvastatin use; by seven years, the figures were 17% and 26%. Thirty-six percent of patients were co-prescribed a contraindicated medicine on >1 occasion; the corresponding proportion for use-with-caution medicines was 84%. For a substantial proportion of those co-prescribed a use-with-caution medicine, the concomitant daily dose of simvastatin exceeded the maximum dose recommended at the time of prescribing. In the majority of cases, the prescriber of simvastatin and the contraindicated or use-with-caution medicine were the same. Co-prescribing of contraindicated medicines varied by sex, age, ethnicity and comorbidity.

CONCLUSIONS: The prescription of contraindicated and use-with-caution drugs to patients taking simvastatin is not uncommon in New Zealand.

Statins play a vital role in the primary and secondary prevention of major cardiovascular events.[1] In recent years, the adoption of an absolute cardiovascular risk reduction approach to prevention has led to an increase in the use of these medicines in New Zealand.[2–7] In 2016, for example, over 1.8 million prescriptions for statins were dispensed.[7]

Three statins are fully funded by the New Zealand Pharmaceutical Management Agency (PHARMAC): simvastatin, atorvastatin, and pravastatin.[8] Simvastatin (and, to a lesser degree, atorvastatin) is metabolised by the isoenzyme cytochrome P450 3A4 (CYP3A4), and the concomitant use of medicines which inhibit CYP3A4 may increase plasma levels of simvastatin, thereby

increasing the risk of adverse events such as myopathy and rhabdomyolysis.[9] Some CYP3A4 inhibitors are completely contraindicated in users of simvastatin, while others should only be used with caution and careful management of simvastatin dose.

Researchers from several countries have reported concerning levels of exposure to CYP3A4 inhibitors among users of CYP3A4-metabolised statins;[10–16] however, the extent of any such co-prescribing in New Zealand is unknown. We undertook a nationwide study to describe the use of contraindicated medicines, and those which should be used with caution, among all patients who initiated simvastatin use in New Zealand between 1 January 2006 and 31 December 2013. The specific aims of the study were to: (i) calculate the proportion of patients for whom a prescription of a contraindicated medicine was filled while on simvastatin, (ii) calculate the proportion of patients for whom a prescription of a use-with-caution medicine was filled while on simvastatin, (iii) ascertain whether the prescribers of simvastatin and a contraindicated medicine were the same, (iv) ascertain whether the prescribers of simvastatin and a use-with-caution medicine were the same and (v) explore factors associated with co-prescription of contraindicated medicines, including age, sex, ethnicity, deprivation and comorbidity.

Methods

Data sources

The study was based on data from four national datasets held by the Ministry of Health: the Pharmaceutical Collection (claims for all publicly funded dispensings of prescription medicines from community pharmacies),[17] the National Health Index (NHI) Collection (demographic information indexed to a unique patient identifier, the NHI),[18] the National Minimum Dataset (NMDS, publicly funded hospital discharges from 1988)[19] and the Mortality Collection (hospital inpatient and community-based deaths).[20] Since 2005, NHIs have been recorded with most dispensing records in the Pharmaceutical Collection and this has allowed the linkage of person-level pharmaceutical, demographic and health information held in the national datasets.

Deriving the study cohort

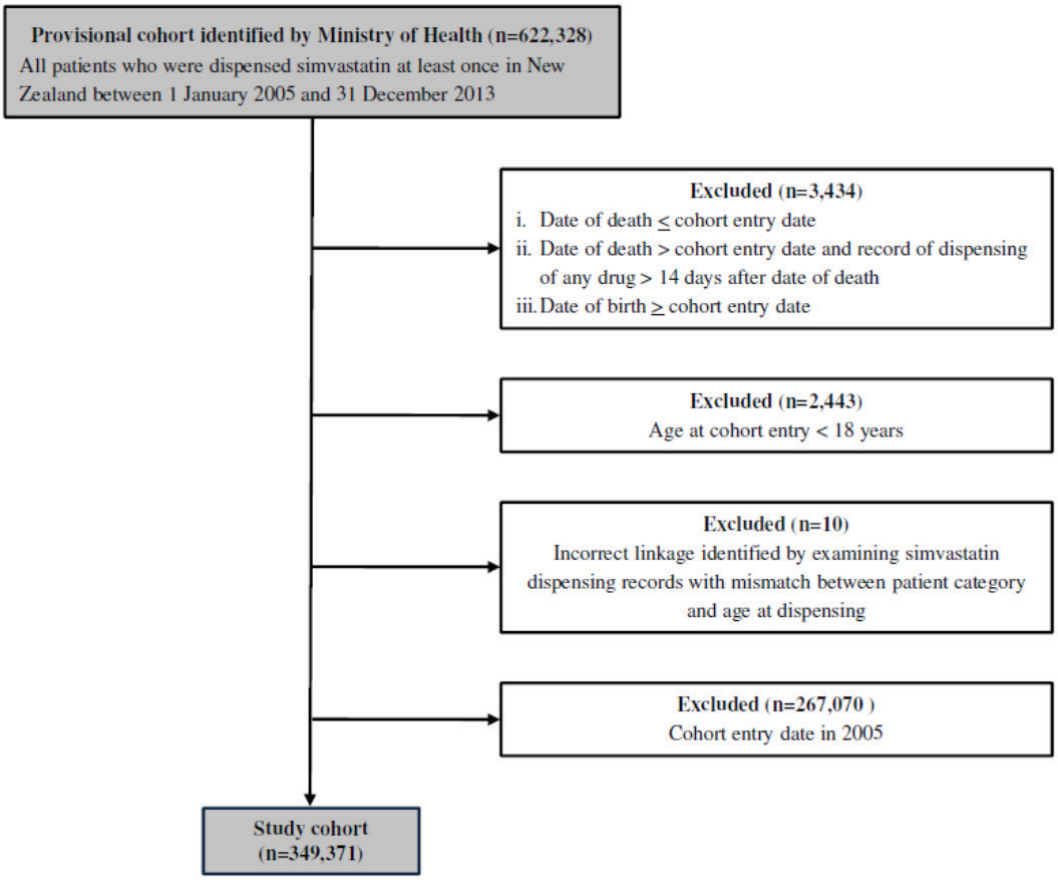
Analytical Services staff at the Ministry of Health searched the Pharmaceutical Collection to identify all patients who were dispensed simvastatin at least once between 1 January 2005 and 31 December 2013 (*the provisional cohort*). The date of the first simvastatin dispensing during that period was taken as the cohort entry date. For each patient, the Ministry provided us with the following data: demographic information (sex, date of birth, date of death, prioritised ethnicity [ie, patients with more than one recorded ethnic group were allocated to one group based on the following hierarchy: Māori, Pacific, Asian, Other, European][21] and an area-based measure of socioeconomic position, NZDep06[22]), details of all dispensings of simvastatin and other medicines (including subsequent dispensings of other statins) from cohort entry, details of any hospital discharges (back to 1988) and details of any deaths.

We undertook two steps to derive *the study cohort* from the provisional cohort identified by the Ministry (Figure 1). First, we excluded the small proportion of linked records where the pharmaceutical dispensing information and the health and demographic data clearly referred to different people. Second, we excluded patients with a cohort entry date in 2005 as we wanted to follow simvastatin users from the initiation of therapy (either as first-time users or as past users who were restarting after a break of at least one year).

Summarising simvastatin exposure

For each cohort member, we summarised simvastatin dispensing data into continuous episodes of use of the same daily dose, using an approach we have employed previously.[23,24] A continuous episode was defined as one in which the gap between the end date of one dispensed supply and the start date of the next was 30 days or less. Episodes were censored (truncated) at the earliest of any of the following: a different daily dose of simvastatin was dispensed, another statin was dispensed, the patient died or the end of the study period was reached (31 December 2013).

Figure 1: Deriving the study cohort.



Identifying exposure to contraindicated and use-with-caution medicines

We used the New Zealand Formulary (NZF)[8] to identify medicines which are contraindicated in simvastatin users, and those which should only be used with caution. Because prescribing advice regarding these medicines changed over time, we also examined archived hard copies of MIMs New Ethicals, which were current during the study period.[25] The contraindicated medicines included azole antifungals, ciclosporin (from January 2012), clarithromycin, danazol (from January 2012), erythromycin, gemfibrozil (from January 2012), omeprazole-amoxycillin-clarithromycin combination therapy and protease inhibitors. The use-with-caution medicines included amiodarone, amlodipine, bezafibrate, ciclosporin (January 2006 to December 2011), danazol (January 2006 to December 2011), diltiazem, gemfibrozil (January 2006 to December 2011), nicotinic acid and verapamil.

For each cohort member, we identified any dispensings of contraindicated and use-with-caution medicines which occurred during a continuous episode of simvastatin use (defined as co-prescribing). Any topical formulations were excluded from the count. In addition, we identified dispensings of amiodarone, amlodipine, bezafibrate, ciclosporin, danazol, diltiazem, gemfibrozil and verapamil to cohort members whose concomitant use of simvastatin exceeded the maximal daily dose recommended at the time of the dispensing. We did not have information about dispensed daily doses of nicotinic acid, so were unable to ascertain whether the dose of simvastatin was inappropriate.

Other information

We calculated a Charlson Comorbidity Score for each cohort member based on hospital discharge diagnoses in the five years before cohort entry, using an ICD-10 SAS macro developed by others.[26]

Statistical methods

Proportions and exact binomial 95% confidence intervals (95% CI)[27] were calculated to describe the crude proportions of simvastatin users who were co-prescribed each and any contraindicated and use-with-caution medicines during the follow-up period. Cumulative incidences of the first prescriptions of contraindicated and use-with-caution medicines were estimated using Kaplan-Meier methods,[28] with duration of simvastatin use as the measure of time. Cox regression methods[29] were used to estimate hazard ratios comparing demographic groups and comorbidity score using the same approach. Missing data were imputed for the Cox regression using chained equations[30] with age, sex, ethnicity, deprivation, Charlson score and outcome in the imputation models (n=10). R version 3.3.2 for Mac OSX and Stata v14 were used for statistical analyses.

Ethical approval

The study received approval from the Northern A Health and Disability Ethics Committee (14/NTA/178/A02).

Results

The study cohort

The provisional cohort identified by the Ministry of Health included 622,328 simvastatin users; a very small proportion had incorrectly linked records (0.9%, n=5,887), while 267,070 were prevalent users (Figure 1). In total, therefore, the study cohort included 349,371 patients who initiated simvastatin therapy in New Zealand between 1 January 2006 and 31 December 2013. The median duration of follow-up was 4.8 years, and the median duration on simvastatin was 2.1 years. The median age of cohort members was 59 years (interquartile range 50–69); just under half were female; 10.3% were Māori, 6.9% Pacific, 8.6% Asian, 66.9% European and 1.1% were classified as belonging to Other ethnic groups; and most had a Charlson Comorbidity Score less than 3 (Table 1). A socio-economic gradient was observed, with higher proportions of cohort members being found in the more deprived versus less deprived NZDep06 quintiles.

Table 1: Characteristics of the study cohort at entry. Values are numbers (%) unless stated otherwise.

Characteristic	Study cohort (n=349,371)
Female sex	157,325 (45.0)
Median age (interquartile range)	59 (50–69)
Ethnicity	
Māori	36,050 (10.3)
Pacific	24,045 (6.9)
Asian	29,893 (8.6)
European	233,757 (66.9)
Other	3,730 (1.1)
Missing	21,896 (6.3)
NZDep06 quintile	
1 (least disadvantaged)	55,825 (16.0)
2	56,805 (16.3)
3	71,862 (20.6)
4	81,611 (23.4)
5 (most disadvantaged)	82,113 (23.5)
Missing	1,155 (0.3)
Charlson Comorbidity Score	
0	271,229 (77.6)
1–2	60,825 (17.4)
3–4	11,279 (3.2)
5–6	3,290 (0.9)
≥7	2,748 (0.8)

Co-prescribing of contraindicated and use-with-caution medicines

Overall, 37,446 (10.72%) cohort members were dispensed at least one contraindicated medicine while they were using simvastatin (Table 2). Erythromycin was co-prescribed to 27,781 (7.95%) patients, while small proportions (between 0.6 and 0.8%) received clarithromycin (alone or in triple therapy), fluconazole, itraconazole and miconazole.

Table 2: Numbers and proportions of cohort members (n=349,371) who were co-prescribed contraindicated medicines on cohort entry date and/or during follow-up.

Medicine*	Cohort members co-prescribed contraindicated medicine	
	Number†	Percentage (95% CI)
Any contraindicated medicine	37,446	10.72 (10.62–10.82)
Clarithromycin	2,306	0.66 (0.63–0.69)
Erythromycin	27,781	7.95 (7.86–8.04)
Fluconazole	2,675	0.77 (0.74–0.80)
Itraconazole	1,992	0.57 (0.55–0.60)
Miconazole	2,593	0.74 (0.71–0.77)
Omeprazole, amoxicillin, clarithromycin combination therapy	2,197	0.63 (0.60–0.66)

*No cohort members were co-prescribed indinavir, nelfinavir or posaconazole, and very small numbers were co-prescribed atazanavir sulphate (n=10), ciclosporin (n=276), danazol (n=6), darunavir (n=3), gemfibrozil (n=100), ketoconazole (n=157), lopinavir with ritonavir (n=8), and ritonavir (n=11). The numbers for ciclosporin, danazol and gemfibrozil relate to dispensings from January 2012 onwards, when the concomitant use of these drugs with simvastatin became contraindicated.

†The number of cohort members co-prescribed at least one contraindicated medicine is less than the sum of the numbers for individual drugs because some people were co-prescribed more than one contraindicated medicine.

Co-prescription of ciclosporin, danazol, gemfibrozil, ketoconazole and protease inhibitors was very uncommon. Just over a third of patients (36.01%, n=13,484) who received a contraindicated medicine while taking simvastatin did so on more than one occasion, and 594 (1.59%) patients had at least 10 such co-prescribing events. The drug most likely to have been repeatedly dispensed was ciclosporin; of those who were dispensed ciclosporin, 96.01% had two or more dispensings, and 61.59% had 10 or more. A very small number (n=263) of patients were co-prescribed, at least once, two or more contraindicated medicines on the same day.

In total, 58,769 (16.82%) cohort members were dispensed at least one use-with-caution medicine during an episode of simvastatin use (Table 3). Amlodipine and diltiazem were the most common co-prescribed medicines (to 6.86% and 6.43% of patients, respectively). Overall, 83.74% (n=49,214) of cohort members who received a use-with-caution drug while taking simvastatin did so on more than one occasion; 46.14% (n=27,118) of patients had at least 10 such co-prescribing events, and 7.63% (n=4,485) had at least 50 events. Only 16 patients were co-prescribed, at least once, two or more use-with-caution medicines on the same day. Of the patients co-prescribed amiodarone, amlodipine, bezafibrate, diltiazem or verapamil, substantial proportions were taking simvastatin at a higher daily dose than recommended at the time of the dispensing.

Figure 2 shows the cumulative incidence of the first co-prescription of a contraindicated medicine, and of the first co-prescription of a use-with-caution medicine. The steep initial rise, particularly for use-with-caution drugs, is likely to be explained by repeats of previously prescribed medications. About 11% (11.2%, 95% CI: 11.1 to 11.3) of cohort members were dispensed a contraindicated medicine in the first two years of simvastatin use, and this increased to 16.7% (95% CI: 16.5 to 16.9) by seven years. The corresponding proportions for a use-with-caution medicine were 15.9% (95% CI: 15.8 to 16.0) and 25.8% (95% CI: 25.5 to 26.1), respectively.

For 21,546 (57.5%) of the first contraindicated medicine dispensings, the prescriber was the same clinician who had written the most recent prescription for simvastatin; just over a third (35.3%, n=7,610) of the dispensings from the same clinician occurred on the same day that simvastatin was dispensed. For 47,099 (80.1%) of the first use-with-caution dispensings, the

Table 3: Numbers and proportions of cohort members (n=349,371) who were co-prescribed use-with-caution medicines on cohort entry date and/or during follow-up, and numbers and proportions for whom concomitant use of simvastatin exceeded maximal daily dose recommendations.

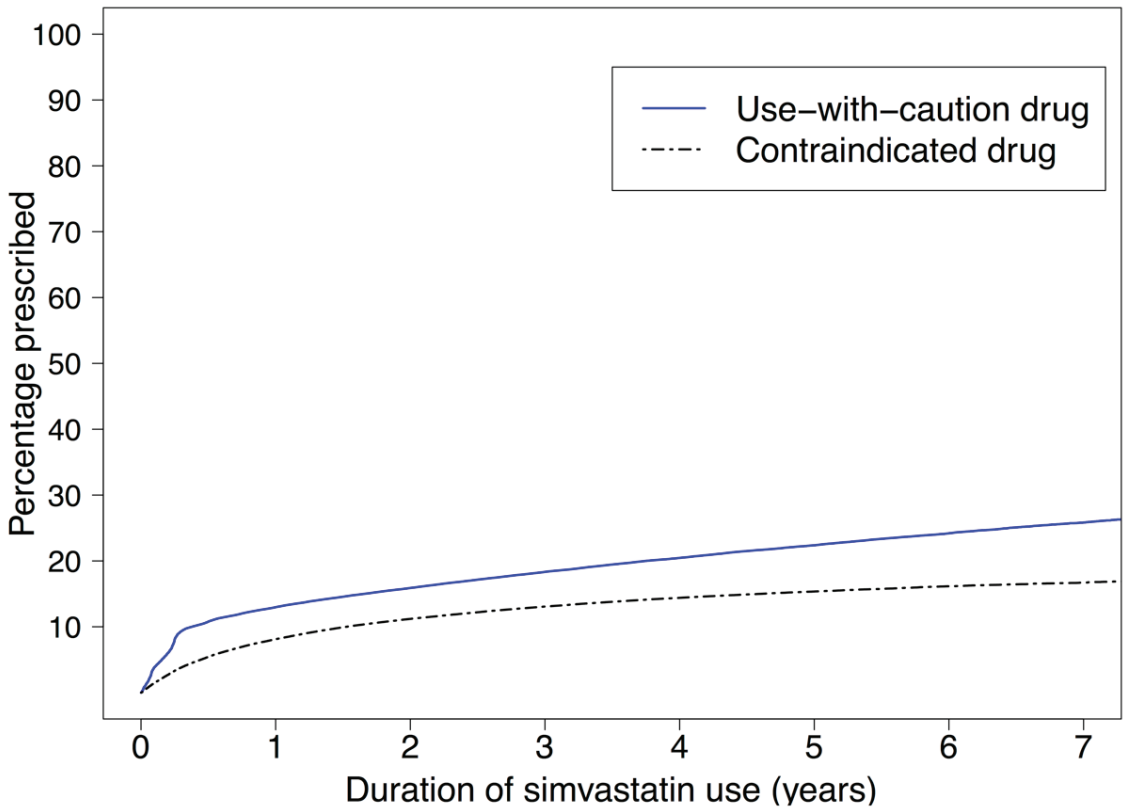
Medicine*	Cohort members co-prescribed use-with-caution medicine†		Cohort members co-prescribed use-with-caution medicine when concomitant use of simvastatin exceeded the recommended maximal daily dose	
	Number	Percentage (95% CI)	Number	Percentage (95% CI)‡
Any use-with-caution medicine	58,769	16.82 (16.70–16.95)	32,484	55.27 (54.87–55.67)
Amiodarone	5,663	1.62 (1.58–1.66)	3,491	61.65 (60.37–62.92)
Amlodipine	23,962	6.86 (6.78–6.94)	11,621	48.50 (47.87–49.14)
Bezafibrate	7,795	2.23 (2.18–2.28)	6,876	88.21 (87.47–88.91)
Diltiazem	22,448	6.43 (6.34–6.51)	11,584	51.60 (50.94–52.26)
Verapamil	2,933	0.84 (0.81–0.87)	1,277	43.54 (41.74–45.36)

*Very small numbers of cohort members were co-prescribed ciclosporin (n=448), danazol (n=21), gemfibrozil (n=50) and nicotinic acid (n=1,072). The numbers for ciclosporin, danazol and gemfibrozil relate to dispensings between January 2006 and December 2011, when it was advised that any co-prescribing of these drugs to patients taking simvastatin should be undertaken with caution.

†The number of cohort members co-prescribed at least one use-with-caution medicine is less than the sum of the numbers for individual drugs because some people were co-prescribed more than one contraindicated medicine.

‡The denominators for the percentages are the number of cohort members who were prescribed the use-with-caution medicines.

Figure 2: Cumulative incidence of co-prescription of contraindicated and use-with-caution medicines.



prescriber of the use-with-caution medicine and simvastatin were the same; for 36,836 (78.2%) of these dispensings the two medicines were dispensed on the same day.

Table 4 shows the results of the Cox regression analysis. Co-prescription of a contraindicated medicine was more common in women and in those with a higher Charlson Comorbidity Score, and less common in older age groups (for whom the time to the first co-prescribing event was longer). Compared with Māori, co-prescription was less common in Pacific and Asian patients, more common in the Other ethnic group and about the same in Europeans. There was no strong socio-economic gradient in co-prescribing.

Table 4: Numbers and proportions of cohort members (n=349,371) co-prescribed at least one contraindicated medicine according to demographic and clinical characteristics, with crude and adjusted hazard ratios.

Characteristic	Cohort members co-prescribed contraindicated medicine (no, %)*	Crude hazard ratio† (95% CI)	Adjusted hazard ratio (95% CI)†‡
Sex			
Female	19,003 (12.1)	1.43 (1.40–1.46)	1.44 (1.42–1.48)
Male	16,669 (8.7)	1.0	1.0
Age (years)			
18–39	1,900 (8.7)	1.0	1.0
40–59	14,957 (9.7)	0.93 (0.89–0.98)	0.89 (0.85–0.93)
60–79	15,956 (10.8)	0.97 (0.92–1.01)	0.86 (0.82–0.90)
≥80	2,860 (11.4)	1.12 (1.06–1.19)	0.83 (0.78–0.89)
Ethnicity			
Māori	3,871 (10.7)	1.0	1.0
Pacific	2,221 (9.2)	0.86 (0.81–0.90)	0.87 (0.82–0.91)
Asian	2,693 (9.0)	0.82 (0.78–0.86)	0.90 (0.86–0.95)
European	24,965 (10.7)	0.94 (0.91–0.97)	1.01 (0.98–1.05)
Other	463 (12.4)	1.22 (1.10–1.34)	1.31 (1.19–1.45)
NZDep06 quintile			
1 (least disadvantaged)	5,471 (9.8)	1.0	1.0
2	5,530 (9.7)	1.00 (0.97–1.04)	0.99 (0.95–1.03)
3	7,385 (10.3)	1.06 (1.02–1.10)	1.03 (1.00–1.07)
4	8,612 (10.6)	1.08 (1.05–1.12)	1.04 (1.01–1.08)
5 (most disadvantaged)	8,612 (10.5)	1.10 (1.06–1.14)	1.06 (1.02–1.10)
Charlson Comorbidity Score			
0	25,337 (9.3)	1.0	1.0
1–2	7,654 (12.6)	1.30 (1.26–1.33)	1.32 (1.28–1.35)
3–4	1,759 (15.6)	1.70 (1.62–1.78)	1.73 (1.65–1.82)
5–6	568 (17.3)	2.01 (1.85–2.18)	2.06 (1.89–2.24)
≥7	355 (12.9)	1.64 (1.47–1.82)	1.62 (1.46–1.80)

*Denominator is all cohort members in the category. Ethnicity was unknown for 1,460 cohort members prescribed a contraindicated medicine and NZDep06 quintile was unknown for six.

†Missing data were imputed for estimating the hazard ratios.

‡Adjusted for the other variables in the table.

Discussion

Principal findings

In this national study of all patients who initiated simvastatin use in New Zealand between 2006 and 2013, about 11% and 16% of patients were co-prescribed contraindicated and use-with-caution medicines, respectively, in the first two years of simvastatin use. These co-prescribing events were not always isolated incidents, with sizeable proportions of patients receiving a contraindicated or use-with-caution medicine on more than one occasion. For a substantial proportion of those co-prescribed a use-with-caution medicine, the concomitant daily dose of simvastatin exceeded the maximum dose recommended at the time. In the majority of cases, the prescriber of simvastatin and the contraindicated or use-with-caution medicine were the same. Female sex, younger age, greater comorbidity and ethnicity were all associated with co-prescribing of contraindicated medicines.

Strengths and limitations

The study had several strengths and some limitations which warrant further consideration. First, we were able to establish a national cohort of simvastatin users and follow those users from the initiation of therapy. Second, it is likely we identified virtually all dispensings of simvastatin, as well as contraindicated and use-with-caution medicines, from community pharmacies during the study period as pharmacists are not reimbursed for such dispensings unless they submit a claim. However, medicines dispensed to patients in hospital are not recorded in the Pharmaceutical Collection, so we cannot comment on the prevalence of co-prescribing in the hospital setting. Third, because the study was based on dispensing, rather than prescription, records, it is clear that cohort members recieved supplies of simvastatin and other medicines. However, we do not know whether they took those medicines as directed on the prescription; nor do we know whether patients who were prescribed a short course of a contraindicated or use-with-caution medicine were instructed to temporarily withhold simvastatin or reduce their daily dose. Hence it is possible that we might have overestimated the co-prescription of short-term medicines such as erythromycin, and therefore the overall proportion of cohort members co-prescribed any contraindicated medicine. By contrast, all of the use-with caution medicines which were dispensed to simvastatin users are drugs which are used long-term, so it seems less likely that patients would have been advised to stop or reduce their dose of simvastatin (while at the same time continuing to collect their usual simvastatin supplies from the pharmacy)—therefore our measures of co-prescription of use-with-caution medicines are less likely to be overestimates. For the same reason, we are unlikely to have substantially overestimated the proportions prescribed use-with-caution medicines in combination with daily doses of simvastatin exceeding the recommended levels.

Fourth, we focused on contraindicated and use-with-caution medicines, which were listed in prescribing information sources commonly used by prescribers during the study period (rather than the detailed simvastatin datasheets), so it is possible we might have underestimated the overall co-prescribing of both contraindicated and use-with-caution drugs.

Finally, our study cohort comprised new users of simvastatin who were identified for an earlier study,[24] so we were unable to examine co-prescribing of CYP3A4 inhibitors among users of atorvastatin. However, CYP3A4 inhibitors affect the metabolism of simvastatin more than atorvastatin, so our focus on simvastatin was justifiable. Moreover, because simvastatin was recommended as the first-line statin for the primary and secondary prevention of cardiovascular events during the study period[3,4] and the current guidelines still recommend simvastatin 40mg (or atorvastatin 20mg) for patients with a five-year combined cardiovascular risk of 10–20%,[5] simvastatin is widely used in New Zealand (in 2016, for example, it was the 14th most commonly dispensed medicine, with 650,000 dispensed prescriptions[7]).

Comparison with previous studies

This is the first study, internationally, to have examined the co-prescribing of contraindicated and use-with-caution medicines

in a national cohort of new users of simvastatin, so it is not possible to make direct comparisons with other investigations. In contrast to our study, previous investigations have been based on sub-groups of patients,[10,11,13,15,16] a mix of new and prevalent statin users,[10–16] and some have not differentiated between contraindicated and use-with-caution medicines.[11] However, despite these differences in design, our results are broadly consistent with reports of concomitant use of CYP3A4 inhibitors and CYP3A4-metablised statins in the UK,[13] US,[10,11] Australia,[15] Norway,[12] Sweden[14] and Korea.[16]

Conclusions

Despite the existence of prescribing guidelines and patient management software which alerts prescribers to potential drug interactions, the prescription of contraindicated and use-with-caution drugs to patients taking simvastatin is not uncommon in New Zealand. Further work is required to explore and address the reasons for such co-prescribing, and for the apparent differences in co-prescribing by demographic characteristics. Future studies could also examine the level of co-prescribing of contraindicated and use-with-caution medicines in users of atorvastatin.

Competing interests:
Nil.

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REFERENCES:

1. Taylor F, Huffman MD, Macedo FA, et al. Statins for the primary prevention of cardiovascular disease. Cochrane Database Syst Rev. 2013; 1:CD004816.
2. New Zealand Guidelines Group. The assessment and management of cardiovascular risk. Wellington: New Zealand Guidelines Group, 2003.
3. New Zealand Guidelines Group. New Zealand Cardiovascular Guidelines Handbook: A summary resource for primary care practitioners. 2nd ed. Wellington: New Zealand Guidelines Group, 2009.
4. New Zealand Guidelines Group. New Zealand Primary Care Handbook 2012. 3rd edition. Wellington: New Zealand Guidelines Group, 2012.
5. Ministry of Health. Cardiovascular Disease Risk Assessment. Updated 2013. New Zealand Primary Care Handbook. Wellington: Ministry of Health 2013.
6. Best Practice Advocacy Centre New Zealand. A review of statin use and monitoring. Dunedin: Best

Practice Advocacy Centre New Zealand, 2014.

7. PHARMAC. Year in Review. Wellington: PHARMAC, 2016.
8. New Zealand Formulary. http://nzformulary.org/. Accessed 27 September 2016.
9. Medsafe. Statins and CYP interactions. Prescriber Update. 2014; 35:12–3.
10. Stang P, Morris L, Kempf J, et al. The coprescription of contraindicated drugs with statins: continuing potential for increased risk of adverse events. Am J Ther. 2007; 14:30–40.
11. Ming EE, Davidson MH, Gandhi SK, et al. Concomitant use of statins and CYP3A4 inhibitors in administrative claims and electronic medical records databases. J Clin Lipidol. 2008; 2:453–63.
12. Devold HM, Molden E, Skurtveit S, et al. Co-medication of statins and CYP3A4 inhibitors before and after introduction of new reimbursement policy. Br J Clin Pharmacol. 2009; 67:234–41.
13. Bakhai A, Rigney U, Hollis S, et al. Co-administration of statins with cytochrome P450 3A4 inhibitors in a UK primary care population. Pharmacoepidemiol Drug Saf. 2012; 21:485–93.
14. Settergren J, Eiermann B, Mannheimer B. Adherence to drug label recommendations for avoiding drug interactions causing statin-induced myopathy: a nationwide register study. PLOS ONE. 2013; 8:e69545.
15. Kerr KP, Mate KE, Magin PJ, et al. The prevalence of co-prescription of clinically relevant CYP enzyme inhibitor and substrate drugs in community-dwelling elderly Australians. J Clin Pharm Ther. 2014; 39:383–9.
16. Yang BR, Seong J-M, Choi N-K, et al. Co-medication of statins with contraindicated drugs. PLOS ONE. 2015; 10:1–11.
17. Ministry of Health. Pharmaceutical Collection. http://www.health.govt.nz/nz-health-statistics/national-collections-and-surveys/collections/pharmaceutical-collection. Accessed 24 May 2017.
18. Ministry of Health. National Health Index. http://www.health.govt.nz/our-work/health-identity/national-health-index. Accessed 24 May 2017.
19. Ministry of Health. National Minimum Dataset (Hospital Events) data dictionary. http://www.health.govt.nz/publication/national-minimum-dataset-hospital-events-data-dictionary. Accessed 24 May 2017.
20. Ministry of Health. Mortality Collection. http://www.health.govt.nz/nz-health-statistics/national-collections-and-surveys/collections/mortality-collection. Accessed 24 May 2017.
21. Ministry of Health. Ethnicity data protocols for the health and disability sector. Wellington, 2004.
22. Salmond C, Crampton P, Atkinson J. NZDep2006 Index of Deprivation User's Manual. Wellington: University of Otago, 2007.
23. Parkin L, Paul C, Herbison P. Simvastatin dose and risk of rhabdomyolysis: Nested case-control study based on national health and drug dispensing data. Int J Cardiol. 2014; 174:83–9.
24. Parkin L, Sharples KJ, Barson DJ, et al. Simvastatin dose and acute kidney injury without concurrent serious muscle injury: a nationwide nested case-control study. PLOS ONE. 2017; 12:e0182066.
25. MIMS New Ethicals. http://www.mims.co.nz/MIMSNewEthicals.aspx. Accessed 24 May 2017.
26. Manitoba Centre for Health Policy. Concept: Charlson Comorbidity Index http://mchp-appserv.cpe.umanitoba.ca/viewConcept.php?conceptID=1098. Accessed 1 July 2015.
27. Clopper CJ, Pearson ES. The use of confidence or fiducial limits illustrated in the case of the binomial. Biometrika. 1934; 26:404–13.
28. Kaplan EL, Meier P. Nonparametric estimation from incomplete observations. J Am Stat Assoc. 1958; 53:457–81.
29. Cox DR. Regression models and life-tables (with discussion). J R Stat Soc, Series B. 1972; 34:187–220.
30. van Buuren S. Multiple imputation of discrete and continuous data by fully conditional specification. Stat Methods Med Res. 2007; 16:219–42.

Off label or on trend: a review of the use of quetiapine in New Zealand

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This paper will review the use of quetiapine in New Zealand. Quetiapine, a dibenzothiazepine derivative, is a second-generation antipsychotic, licensed in the US by the FDA for the treatment of schizophrenia and bipolar disorder and as adjunctive treatment for major depressive disorder.[1] In New Zealand, quetiapine is approved for the treatment of schizophrenia, acute mania associated with bipolar I disorder and maintenance treatment of bipolar I disorder.[2] However, in New Zealand and in a number of other countries,[3] there is growing evidence that quetiapine is largely prescribed 'off-label', ie, not for the licensed indication.

At low doses (25mg), quetiapine is a histamine-1 receptor and alpha-1 adrenergic antagonist. At doses between 50–200mg, it increasingly antagonises serotonin receptors, and at higher doses (above 300mg) it antagonises dopamine-2 receptors.[4,5] Low-dose 'off label' use exploits the histamine-1 receptor blockade causing sedation and the antagonism of the alpha-1 adrenergic receptors for its anxiolytic effect. The higher doses acting on the serotonergic and dopaminergic receptors provide the antidepressant and antipsychotic effects respectively.

In an article in the Australian Prescriber, Jonathan Brett reported that in Australia between 2000 and 2011, quetiapine's use had increased from 0.01 to 2.3 defined daily doses/1,000 population/day and noted that these changes cannot be accounted for by patients being switched from older to newer antipsychotic drugs or changes in the diagnosis of long-term mental illness.[6,7]

McKean and Monasterio reported that off-label use of quetiapine accounted for about 17% of the budget for atypical antipsychotics in New Zealand,[8] while Huthwaite and colleagues reported that in an audit of the hypnosedative prescribing patterns of New Zealand community psychiatrists, quetiapine was the most commonly hypnosedative, with 38.4% of the patients being prescribed it for this purpose.[9] Ilyas and Moncrieff reported that in 2010, quetiapine accounted for 23% of antipsychotic prescription items in England with 54% of these prescriptions, for the 25mg tablets.[10] The Drug Utilisation Sub-Committee of the Pharmaceutical Benefits Advisory Committee in Australia reported that off-label use was most evident for the 25mg strength of quetiapine.[11] The prescribing of quetiapine for the treatment of insomnia has become common practice despite the paucity of evidence to support its efficacy as a hypnotic.[12]

A concerning trend are the reports of quetiapine having street value, being used to recover from or enhance the effects of drugs of misuse.[13] In Australia and the US, quetiapine misuse is now increasingly documented in case reports, case series and emergency department presentations with increasing reports of overdosing, poison information center data and coronial data and quetiapine overdoses have been reported as causing hypotension, respiratory depression, sinus tachycardia, delirium, coma or death and that these complications were more likely to occur with quetiapine than with overdoses by all the other antipsychotic drugs put together.[14,15]

To aid the understanding of quetiapine prescribing in general practice, a retrospective audit of the prescribing of quetiapine in 57 practices in the Compass Health Primary Health Organisation (PHO) was undertaken. This was in response to a concern by the Clinical Quality Board of Compass Health that quetiapine was being prescribed off label.

Method

The audit was conducted from January 2015 to January 2016 in 57 general practices in the Compass Health Network. The network is located in the lower North Island and at the time included 59 practices. The auditors were PHO employed pharmacists. Data regarding the quetiapine prescriptions were extracted from the clinical records in the shared Practice Management Systems (PMS) and therefore represented prescribing data not dispensing data. Using the list of indications in quetiapine's data sheet, the auditors made an a priori decision about what indications would be considered licensed and which would be considered 'off-label'. The clinical notes and relevant correspondence (eg; psychiatrist letters, discharge summaries) were scrutinised to determine the indication for its use. Approval for this audit of Medical Practice Activity was gained from the Royal New Zealand College of General Practitioners. Data were entered in a Microsoft Excel (2010) spreadsheet and statistical analyses were conducted using Microsoft Excel.

Results

Two hundred and seventy prescribing general practitioners in 57 practices were audited. A total of 2,161 patients were prescribed quetiapine in the one year of the audit. Only 460 (21.3%) were prescribed quetiapine for a licensed indication, with 1,556 (72%) receiving quetiapine for an 'off-label' indication. For the remaining 6.7%, the prescribing indication was unclear. In over half the sample (56.2%), the quetiapine prescribing was initiated in primary care, 39% in secondary care, while for 4.8% of the sample it was unclear who had initiated the prescribing. In the primary care initiated group, full consent for the 'off-label' prescribing was documented in 11% of the patient's records. (The "Prescribing Unapproved Medicines" section of the New Zealand Medical Council statement "Good Prescribing Practice" was used as a guide to determine consent). Table 1 shows the gender and age demographics of those persons prescribed quetiapine.

Table 2 shows the duration of use and Table 3 lists the non-approved indications for which quetiapine was prescribed.

Table 1: Demographics.

Gender	
Female	58%
Male	42%
Age bands in years	
14–19	6.3%
20–29	19.5%
30–39	16.1%
40–49	23.8%
50–59	17.2%
60–69	8.2%
70–79	4.3%
80–89	4.0%
90–96	0.6%

Table 2: Duration of the prescribing of quetiapine (off label).

Duration	**Total number**	**Percentage %**
Short term (<1 month)	268	17.2%
Intermittent use (from time to time)	435	28%
Long term (>1 month continuous prescribing)	846	54.4%
Unknown	8	0.4%

Figure 1 shows the percentage for the groups of non-approved conditions for which quetiapine was prescribed.

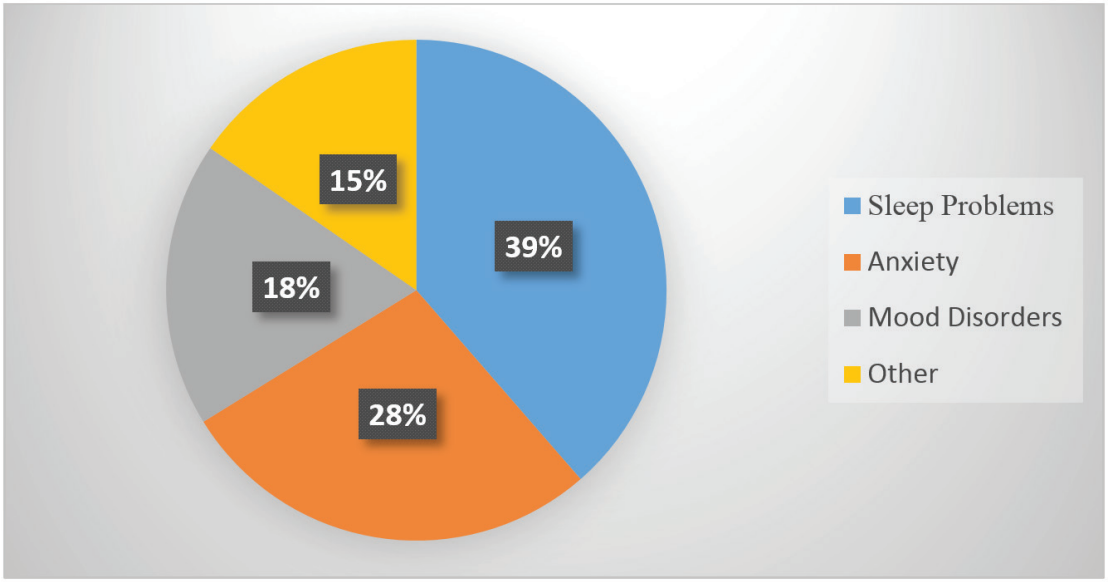
Full metabolic monitoring was recorded as being done in only 2.3%, while partial monitoring occurred in 68% and no monitoring in 29.7%. Full monitoring comprised all the tests listed in the Capital and Coast District Health Board's antipsychotic metabolic monitoring guidelines. Partial monitoring included those with three or more of the recommended tests.

The dose range for 'off-label' prescribing was between 6.25mg–800mg, with 91% (1,416) being prescribed less than 100mg daily (see Figure 2). Only 2.3% (36) of those prescribed quetiapine for an 'off–label' indication were prescribed more than

Table 3: 'Off-label' prescribing of quetiapine: non-approved conditions for which quetiapine was prescribed.

Sleep problems	Anxiety/generalised anxiety disorder
Anxiety with depression	Post-traumatic stress disorder
Anger	Borderline personality disorder
Agitation	Cannabis dependence and withdrawal
Tinnitus	Obsessive compulsive disorder
Mood	Borderline personality disorder
Epilepsy	Stress
Dysthymia	Mental retardation
When starting an SSRI to limit emergence of anxiety symptoms	Cyclothymia
Alcohol dependence and withdrawal	Aggression
Panic	Pain/headache
Behaviour	Grief
Autistic spectrum disorders	Behavioural tic
Nightmares	Suicide risk
Impaired behavior	Post suicide attempt
Adjustment disorder	Drug overdose

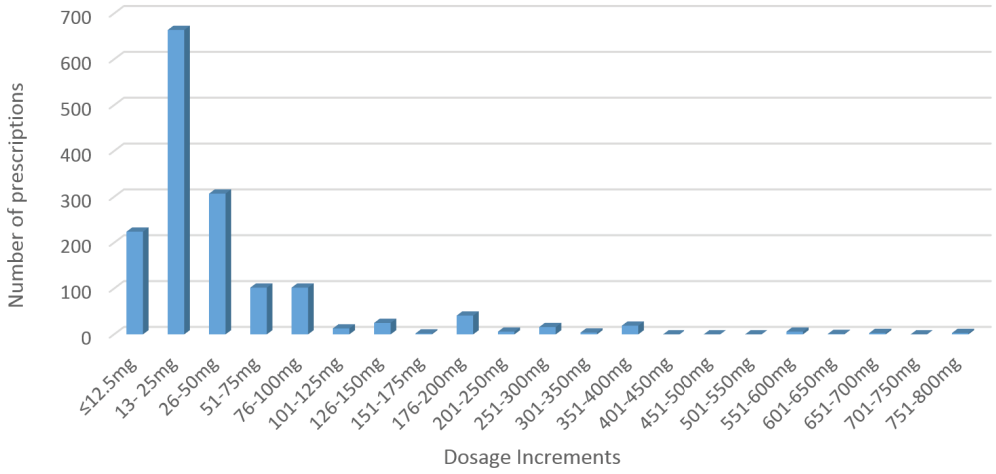
Figure 1: Non-approved conditions for which quetiapine was prescribed.



300mg daily. A relatively wide dose range was noted in many cases, for example: 25 to 100mg at night (or daily) as required, with the largest of these being 6.25 to 300mg daily as required.

It was noted during this study that several patients asked for quetiapine, claiming that a "neighbour, relative or friend" had given them some.

Figure 2: Dose range for 'off-label' prescribing.



Discussion

This audit confirms previous New Zealand studies that quetiapine is largely being used 'off-label' and that there is a growing trend for it to be prescribed to exploit the sedating effects and mild anxiolytic effects in the lower dose range. The results of this audit indicate that there is little monitoring of the metabolic side effects. At the recommended doses for the licensed indications (ie, the treatment of mania and schizophrenia), quetiapine is associated with metabolic adverse events (ie, diabetes, hyperlipidemia and obesity) and other serious adverse events, including QT interval prolongation, orthostatic hypotension, hyperprolactinemia, extrapyramidal symptoms, tardive dyskinesia and neuroleptic malignant syndrome. There is some evidence (one review and two data papers) that these adverse effects can occur at low doses;[16,17] more studies are needed. Prescribers, using low doses may erroneously presume that because the drug is not being prescribed as an atypical antipsychotic, and in the lower dose range, that metabolic monitoring is not desirable. When prescribing in the real world, 'off-label' prescribing may be warranted and even advantageous, limiting the inappropriate use of benzodiazepines and zopiclone and their associated problems of dependence and abuse. Prescribers making decisions to prescribe quetiapine in this manner may resent the implication that they are doing something wrong.[18]

However, prescribers should be aware of the currently available risk-benefit profile for the relevant non-approved indication in each patient, noting the rationale behind their decision to use this drug at this dose. Even when 'off-label low doses' are being prescribed, the prescriber should be aware that the dose equivalent for the elderly patient (especially the female elderly patient) is about half that used for the younger patient[19] and that the elderly are at increased risk of the adverse effects described above.[8]

The 'off-label' use should be discussed with the patient. The prescriber should ensure that the patient is making an informed decision about using the quetiapine in this manner and this should all be clearly documented in the clinical record.[20] This places all the onus of the prescriber, while the pharmaceutical companies passively enjoy the profits of 'off-label' on trend prescribing. It is interesting to note that in April 2010, Astra-Zeneca signed a civil settlement to pay $US 520 million to "resolve allegations" that it had illegally marketed Seroquel (original brand of quetiapine) for uses not approved as safe and effective by the FDA.[21] Then in March 2011, it agreed to pay a further $US 68.5 million in a multi-state agreement over off-license marketing of the same drug. Other substantial settlements within the US over the marketing of unapproved uses have also been reached.

Conclusion

Most quetiapine prescriptions reviewed in an audit of a large PHO were for 'off -label' use. While it is commonly accepted that prescribing off-label is at the prescriber's discretion, and not necessarily a "bad thing to do", the authors suggest that when prescribing quetiapine for a non-approved condition, or to a specific clinical population (the elderly and the young), the thoughtful prescriber will carefully document not only the clinical rationale for this prescribing but also that they have discussed this with their patient (and in some instances their families or caregivers).[22] It is unlikely that the pharmaceutical suppliers of quetiapine will apply for new approved indications for its use. The respective Colleges and other representative bodies (like BPAC or Medsafe) may wish to develop guidelines for the non-approved prescribing of quetiapine to allow prescribers to act in accordance with accepted practice and current best practice guidelines.

Competing interests:
Dr McBain is a practicing general practitioner—there are patients included in the audit who are enrolled at Dr McBain's practice. Dr McBain is currently a contracted employee at Compass Health PHO.

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REFERENCES:

1. Drugs@FDA. (2017). http://www.accessdata.fda.gov/scripts/cder/drugsatfda/index.cfm. Accessed 20 April, 2017.
2. AstraZeneca. (2010). Seroquel film coated tablet. Auckland, New Zealand: Medsafe, Ministry of Health.
3. Kamphuis J, Taxis K, Schuiling-Veninga CC, Bruggeman R, Lancel M. (2015). Off-label prescriptions of low-dose quetiapine and mirtazapine for insomnia in The Netherlands. Journal of clinical psychopharmacology, 35(4):468–470.
4. Cheer SM, Wagstaff AJ. (2004). Quetiapine. CNS drugs, 18(3):173–199.
5. Schwartz TL, Stahl SM. (2011). Treatment strategies for dosing the second generation antipsychotics. CNS neuroscience & therapeutics, 17(2):110–117.
6. Brett J. (2015). Concerns about quetiapine. Australian Prescriber, 38(3):95–97.
7. Stephenson CP, Karanges E, McGregor IS. (2012). Trends in the utilisation of psychotropic medications in Australia from 2000 to 2011. Australian & New Zealand Journal of Psychiatry, 47(1):74–87. doi:10.1177/0004867412466595
8. McKean A, Monasterio E. (2015). Indications of atypical antipsychotics in the elderly. Expert review of clinical pharmacology, 8(1):5–7.
9. Huthwaite MA, Andersson V, Stanley J, Romans SE. (2013). Hypnosedative prescribing in outpatient psychiatry. International Clinical Psychopharmacology, 28(4):157–163. doi:10.1097/YIC.0b013e32836248f1

10. Ilyas S, Moncrieff J. (2012). Trends in prescriptions and costs of drugs for mental disorders in England, 1998–2010. The British Journal of Psychiatry, 200(5):393–398. doi:10.1192/bjp.bp.111.104257
11. Sub-Committee, D. U. (2013). DUSC review on the utilisation of antipsychotics–August 2013. Public Summary Document. Canberra: Australian Government Department of Health.
12. Thompson W, Quay TAW, Rojas-Fernandez C, Farrell B, Bjerre LM. (2016). Atypical antipsychotics for insomnia: a systematic review. Sleep Med, 22:13–17. doi:10.1016/j.sleep.2016.04.003
13. Tcheremissine OV. (2008). Is quetiapine a drug of abuse? Reexamining the issue of addiction. Expert Opinion on Drug Safety, 7(6):739–748. doi:10.1517/14740330802496883
14. Balit CR, Isbister GK, Hackett LP, Whyte IM. (2003). Quetiapine poisoning: A case series. Annals of Emergency Medicine, 42(6):751–758. doi:http://dx.doi.org/10.1016/S0196-0644(03)00600-0
15. Ngo A, Ciranni M, Olson KR. (2008). Acute Quetiapine Overdose in Adults: A 5-Year Retrospective Case Series. Annals of Emergency Medicine, 52(5):541–547. doi:http://dx.doi.org/10.1016/j.annemergmed.2008.03.016
16. Coe HV, Hong IS. (2012). Safety of low doses of quetiapine when used for insomnia. Annals of Pharmacotherapy, 46(5):718–722.
17. Williams SG, Alinejad NA, Williams JA, Cruess DF. (2010). Statistically Significant Increase in Weight Caused by Low-Dose Quetiapine. Pharmacotherapy: The Journal of Human Pharmacology and Drug Therapy, 30(10):1011–1015.
18. MacDonald J, Garvie C, Gordon S, Huthwaite M, Mathieson F, Wood A-J, Romans S. (2015). 'Is it the crime of the century?': factors for psychiatrists and service users that influence the long-term prescription of hypnosedatives. International Clinical Psychopharmacology, 30(4):193–201. doi:10.1097/yic.0000000000000073
19. Castberg I, Westin AA, Skogvoll E, Spigset O. (2017). Effects of age and gender on the serum levels of clozapine, olanzapine, risperidone, and quetiapine. Acta Psychiatr Scand, 136(5):455–464. doi:10.1111/acps.12794
20. Ghinea N, Lipworth W, Kerridge I, Day R. (2012). No evidence or no alternative? Taking responsibility for off-label prescribing. Internal medicine journal, 42(3):247–251.
21. United States, D. o. J. (2010). Retrieved from http://www.justice.gov/opa/pr/pharmaceutical-giant-astrazeneca-pay-520-million-label-drug-marketing
22. NZMC. (2016). Good-prescribing-practice.

Outcomes following therapeutic lymphadenectomy for Stage III malignant melanoma in a single unit

Rahul Jayakar, Emily Yassaie, Christopher Adams

ABSTRACT

BACKGROUND: Malignant melanoma is the fourth most common cancer in New Zealand. Surgery is the only treatment modality that can achieve high cure rates for regional disease, but is associated with high complication rates. Our study documents the morbidity associated with regional lymphadenectomy; audits nodal harvest numbers and considers nodal harvest targets.

METHODS: We retrospectively reviewed regional lymphadenectomies for Stage III melanoma at a single tertiary centre from 2004 to 2014. Data was collected on patient demographics, site of operation, number of lymph nodes recovered, all complications within six months of surgery, loco-regional recurrence, distal progression and five-year survival. We also used key performance indicators (KPI) to assess the quality of dissection.

RESULTS: A total of 219 lymphadenectomies were carried out. Forty-three percent of all patients experienced at least one complication. This was markedly higher for those undergoing a groin dissection. Recurrence, progression and survival rates did not vary between nodal basins. There was a mean of 31.6, 17.6 and 10.9 nodes recovered from neck, axillary and groin dissection groups respectively. Our KPIs were achieved in 80%, 86.6% and 90% of cases and resulted in a significant improvement in recurrence and progression rates.

CONCLUSION: Lymphadenectomy has a high risk of post-operative complications, especially for groin dissections. Quality of lymphadenectomy can be assessed by monitoring nodal harvest numbers, and achieving nodal harvest targets provides significant prognostic information. We support the development of national tumour standards, including key performance indicators, for management of Stage III melanoma.

In New Zealand, malignant melanoma is the fourth most common cancer and the sixth most common cause of cancer-related mortality.[1] Stage I and II melanomas have high cure rates, however Stage III melanoma is associated with significantly higher mortality and morbidity.[2]

Sentinel lymph node biopsy (SNLB) has become a key part in staging cutaneous malignant melanoma and its status is the most important prognostic factor in determining the risk of mortality and recurrence.[3] For those with known Stage III disease, regional lymphadenectomy (RL) is the only proven treatment that prolongs disease-free survival.[4] RL is associated with a high risk of surgical complications with estimates ranging from 30 to 80%.[5] There is a paucity of information on quality of lymph node dissections, survival outcomes and morbidity rates in New Zealand following RL.

In 2013, the New Zealand Ministry of Health proposed the development of national tumour standards for management of melanoma, and draft standards of service provision have been published.[6] These standards have not formally recommended specific lymph node harvest targets.

In 2009, Spillane et al[7] from the Sydney Melanoma Unit (SMU) published their recommendations for quality of lymphadenectomies. They recommend that greater than 90% of dissections have a minimum recovery of 10 axillary nodes, seven groin nodes and 20 neck nodes (if four or more levels dissected) (Table 1).

Table 1: SMU recommended guidelines. Nodal harvest lymph node count greater than 90% of the time.

Site	Nodal count (NZ standards[6])	Nodal count (Spillane et al[7])
Axilla	>18	≥10
Inguinal	>8	≥7*
Ilio-inguinal	>15	
Neck	>20 (>4 levels dissected)	≥20 (>4 levels dissected)
	>10 (if 3 levels dissected)	

*Data for inguinal and ilioinguinal dissections was combined.

The Wellington regional Plastic, Maxillofacial and Burns unit provides for the surgical management of Stage III melanoma through the Wellington multidisciplinary melanoma clinic. A multidisciplinary approach is implemented in the assessment and treatment of those with advanced melanoma in the Wellington region.

Objectives

The aims of the study were: to document the morbidity associated with regional lymphadenectomy (RL) at a New Zealand specialist melanoma unit; to document the quality of dissection, and its influence on disease outcomes in terms of five-year disease specific mortality; and to audit nodal harvest numbers.

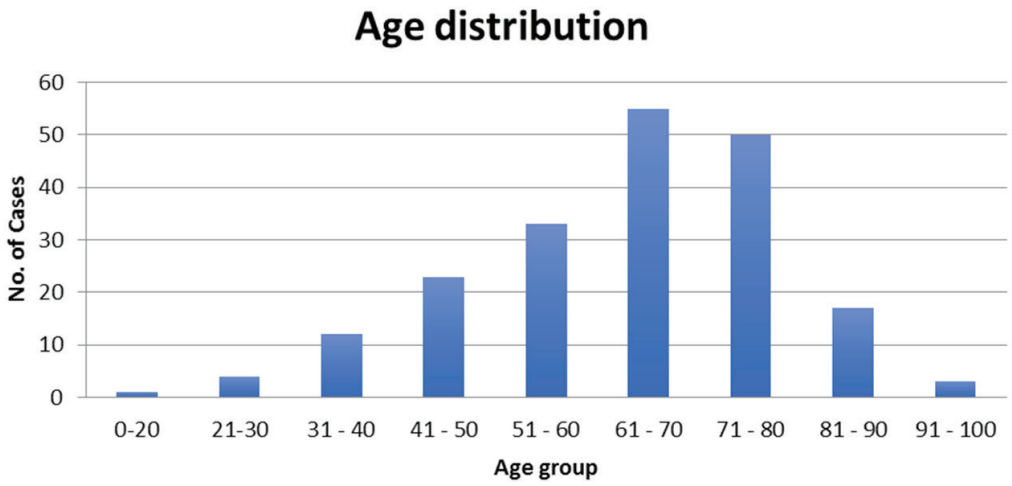
Methods

All patients who underwent regional lymphadenectomy (RL) for metastatic malignant melanoma through the Wellington regional plastic surgery service at Hutt Hospital, Lower Hutt, from July 2004 to June 2014 were identified from the hospital database. Data collected from the hospital electronic and written records included: patient demographics; site of operation; number of lymph nodes recovered; all complications that occurred within six months of the initial surgery and their management including re-admission and return to theatre. This included chronic complications present at six months post-surgery. We also recorded the Breslow thickness of primary lesions, local recurrence rates, distal progression, sentinel lymph node status, five-year survival rate and whether adjuvant radiotherapy was offered. These were entered into a Microsoft Excel® spread sheet (Microsoft Corporation, Redmond, WA, USA). This study meets the New Zealand Health and Disability ethics committee approval criteria for audit.

Unit policy

The Wellington multidisciplinary melanoma clinic reviews all referrals with Stage III melanoma to plan appropriate treatment. The team is made up of plastic and reconstructive surgeons, general surgeons, medical oncologists, radiation oncologists, radiologists, pathologists and clinical nurse specialists. Sentinel node biopsy (SNB) is performed in those patients with Stage 1b-2a melanoma, and a completion lymphadenectomy is offered to those with positive sentinel nodes.[8] Patients with clinical or radiological disease are offered regional lymphadenectomy (RL) wherever possible, even with advanced disease. We perform inguinal node dissections (groin dissection) only in those with inguinal lymphadenopathy and do not routinely perform ilio-inguinal node dissection. Patients with pelvic node involvement are referred for pelvic node dissection or to radiation oncology for further treatment. Patients undergoing RL are routinely discharged with wound drains in situ until the output decreases. There is an exception for lymph node clearance in the neck where patients will often remain in hospital until the drains are removed. Adjuvant radiotherapy is offered to all patients who reach criteria as specified in the TROG trial.[9] These are: palpable (macroscopic) metastatic nodal involvement of one or more parotid node, two or more neck or axillary nodes, or three or more groin nodes; extranodal spread; and/or a maximum metastatic node diameter of ≥3cm in the neck or ≥4cm in the axilla or groin.

Figure 1: Number and age distribution of 198 patients undergoing lymphadenectomy for Stage III melanoma.



Results

Patients

A total of 198 patients underwent regional lymphadenectomy (RL) for Stage III melanoma during the study period. The incidence of Stage III disease increased with age peaking in the seventh decade of life (Figure 1). The mean age at time of surgery was 64 years (median = 66; range = 19–93). The Breslow thickness of the primary lesion was documented in 158 cases (80%) with a mean thickness of 3.93mm (median = 3.0mm; range = Melanoma in situ – 20.0mm). Twenty-two (11%) patients had Stage III disease diagnosed without identification of a primary lesion, and 18 (9%) patients did not have the Breslow thickness of the primary lesion documented.

Procedures

A total of 219 regional lymphadenectomies (RL) were performed in 198 patients. Sixteen patients underwent two procedures, one patient underwent three procedures and one patient underwent four procedures (This was due to disease progression to multiple nodal basins). A total of 85 groin dissections were performed, making this the most common procedure. There were 68 axillary dissections and 66 neck dissections.

Outcomes

Ninety-four (43%) of the 219 procedures were associated with an acute post-operative complication. This was defined as any adverse event occurring within six weeks of surgery. Seroma requiring serial aspiration was the most common acute complication recorded (16% of total) followed by wound infection (10%) (Table 2). Forty-two (19%) patients required an acute admission for management of their complication and 37 (17%) patients required an acute return to an operating theatre. Fifty-two (24%) patients were noted to have a chronic complication at six months following their RL. This included 45 (20%) cases of significant lymphoedema making it the most common chronic complication. Significant lymphedema was defined as lymphoedema contributing to patient morbidity as documented at six months and requiring ongoing input from outpatient lymphoedema nurse specialists.

Table 2: Distribution of 94 acute post-operative complications following 219 regional lymphadenectomies.

Acute complication	No. of cases (%)
Seroma requiring aspiration*	36 (16)
Wound infection	23 (10)
Post op haematoma	15 (7)
Infected seroma	10 (4)
Wound dehiscence/breakdown	6 (2)
Other	4 (1)
Total	94 (43)

*Three patients had both haematoma and seroma. These have been included in the seroma group as this was the primary complication documented.

Loco-regional recurrence was identified in 70 patients (35%) and distant progression (Stage IV disease) was documented in 90 patients (45%) in the follow-up period. For those patients with five-year follow up data, we calculated the five-year disease progression rate at 52.75%. The five-year disease specific mortality rate for patients undergoing regional lymphadenectomy (RL) was 50.5% (47/93) and all-cause mortality was 56.9% (53/93). Thirteen of these patients had Stage IIIC disease on review of the histology and the five-year disease specific mortality for this group was 69.2% (CI 50–90%).

Neck dissections

We performed 66 neck dissections on 61 patients with a mean age of 64. All neck dissections were pooled into a single group, as sub-stratification of these provided no significant data. There were 39 men (64%) and 22 women (36%). Three patients had a sentinel lymph node biopsy (SLNB) prior to their neck RL. There were three concurrent and two staged bilateral neck dissections.

Ten (15%) acute complications were recorded with seven (10%) of these requiring an acute return to theatre. Two patients required readmission following discharge for management of a complication and one patient developed a chronic complication. The most common complication recorded was post-operative haematoma (n=7; 10%) (Table 3).

Table 3: Eleven complications following neck dissections.

Complication	No. of cases (%)
Haematoma	7 (64)
Chyle leak	1 (9%)
Cardiac arrest	1 (9%)
Wound infection	1 (9%)
Chronic discharging sinus	1 (9%)

Loco-regional recurrence was documented in 20 patients (33%) and distant progression in 29 patients (47%). Five-year disease specific mortality within this group was 50% (17/34).

A total of 2,058 lymph nodes were recovered in 65 procedures with a mean of 31.6 nodes per procedure (median = 30; range 4–64). One patient had diffuse subcutaneous metastases. We used recovery of a minimum of 20 nodes as our key performance indicator (KPI) as recommended by Spillane et al.[7] Fifty-two out of 65 procedures recovered 20 or more nodes. Thus, our KPI was achieved in 80% of neck dissections.

Axillary dissections

Sixty-eight axillary dissections were performed on 60 patients with a mean age of 61. There were 36 men (60%) and 24 women (40%) in this group. There were four concurrent and three staged bilateral dissections and one revision ipsilateral dissection.

There were 26 (38%) acute complications reported within six weeks of surgery with four (6%) patients requiring an acute return to theatre and six (9%) requiring readmission. Eleven patients (16%) developed a chronic complication. The most common acute complication reported was a seroma requiring aspiration while the most common chronic complication was lymphoedema (Table 4).

Loco-regional recurrence was documented in 18 patients (30%) and 22 (36%) developed distal progression. Five-year disease specific mortality was 50% (12/24).

A total of 1,177 lymph nodes were recovered following 67 procedures with a mean of 17.6 nodes per procedure (median = 18; range = 3–44). One patient had multiple matted nodes and a node count could not be made. We used a minimum recovery of 10 nodes as our KPI in this group.[7] Fifty-eight procedures recovered 10 or more nodes. Thus, our KPI was achieved in 86.6% of axillary dissections.

Groin dissections

There were 85 groin dissections performed in 83 patients with a mean age of 64. There were 43 (52%) men and 40 (48%) women in this group. One patient underwent a revision ipsilateral dissection while another underwent staged bilateral dissections.

There were 58 (68%) acute complications within six weeks of surgery and 40 (47%) chronic complications reported at the six-month mark. Thirty-four (40%) patients were readmitted for management of an acute complication, and 25 (29%) patients required an acute return to an operating

Table 4: Twenty-six acute and 11 chronic complications following axillary dissection.

Acute complication	No. of cases (%)	Chronic complication	No. of cases (%)
Seroma requiring aspiration	18 (68)	Lymphoedema	10 (91)
Wound infection	2 (8)	Chronic Seroma	1 (9)
Haematoma	2 (8)		
Infected seroma	1 (4)		
Wound dehischence	1 (4)		
Axillary vein thrombosis	1 (4)		
Seroma and haematoma	1 (4)		

theatre. Post-operative wound infection was the most common acute complication reported while lymphoedema was the most common chronic complication (Table 5).

Loco-regional recurrence was documented in 34 patients (41%) and distal progression was documented in 42 patients (51%). Five-year disease specific mortality was 51.4% (18/35).

A total of 883 nodes were recovered from 81 procedures at a mean of 10.9 nodes per procedure (median = 10; range 0–27). Four procedures resulted in the recovery of multiple matted nodes and a node count could not be made. The KPI for the groin dissection group was minimum recovery of seven lymph nodes.[7] Seventy-three procedures recovered seven or more lymph nodes. Thus, our KPI was achieved in 90% of groin dissections.

Radiotherapy

Sixty-one (28%) patients received adjuvant radiotherapy following lymphadenectomy and discussion at the regional multidisciplinary clinic. Radiotherapy was provided following 20 neck dissections, 20 axillary dissections and 21 groin dissections and was only offered to patients who had a predicted high risk of nodal recurrence, as per the TROG criteria.[9] Regional recurrence rates following adjuvant treatment were documented at 45% in neck dissections, 33% in axillary dissections and 38% in groin dissections. Forty percent of those in the axillary dissection group and 58% in the groin dissections group developed significant lymphoedema following radiotherapy.

Statistical analysis

Univariate analysis was performed using Chi-squared and Fisher's exact test. The type of dissection had a significant effect on the number of complications. Sixty-eight percent of groin dissections developed acute complications compared to 38% of axillary dissections and 15% of neck dissections ($\chi 2=41.834$; $p<0.001$); and only 1.5% of neck dissections developed chronic complications compared to 16% of axillary dissections and 45% of groin dissections ($\chi 2=42.566$;

Table 5: Fifty-eight acute and 40 chronic complications post groin dissection.

Acute complication	No. of cases (%)	Chronic complication	No. of cases (%)
Wound infection	21 (36%)	Lymphoedema	35 (87%)
Seroma requiring aspiration	15 (26%)	Chronic seroma	5 (13%)
Haematoma	6 (10%)		
Infected seroma	8 (14%)		
Wound breakdown/dehiscence	4 (7%)		
Seroma and haematoma*	3 (5%)		
High drain output	1 (2%)		

* Three patients with a seroma also developed a haematoma. These have been included as a separate group.

p<0.001). The nodal basin dissected did not have a significant impact on regional recurrence ($\chi2$=1.747; p=0.417), distant progression ($\chi2$=3.163, p=0.206) and disease specific mortality ($\chi2$=0.176; p=0.916).

Multivariate analysis revealed that achieving our nodal harvest targets correlated with significantly lower regional recurrence (30.6% vs 55.6%; p=0.007), and disease progression (41.0% vs 65.6%; p=0.018). Five-year disease specific mortality was also lower (47% vs 55%) but this trend did not reach statistical significance (p=0.678).

Discussion

In 2012, New Zealand had a total of 2,324 registered cases of malignant melanoma with 354 deaths.[1] It was the second most commonly registered cancer among men and women aged 25–64.[1] Regional lymphadenectomy is a common procedure performed for the treatment of advanced disease but there is little published data available on morbidity and mortality following this procedure in New Zealand, and only a few detailed studies have been published internationally.[4,10–14]

A review of this literature reveals that complication rates vary between 20% and 51% following axillary dissections, while those following groin dissections range from 30–90%.[4,10–16] Two large multi-centre trials, The Sunbelt melanoma trial[15] and MSLT-1,[16] reported overall complication rates of 23% and 37% respectively. The Sunbelt melanoma trial further stated regional complications rates as 10% for neck dissections, 20% for axillary dissections and 51% for groin dissections.

Serpell et al[13] reported that in their series of 28 groin dissections, 44% developed seromas requiring serial aspiration. They concluded that given this high rate, post-operative seroma formation should be considered a known and acceptable outcome of groin dissection rather than a complication. Our series found that 26 of 85 (30%) groin dissections developed seromas with 11 (12%) of these developing secondary acute complications (haematoma = 3 or wound infection = 8). We performed a Sartorius switch procedure in 62 groin dissections (73%) and found a similar rate of seroma formation in both groups (32% vs 26%).

Twenty of 68 (29%) axillary dissections also developed seromas with two (3%) of these developing a secondary acute complication. There were no seromas identified in our neck dissection group, confirming this as a rare complication following neck dissection.[4,11]

Wound infection was a commonly reported complication in our study with a total of 17.8% of wounds developing an infection or breakdown. This was 1.5% for neck dissections, 5.8% for axillary dissections and 38.8% for groin dissections. This compares well with a large series published by Van Akkooi et al[17] who reported an overall infection rate of 18% (groin dissection = 29%; axillary dissection = 6%; neck dissection = 3%) and is within the range of 13–25% reported by other studies.[10,13,17–19]

There is limited reliable data on loco-regional and distant recurrence rates following regional lymphadenectomy (RL). Our figures documented a loco-regional recurrence rate of 35% (neck dissection = 30%; axillary dissection = 33%; groin dissection = 41%). The range of reported data is extremely wide with local recurrence rates reported at of 5–50% and nodal recurrence rates at 4–30%.[4,20] Our data does not show a statistical difference in recurrence between nodal basins. This differs from a series conducted by Guggenheim et al[4] who reported nodal recurrence rates as high as 33.3% in the neck, followed by 11.9% for groin dissections and 4.3% for axillary dissections. We also report an overall distant progression rate of 45%. This falls within the range of reported distant progression rates of 11–55%.[4,20–22] There were no significant differences in distant progression rates between neck, groin and axillary dissection groups.

Adjuvant radiotherapy is considered for those meeting the TROG criteria.[9] It reduces the risk of regional recurrence without affecting disease-free survival.[23] We found that patients undergoing adjuvant radiotherapy had regional recurrence rates of 45%, 33% and 38% following neck, axillary and groin dissection respectively. These rates are marginally higher than our overall recurrence rates, however these patients had a high disease burden, and therefore were considered to have a significantly higher risk of recurrence.

Previous publications by the American Joint Committee on Cancer (AJCC) have reported an overall 50% five-year mortality rate in Stage III patients[24] with this being further categorised as 22% for Stage IIIA, 41% for Stage IIIB and 60% for Stage IIIC disease.[25] These are overall trends in reported survival and there is limited published survival data from large volume specialist melanoma centres. We report an overall five-year disease specific mortality rate of 50.5% for all Stage III disease and a 69.2% disease specific mortality rate for Stage IIIC disease.

Chan et al[26] demonstrated that the number of lymph nodes removed is of significant prognostic importance and corresponds to survival. When analysed by quartiles, patients in the highest quartile had a five-year survival of 44% compared to 23% for those in the lowest quartile. Rossi et al.[27] also concluded that the number of excised lymph nodes was a significant and independent predictor of melanoma specific survival. They suggest that a minimum of 14 neck, 11 axillary and 10 groin nodes be retrieved for correct staging of patients.

The current clinical practice guidelines for melanoma management in Australia and New Zealand do not provide a nodal harvest target for regional lymphadenectomies.[8] We acknowledge that nodal harvest numbers have some dependence on the reporting pathologist, just as there is variation in harvest numbers between individual surgeons. These variations can be accounted for by analysing data across an entire service.

Spillane et al from the Sydney Melanoma Unit (SMU) have published quality assurance standards and acceptable ranges for lymph node harvest (Table 1).[7] Our study confirms that achievement of these specified lymph node harvest targets is correlated with a significant reduction in local recurrence and distant progression rates. There was also a reduction in five-year disease specific mortality that did not reach statistical significance.

We used the standards published by Spillane et al[7] as our KPIs. This resulted in our targets being achieved in 80% of neck dissections, 86.6% of axillary dissections and 90% of groin dissections. The high achievement rates coupled with a significant reduction in loco-regional recurrence and distant progression support the adoption of nodal harvest targets as set out by Spillane et al.[7]

We support the development of national tumour standards, including key performance indicators for the management of Stage III melanoma. To our knowledge, we are the first New Zealand centre since Shaw et al (1990)[28] to publish our findings on outcomes following lymphadenectomy for melanoma and the first to report on quality of lymph node dissections and nodal harvest targets for melanoma in New Zealand.

We recommend that regional lymphadenectomies for metastatic melanoma should aim to retrieve a minimum of 10 axillary nodes, seven groin nodes and 20 neck nodes. We would like to urge the New Zealand melanoma tumour standards working group to review our data and consider amending the proposed monitoring requirements (MR8E) to reflect our findings.[6]

We conclude that achieving these nodal harvest targets gives strong prognostic information for patients with Stage III melanoma and may predict survival benefit.

Competing interests:
Nil.

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REFERENCES:

1. Ministry of Health. 2015. Cancer: New registrations and deaths 2012. Wellington: Ministry of Health.
2. Bilimoria K, Balch C, Bentrem D, et al. Complete lymph node dissection for sentinel node-positive melanoma: assessment of practice patterns in the United States. Ann Surg Oncol 2008; 15(6):1566–76.
3. Balch C, Soong S, Gershenwald J, et al. Prognostic factors analysis of 17,600 melanoma patients: validation of the American Joint Committee on Cancer melanoma staging system. J Clin Oncol. 2001; 19:3622–3634.
4. Guggenheim M, Hug U, Jung F, et al. Morbidity and Recurrence After Completion Lymph Node Dissection Following Sentinel Lymph Node Biopsy in Cutaneous Malignant Melanoma. Ann Surg. 2008; 247(4):687–93.
5. Dzwierzynski W. Complete lymph node dissection for regional nodal metastases. Clin Plastic Surg. 2010; 37:113–125.
6. National Melanoma Tumour Standards Working Group. 2013. Standards of Service Provision for Melanoma Patients in New Zealand - Provisional. Wellington: Ministry of Health.
7. Spillane A, Cheung B, Stretch J, et al. Proposed Quality standards for regional lymph node dissections in patients with melanoma. Ann Surg. 2009; 249:473–480.
8. Australian Cancer Network Melanoma Guidelines Revision Working Party. Clinical Practice Guidelines for the Management of Melanoma in Australia and New Zealand. The Cancer Council Australia and Australian Cancer Network, Sydney and New Zealand Guidelines Group, Wellington (2008).
9. Trans-Tasman Radiation Oncology Group. A randomised clinical trial of surgery versus surgery plus adjuvant radiotherapy for regional control in patients with completely resected macroscopic nodal metastatic melanoma. Australian and New Zealand Melanoma Trials Group, Melbourne (2007).
10. Karakousis CP, Hena MA, Emrich LJ, et al. Axillary node dissection in malignant melanoma: results and complications. Surgery. 1990; 108:10–17.
11. Urist MM, Maddox WA, Kennedy JE, et al. Patient risk factors and surgical morbidity after regional lymphadenectomy in 204 melanoma patients. Cancer. 1983; 51:2152–2156.
12. Hughes TMD, A'Hern RP and Thomas JM. Prognosis and surgical management of patients with palpable inguinal lymph node metastases from melanoma. Br J Surg. 2000; 87:892– 01.
13. Serpell JW, Carne PWG, Bailey M. Radical lymph node dissection for melanoma. ANZ J Surg. 2003; 73:294–299.
14. Beitsch P, Balch C. Operative morbidity and risk factor assessment in melanoma patients undergoing inguinal lymph

node dissection. Am J Surg. 1992; 164:462–466.

15. McMasters KM, Noyes RD, Reintgen DS, et al. Lessons learned from the Sunbelt Melanoma Trial. J Surg Oncol. 2004; 86:212–223.
16. Morton DL, Cochran AJ, Thompson JF, et al. Sentinel node biopsy for early-stage melanoma: accuracy and morbidity in MSLT-I, an international multicenter trial. Ann Surg. 2005; 242:302–311.
17. Van Akkooi A, Bouwhuis M, van Geel A, et al. Morbidity and prognosis after therapeutic lymph node dissections for malignant melanoma. Eur J Surg Oncol. 2007; 33:102–108.
18. Hughes T, A'Hern R, Thomas J. Prognosis and surgical management of patients with palpable inguinal lymph node metastases from melanoma. Br J Surg. 2000; 87(7):892–901.
19. Karakousis C, Driscoll L. Groin dissection in malignant melanoma. Br J Surg. 1994; 81:1771–1774.
20. Clary B, Mann B, Brady M, et al. Early recurrence after lymphatic mapping and sentinel node biopsy in patients with primary extremity melanoma: a comparison with elective lymph node dissection. Ann Surg Oncol. 2001; 8:328–337.
21. Morton DL, Thompson JF, Cochran AJ, et al. Sentinel-node biopsy or nodal observation in melanoma. N Engl J Med. 2006; 355:1307–1317.
22. Berk DR, Johnson DL, Uzieblo A, et al. Sentinel lymph node biopsy for cutaneous melanoma: the Stanford experience, 1997–2004. Arch Dermatol. 2005; 141:1016–1022.
23. Burmeister BH, Henderson MA, Ainslie J, et al. Adjuvant radiotherapy versus observation alone for patients at risk of lymph-node field relapse after therapeutic lymphadenectomy for melanoma: a randomised trial. Lancet Oncol. 2012; Vol. 13; 6:589–597.
24. American Joint Committee on Cancer. AJCC Staging Handbook (5th ed.) Lippincott-Raven, Philadelphia (1998).
25. Balch C, Gershenwald J, Soong S, et al. Final Version of 2009 AJCC Melanoma Staging and Classification. J Clin Oncol. 2009 Dec 20; 27(36):6199–6206.
26. Chan A, Essner R, Wanek L, et al. Judging the therapeutic value of lymph node dissections in melanoma. J Am Coll Surg. 2000; 191:16–23.
27. Rossi C, Mozillo N, Maurichi A, et al. The number of excised lymph nodes is associated with survival of melanoma patients with lymph node metastasis. Ann Oncol. 2014; 25: 240–246.
28. Shaw JH, and Rumball EM. Complications and local recurrence following lymphadenectomy. BJS. 1990; 77: 760 – 764.

Confidence in the safety of standard childhood vaccinations among New Zealand health professionals

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ABSTRACT

AIMS: To investigate the level of confidence in the safety of standard childhood vaccinations among health professionals in New Zealand.

METHOD: Data from the 2013/14 New Zealand Attitudes and Values Study (NZAVS) was used to investigate the level of agreement that "it is safe to vaccinate children following the standard New Zealand immunisation schedule" among different classes of health professionals (*N*=1,032).

RESULTS: Most health professionals showed higher levels of vaccine confidence, with 96.7% of those describing their occupation as GP or simply 'doctor' (GPs/doctor) and 90.7% of pharmacists expressing strong vaccine confidence. However, there were important disparities between some other classes of health professionals, with only 65.1% of midwives and 13.6% of practitioners of alternative medicine expressing high vaccine confidence.

CONCLUSION: As health professionals are a highly trusted source of vaccine information, communicating the consensus of belief among GPs/doctors that vaccines are safe may help provide reassurance for parents who ask about vaccine safety. However, the lower level of vaccine confidence among midwives is a matter of concern that may have negative influence on parental perceptions of vaccinations.

Scepticism about the safety of childhood vaccinations is an issue of pressing concern.[1] Despite the abundance of comprehensive and reliable scientific evidence on the safety and effectiveness of standard vaccinations,[2–4] many parents continue to express fear and mistrust of vaccinations.[1] Such scepticism may be fostered or enabled by the increased accessibility of pseudo-scientific anti-vaccination information online and previous fraudulent studies on vaccinations.[1] This includes Andrew Wakefield's now retracted study on the unwarranted link between the measles, mumps and rubella vaccine (MMR) and autism.[5] In order to maintain high vaccination coverage, it is essential to correct current misconceptions about vaccinations among the general public.

Health professionals have crucial impact on parental decisions regarding their children's vaccinations. Numerous studies suggest that physician recommendation and positive communication with doctors are associated with an increased likelihood of vaccination uptake.[6–9] Smith et al[8] found that parents who express vaccine safety concerns were much more likely to vaccinate their child when their decisions were influenced by their health professional. Hence, it is essential to ensure that health professionals have strong vaccine confidence and accurate vaccine knowledge to positively influence parental vaccination decisions.

Vaccinations in the context of New Zealand

The New Zealand National Immunisation Schedule offers publicly funded vaccinations to all New Zealanders at various recommended ages.[10] This includes the influenza and whooping cough vaccine for pregnant women, and rotavirus and diphtheria-tetanus-pertussis vaccine for babies six weeks after birth.[10] As pregnancy is not officially defined as a category on the National Immunisation Register, it is difficult to quantify

accurate vaccination coverage rates among pregnant women. Immunisation coverage for children who turned one of the milestone ages during 2017 are relatively high (from 78.7% to 93.4%), but a small subset (around 4%) of parents continue to decline at least one vaccination every year.[11] Somewhat in line with these coverage rates, a recent study using data from the 2013/14 NZAVS found that the majority of New Zealand adults (68.5%) strongly agree that standard vaccinations following the National Immunization Schedule are safe, but 26% express uncertainty and 5.5% are strongly opposed.[12]

Unsurprisingly, parents who receive discouraging information on vaccinations are less likely to immunise their children.[13,14] The Growing Up in New Zealand Study[14] found that information which encourages immunisations did not increase the likelihood of timely vaccination uptake, suggesting that exposure to negative information has a particularly salient impact on parental vaccination decisions. On the contrary, Wroe, Turner and Owens[15] found that, in comparison to parents who received standard immunisation information, those who received more sophisticated decision-making aids showed a significantly higher likelihood of timely immunisations and decreased risk perceptions of vaccinations. This finding suggests that the comprehensiveness and adequacy of the way in which positive vaccination information is provided determines its impact on parental vaccination decisions.

Health professionals in New Zealand

Similar to past international research,[6,7] earlier New Zealand studies suggest that characteristics or attitudes of health professionals influence parental decisions on childhood vaccinations.[13,16,17] For instance, the belief that parental apathy is a barrier to immunisation among nurses has been associated with increased timeliness of vaccinations,[13] and practices with doctors who were confident in their vaccination knowledge had higher vaccination coverage.[17] As the way in which health professionals present pro-immunisation information is likely to determine its effectiveness, it is vital they have sufficient vaccine knowledge and can adequately communicate their confidence in vaccine safety to parents.

Previous studies indicate inconsistencies in perceptions of vaccinations across different classes of health professionals. A 2002 survey on health professionals in Rotorua (*N*=200) which assessed participants' level of agreement to various statements about immunisations (1= strongly disagree, 5= strongly agree) found that most health professionals agreed that childhood immunisations should be recommended (95%).[18] However, "41% of nurses (35/86), 45% (13/29) of midwives and 21% of doctors (16/76) were unsure whether the MMR vaccine was associated with autism or Crohn's disease."[18] Moreover, while 80% of doctors and nurses disagreed or strongly disagreed that "immunisations have unacceptable dangers", only 45% of midwives disagreed, with 28% being uncertain and 28% agreeing.[18] In other studies, some GPs identified inaccurate vaccine information distributed by midwives as a barrier to childhood vaccination,[19] and a higher proportion of pregnant women reported receiving vaccine discouraging information from midwives (11%) compared to GPs (3%).[14] Yet, a greater number of mothers also reported receiving vaccine encouraging information from their midwife (62%) compared to GPs (36%).[14]

Extending on past research, the current study leverages data from the 2013/14 NZAVS to directly assess up-to-date differences in levels of confidence in the safety of standard immunisations across different classes of health professionals in New Zealand. We aim to identify which classes of health professionals exhibit strong vaccine confidence, and which classes may require greater access to training and resources about vaccine safety.

Methods

Sampling procedure

The NZAVS is a longitudinal panel study with a probability sample of New Zealand adults. This study has been approved by the University of Auckland Human Participants Ethics Committee. Time 1 (2009) wave of the NZAVS was initially sampled from the electoral roll (response rate: 16.6%), with various booster samples collected during

Time 3 (2011), 4 (2012) and 5 (2013) to increase representativeness of our sample.[20] The current study uses data from the Time 5 sample (*N*=18,261, 81% retention rate from Time 4), specifically focusing on health professionals who completed the item assessing vaccine confidence (*N*=1,032).

Participants

As seen in Table 1, most health professionals in our sample were European (86.7%) and female (84.1%). The median age for all health professionals was 48 years (SD = 12). Doctors who listed a speciality other than GP ($150,000) and those describing their occupation as GP or simply 'doctor' ($120,000) had the highest median personal income, whereas midwives, physiotherapists ($50,000) and practitioners of alternative medicine ($52,000) had the lowest median income.

Measures

Occupation was assessed using the open-ended question "What is your occupation?" Health professionals were identified using the statistical standard provided by the Australian and New Zealand Standard Classification of Occupations.[21] This measure was validated by matching participants' self-reports against their occupation as listed in the original sample frame drawn from the electoral roll. We then created our own coding scheme within this Level 3 tier to classify health professionals into the 11 categories described in Table 1. Participants simply listing 'doctor' as their occupation were included in the GP category, as more specific information about their medical speciality was not available. Doctors listing a specific speciality other than GP (eg, anaesthetist, surgeon) were grouped into a category representing 'other specialist doctors.' Participants were also asked about their demographic characteristics.

Vaccine confidence was assessed using the likert item (1 = Strongly Disagree, 7 = Strongly Agree); "It is safe to vaccinate children following the standard NZ immunisation schedule". This item was developed for the NZAVS in consultation with medical professionals.

Statistical analyses

A one-way ANOVA was conducted to assess mean differences in levels of vaccine confidence across different classes of health professionals. This was followed by an ANCOVA which included participants' age, gender, ethnicity, parental and partner status, religiosity and region of residence as covariates. Lastly, a Chi-square test was conducted to investigate differences in proportions of strong vaccine confidence across the different classes of health professional. All analyses were conducted on SPSS.

Results

Analysis of mean differences

The ANOVA assessing differences in agreement with the Likert item "It is safe to vaccinate children following the standard NZ immunisation schedule" across the 11 classes of health practitioners was significant ($F_{(10,1021)}$=18.64, p<.001, partial eta squared = .154). Observed power for the F-ratio was >.99. Mean levels of vaccine confidence for each class of health professionals are presented in Figure 1.

GPs/doctors expressed the highest level of agreement that vaccinations following the standard schedule were safe (*M*=6.84). Bonferroni post-hoc tests indicated that midwives expressed significantly lower levels of belief in the safety of vaccinations relative to GPs/doctors (p<.001), pharmacists (p<.001), nurses (p=001), dentists (p=.01), physiotherapists (p=.005) and other specialist doctors (p=.025). Midwives' mean level of belief in the safety of vaccinations following the standard schedule (*M*=5.30) was marginally lower than that of the general population (*M*=5.72). However, this was not a significant difference.

Practitioners of alternative medicine (eg, homeopathy and osteopathy) expressed the lowest level of vaccine confidence (*M*=3.18). Bonferroni post-hoc tests indicated that they showed significantly lower agreement that vaccinations are safe relative to all other classes of health professionals (p<.001).

The ANCOVA assessing differences in levels of vaccine confidence across health professionals was significant ($F_{(10, 958)}$=16.57, p<.001, partial eta squared=.147). Observed power for the overall F-ratio was >.99. Age, gender, ethnicity (Māori, Asian, Pacific or European), parental and partner status, religiosity and region of residence were included as covariates. GPs continued to show the highest mean level of vaccine

safety (*M*=6.78), while midwives (*M*=5.53) and practitioners of alternative medicine (*M*=3.13) showed the lowest level of agreement. Bonferroni post-hoc tests indicated that midwives expressed significantly lower vaccine confidence relative to GPs/doctors ($p<.001$) and pharmacists ($p=.008$). However, practitioners of alternative medicine continued to show significantly lower levels of vaccine confidence compared to all other health professionals ($p<.001$).

Strong vaccine confidence

The number of participants who selected each rating on our measure of vaccine confidence is presented in Table 2. The distribution of confidence in vaccine safety tended to be skewed towards strong agreement for most classes of health professionals. Following the coding scheme proposed by Lee et al,[12] ratings of 6 or 7 on the vaccination item were described as *strong vaccine confidence*. A chi-square test indicated that there were reliable differences across the classes of health professional in strong support for vaccinations ($\chi^2_{(10;\, N = 1032)}=107.73$, $p<.001$). As shown in Figure 2, GPs/doctors exhibited the highest proportion of strong vaccine confidence (96.7%), while practitioners of alternative medicine (13.6%) and midwives (65.1%) showed the lowest proportions.

Discussion

The current study used data from the 2013/14 NZAVS to investigate the level of confidence in the safety of standard childhood vaccinations among different classes of health professionals. We found that GPs/doctors (96.7%), pharmacists (90.7%) and dentists (86.2%) exhibited the highest levels of strong vaccine confidence, while midwives (65.1%) and practitioners of alternative medicine (13.6%) exhibited the lowest level of strong confidence. As reported by Lee et al,[12] the 2013/14 NZAVS data suggests that the majority of New Zealanders believe in the safety of vaccinations (68.5%). Although most health professionals exhibit considerably higher levels of vaccine confidence compared to the general public, practitioners of alternative medicine show substantially lower and midwives show marginally lower levels of strong confidence.

Irrespective of whether we controlled for key demographic factors, practitioners of alternative medicine showed a significantly lower mean level of vaccine confidence compared to all other health professionals. Moreover, midwives showed a significantly lower level of confidence compared to most other health professionals and continued to

Table 1: Demographic details of participants within each class of health professionals and the full sample.

	Female		European		Religion		Urban		Age		Personal income	
	N	%	N	%	N	%	N	%	Median	SD	Median	SD
GPs/doctors	68	55.7%	99	81.1%	48	41.0%	74	69.8%	45.00	12.44	$120,000	$106,595
Pharmacists	32	74.4%	33	76.7%	24	58.5%	29	67.4%	45.00	13.45	$72,000	$46,242
Dentists/dental surgeons	17	58.6%	25	86.2%	9	32.1%	23	82.1%	45.00	13.29	$112,500	$99,028
Doctors - other specialists	14	43.8%	29	90.6%	10	31.3%	25	78.1%	51.10	9.31	$150,000	$137,497
Physiotherapists	51	85.0%	55	91.7%	18	31.0%	46	78.0%	41.00	10.85	$50,000	$29,109
Nurses	495	94.5%	457	87.2%	236	47.3%	328	63.0%	50.00	11.51	$58,000	$22,796
Radiographers	23	85.2%	27	100.0%	9	33.3%	20	76.9%	41.00	12.38	$80,000	$21,745
Health professionals - other	85	78.0%	92	83.6%	48	41.0%	74	69.8%	45.50	12.03	$59,000	$27,903
Occupational therapists	21	100.0%	21	95.5%	7	33.3%	15	68.2%	52.00	9.08	$63,000	$20,097
Midwives	43	100.0%	38	88.4%	17	44.7%	28	65.1%	50.00	11.47	$50,000	$29,716
Practitioners of alt. medicine	20	90.9%	21	95.5%	3	13.6%	16	72.7%	45.50	9.98	$52,000	$21,452
Total - health professionals	870	84.1%	897	86.7%	429	43.2%	692	67.8%	48.00	11.76	$62,000	$67,535
Total - full sample	11,460	62.80%	15,607	85.50%	6,879	39.40%	12,151	67.20%	49.00	14.07	$48,000	$52,470

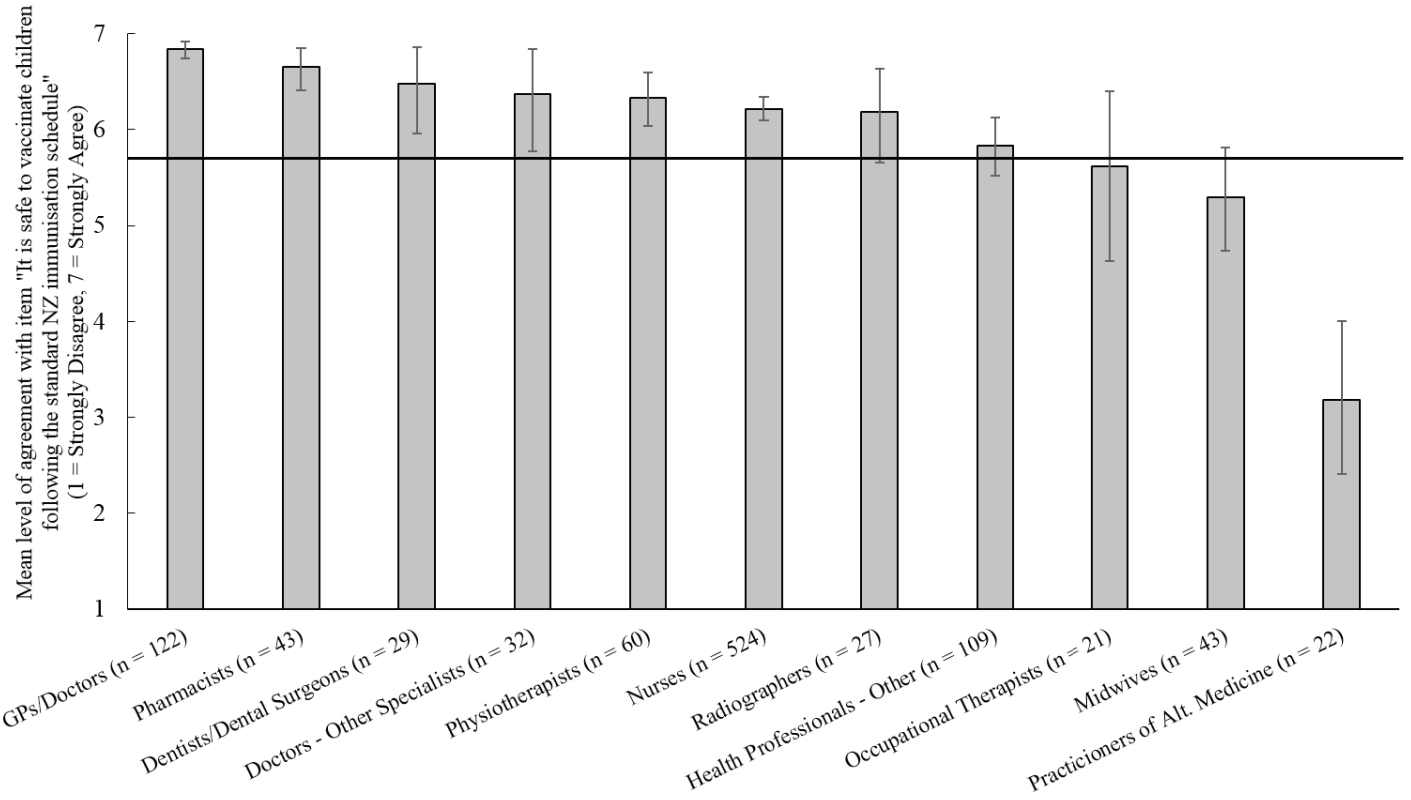
Notes: 'N' and '%' refer to the number of people classified within each demographic category for the different classes of health professionals. The median age and median personal income for people within each class of health professionals, all health professionals together and the full sample of the 2013/14 NZAVS (including health professionals) are also reported.

Table 2: Mean ratings of agreement with the item on vaccine safety and percentage of respondents expressing strong vaccine confidence.

	Mean	SD	Lower 95% CI	Upper 95% CI	N	Percent strong	Frequency count of Likert scale ratings (1 = Strongly Disagree, 7 = Strongly Agree)						
							1	2	3	4	5	6	7
GPs/doctors	6.84	0.49	6.74	6.92	122	96.7%	0	0	0	1	3	11	107
Pharmacists	6.65	0.72	6.41	6.85	43	90.7%	0	0	0	1	3	6	33
Dentists/dental surgeons	6.48	1.15	5.96	6.86	29	86.2%	0	1	0	1	2	3	22
Doctors - other specialists	6.38	1.41	5.77	6.84	32	87.5%	1	0	1	2	0	4	24
Physiotherapists	6.33	1.05	6.04	6.60	60	85.0%	0	0	3	1	5	15	36
Nurses	6.22	1.34	6.10	6.34	524	83.6%	9	11	13	23	30	119	319
Radiographers	6.19	1.24	5.66	6.64	27	77.8%	0	0	2	1	3	5	16
Health professionals - other	5.83	1.60	5.52	6.13	109	72.5%	3	4	5	8	10	25	54
Occupational therapists	5.62	1.91	4.63	6.40	21	81.0%	2	0	2	0	0	9	8
Midwives	5.30	1.77	4.74	5.81	43	65.1%	2	3	3	3	4	17	11
Practitioners of alt. medicine	3.18	1.89	2.41	4.00	22	13.6%	6	3	4	3	3	2	1
Population estimate	5.71	1.54	5.69	5.73	18,154	68.5%	543	455	664	2,054	2,010	4,885	7,543

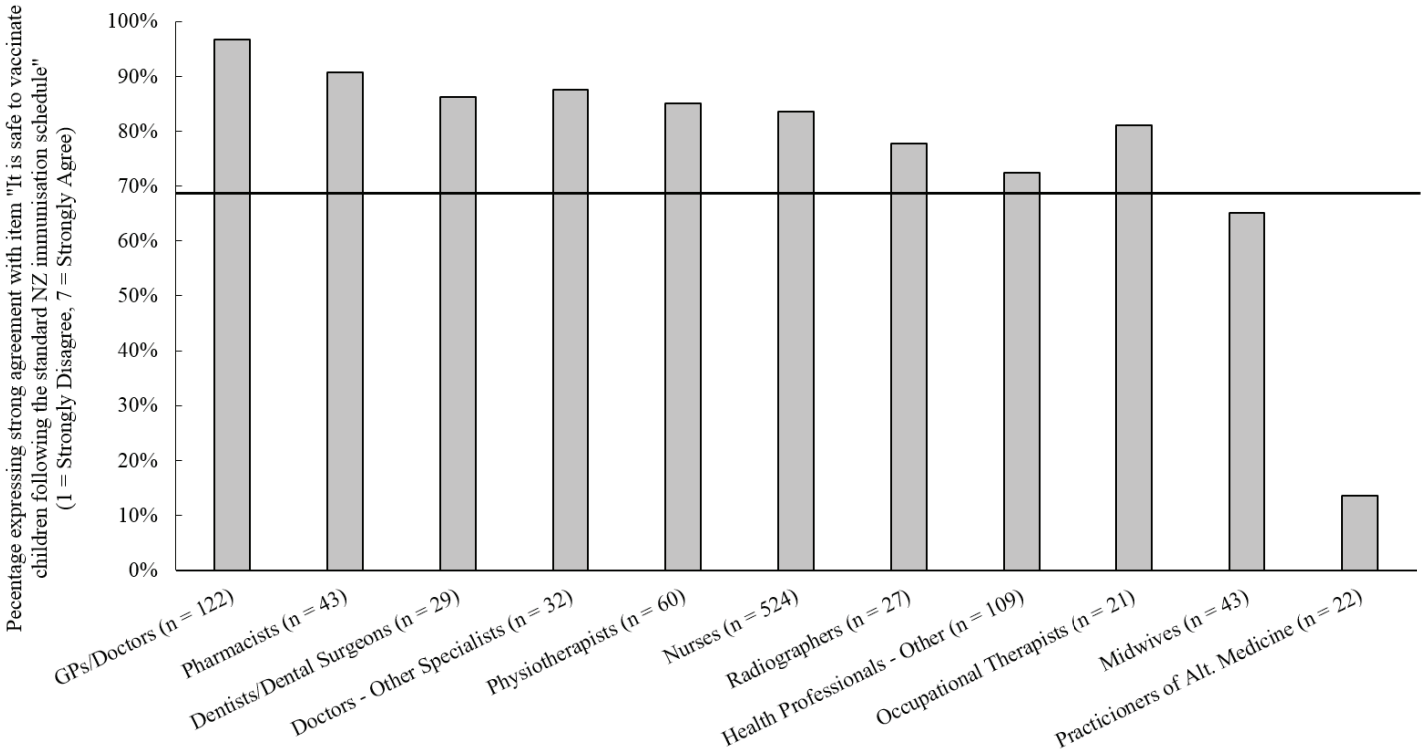
Notes: The estimate of 'percent strong' represents the percentage of people rating a '6' or '7' (ie, strong agreement) with the Likert scale item "It is safe to vaccinate children following the standard NZ immunisation schedule". 95% confidence intervals of the mean were obtained using 5,000 bootstrap resamples. After applying the standard NZAVS post-stratification sample weighting adjustment the population estimate (using the total sample) was 5.72 and associated 95% confidence interval was 5.70, 5.74 (These estimates are different to values presented in table as bootstrapping was not possible in conjunction with weighting).

Figure 1: Mean level of agreement with the Likert item "It is safe to vaccinate children following the standard NZ immunisation schedule" for different classes of health professionals.



Note. Error bars represent 95% confidence interval of the mean using 5,000 bootstrap resamples. The bold horizontal line represents the estimated population mean level of vaccine confidence using the full sample (N=18,153) and applying NZAVS post-stratification sample weighting adjustment.

Figure 2: Percentage of different classes of health professionals expressing strong vaccine confidence.



Notes. Strong vaccine confidence indicated by ratings of 6 or 7 the Likert item "It is safe to vaccinate children following the standard NZ immunisation schedule." The bold horizontal line represents the estimated population mean level of vaccine confidence using the full sample (*N*=18,153) and applying NZAVS post-stratification sample weighting adjustment.

exhibit lower confidence than GPs/doctors and pharmacists after controlling for demographic factors. This finding is consistent with previous studies in which a greater proportion of midwives were found to exhibit vaccine safety concerns or distribute negative vaccine information.[14, 18] The large effect size observed in our ANOVA of differences across occupation (partial eta squared = .154) suggest that the type of occupation held by a health professional has important influence on their level of vaccine confidence. Future studies should investigate how more specific factors, such as differences in vaccination education or working environments, may be driving these disparities in confidence.

Strong vaccine confidence among GPs/doctors

According to Freed et al,[22] most parents tend to view their children's doctors as a highly trusted source of vaccine information. Parents are more likely to vaccinate their children when their doctor is confident in their vaccine knowledge or take their vaccine concerns seriously.[9,17] Hence, the consensus of belief in the safety of immunisations among New Zealand GPs/doctors is an encouraging finding that is likely to have a positive impact on parental vaccination decisions. If GPs/doctors can adequately communicate their confidence in vaccine safety, they may be able to encourage sceptical parents to immunise their children.

Simply distributing information about vaccine safety may not be the best strategy to promote vaccinations.[23, 24] To sufficiently influence parental vaccination attitudes, Wroe et al [25] suggest that it is important to address omission bias; the tendency of people to exhibit greater fear regarding the harm resulting from action (ie, immunising) than from inaction (ie, not immunising). Accordingly, providing parents with a comprehensive information aid that addressed omission bias, and enabled more accurate comparisons between the risks of adverse immunisation side effects versus serious illnesses was found to increase positive perceptions of vaccinations and the likelihood of timely vaccinations.[15] Thus, it may be useful to inform and train health

professionals about how to effectively convey their confidence in vaccine safety and emphasise the risks of not immunising.

Additionally, explicitly stating to parents the statistic that "96.7% of GPs/doctors agree that standard childhood vaccinations are safe" may help provide further reassurance to parents. In the context of climate change belief, the presentation of statistics citing the near-universal consensus in the published literature that "climate change is happening and caused by humans" has been employed as a strategy to reduce scepticism towards this issue.[26] In a similar way, the fact that the view of GPs/doctors, a highly trusted source of vaccine information,[22] are consistent with the large body of high-quality scientific research showing that standard vaccinations are safe[2–4] may help alleviate vaccine safety concerns among some parents.

Lower vaccine confidence among midwives

In contrast to GPs/doctors, only two in three midwives showed strong vaccine confidence in our study. The 2002 survey in Rotorua had also found that midwives show a wide spectrum of beliefs regarding the dangers of vaccinations,[18] suggesting that a fair proportion of midwives persistently exhibit uncertainty about vaccine safety. Perhaps due to this uncertainty, some midwives are hesitant about recommending vaccinations to mothers. A midwife interviewed by Litmus[23] stated believing that it is up to parents to make immunisation decisions, with another stating that they preferred not to be involved in such a controversial issue and desired more vaccination information. From the perspective of parents, while some reported having informed conversations with their midwife, others felt that their midwife did not sufficiently explain the benefits of vaccinations and therefore were not motivated to vaccinate their child.[23]

Midwives are chosen by most New Zealand women to be their lead maternity carer and are most directly involved with parents in the lead up to birth.[27] As most parents make immunisation decisions during pregnancy,[14] this is an important time to educate parents-to-be about the benefits of vaccinations. Hence, the relatively low level of vaccine confidence among midwives may have important implications for understanding the resistance to change of anti-vaccination attitudes in the population. Previously, Lee et al[12] found that vaccine scepticism tends to be higher among Māori individuals, those living in rural areas, with lower education and income, and those with higher subjective health and Openness to Experience. In addition to these factors, the lack of vaccine confidence among midwives may also be contributing to the persistence of vaccine scepticism in New Zealand.

Over the years, there has been a substantial improvement in vaccination coverage rates,[28] and currently there are numerous immunisation training courses available for health professionals.[29] However, the lower level of vaccine confidence among midwives suggests there is a need to provide increased resources for this particular group. Further research on the specific concerns of midwives and the impact that their vaccination attitudes have on parental vaccination decisions is crucial. Such findings will inform the development of interventions and training protocols that aim to increase vaccine confidence among midwives and the general public.

Limitations

As the current study used cross-sectional data and a single-item measure to assess vaccine confidence, we were unable to track changes in attitudes of health professionals over time or identify the reasons why they expressed high or low confidence. There may also have been disparities in the way health professionals interpreted the term 'safety'. Midwives may not regard vaccinations as entirely safe as they are concerned about any sort of harm caused by vaccinations, including minor side effects. Conversely, doctors may view transitory side effects of vaccinations as insignificant when compared to more serious health issues such as heart attacks or broken bones.

As noted by Robertson and Sibley,[30] people with different demographic characteristics (eg, gender, occupation) are not equally likely to respond to the NZAVS. For instance, women and those with professional occupations tend to show higher response rates.[30] This suggests that there may be some degree of response bias in our study, and certain groups may have been over-represented or more heavily determined the types of

occupations held by those in our sample of health professionals. On the other hand, as the NZAVS does not solely focus on health-related issues or specifically target health professionals, health professionals are less likely to have made participation decisions based on their health beliefs or consciously answered questions in a way deemed appropriate for someone in their profession.

Concluding comments

Using data from the 2013/14 NZAVS, the present study investigated the level of confidence in standard childhood immunisations among New Zealand health professionals. Most health professionals, especially GPs/doctors (96.7%) and pharmacists (90.7%), showed high levels of strong vaccine confidence, but midwives (65.1%) and practitioners of alternative medicine (13.6%) exhibited relatively lower levels of strong confidence. The consensus of belief in the safety of vaccinations among GPs/doctors is an encouraging finding and could be used to provide reassurance to vaccine sceptical parents. However, the low level of confidence among midwives is a major concern and may be contributing to the persistence of vaccine scepticism among the general public. Further research is warranted to identify the most effective ways GPs/doctors can convey their vaccine confidence to parents, as well as how to increase vaccine confidence among midwives.

Competing interests:
Nil.

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URL:
https://www.nzma.org.nz/journal/read-the-journal/all-issues/2010-2019/2018/vol-131-no-1474-4-may-2018/7558

REFERENCES:

1. Dub E, Vivion M, MacDonald NE. Vaccine hesitancy, vaccine refusal and the anti-vaccine movement: influence, impact and implications. Expert review of vaccines. 2015; 14:99–117.
2. Plotkin S, Gerber JS, Offit PA. Vaccines and autism: a tale of shifting hypotheses. Clin Infect Dis. 2009; 48:456–61.
3. Vichnin M, Bonanni P, Klein NP, et al. An overview of quadrivalent human papillomavirus vaccine safety: 2006 to 2015. Pediatr Infect Dis J. 2015; 34:983–91.
4. Velzquez RF, Linhares AC, Muoz S, et al. Efficacy, safety and effectiveness of licensed rotavirus vaccines: a systematic review and meta-analysis for Latin America and the Caribbean. BMC paediatrics. 2017; 17:14.
5. Deer B. How the case against the MMR vaccine was fixed. BMJ. 2011; 342:c5347.
6. Swennen B, Van Damme P, Vellinga A, et al. Analysis of factors influencing vaccine uptake: perspectives from Belgium. Vaccine. 2001; 20:S5–7.

7. Gargano LM, Herbert NL, Painter JE, et al. Impact of a physician recommendation and parental immunization attitudes on receipt or intention to receive adolescent vaccines. Human Vaccines & Immunotherapeutics. 2013; 9:2627–33.
8. Smith PJ, Kennedy AM, Wooten K, et al. Association between health care providers' influence on parents who have concerns about vaccine safety and vaccination coverage. Pediatrics. 2006; 118:e1287–92.
9. Marlow LAV, Waller J, Wardle J. Trust and Experience as Predictors of HPV Vaccine Acceptance. Human Vaccines. 2007; 3:171–5.
10. Ministry of Health. New Zealand immunisation schedule. 2017. http://www.health.govt.nz/our-work/preventative-health-wellness/immunisation/new-zealand-immunisation-schedule (accessed 07 Feb 2018).
11. Ministry of Health. National and DHB immunisation data. 2017. http://www.health.govt.nz/our-work/preventative-health-wellness/immunisation/immunisation-coverage/national-and-dhb-immunisation-data (accessed 07 Feb 2018).
12. Lee CHJ, Duck IM, Sibley CG. Personality and demographic correlates of New Zealanders' confidence in the safety of childhood vaccinations. Vaccine. 2017; 35:6089–95.
13. Petousis-Harris H, Grant C, Goodyear-Smith F, et al. what contributes to delays? The primary care determinants of immunisation timeliness in New Zealand. Journal of primary health care. 2012; 4:12–20.
14. Growing Up in New Zealand. Growing Up in New Zealand Policy Brief. Who is saying what about immunisation: evidence from Growing Up in New Zealand. 2015.
15. Wroe AL, Turner N, Owens RG. Evaluation of a decision-making aid for parents regarding childhood immunizations. Health Psychol. 2005; 24:539.
16. Petousis-Harris H, Goodyear-Smith F, Turner N, et al. Family practice nurse views on barriers to immunising children. Vaccine. 2005; 23:2725–30.
17. Grant CC, Petousis-Harris H, Turner N, et al. Primary care practice and health professional determinants of immunisation coverage. J Paediatr Child Health. 2011; 47:541–9.
18. Jelleyman T, Ure A. Attitudes to immunisation: a survey of health professionals in the Rotorua District. N Z Med J. 2004; 117:1–12.
19. Petousis-Harris H, Goodyear-Smith F, Turner N, et al. Family physician perspectives on barriers to childhood immunisation. Vaccine. 2004; 22:2340–4.
20. Sibley CG. Sampling procedure and sample details for the New Zealand Attitudes and Values Study. NZAVS Technical Documents. 2014.
21. Statistics New Zealand. Statistical Standard for Occupation. 2013.
22. Freed GL, Clark SJ, Butchart AT, et al. Sources and perceived credibility of vaccine-safety information for parents. Pediatrics. 2011; 127:S107–12.
23. Litmus. Immunisation for Pregnant Women: Audience research with pregnant women. 2015.
24. Horne Z, Powell D, Hummel JE, et al. Countering antivaccination attitudes. Proc Natl Acad Sci. 2015; 112:10321–4.
25. Wroe AL, Turner N, Salkovskis PM. Understanding and predicting parental decisions about early childhood immunizations. Health Psychol. 2004; 23:33–41.
26. Cook J, Nuccitelli D, Green SA, et al. Quantifying the consensus on anthropogenic global warming in the scientific literature. Environmental research letters. 2013; 8:024024.
27. Ministry of Health. Report on Maternity. 2015.
28. Turner N. The challenge of improving immunization coverage: the New Zealand example. Expert review of Vaccines. 2012; 11:9–11.
29. Immunisation Advisory Centre. Education and training. http://www.immune.org.nz/health-professionals/education-training (accessed Oct 26, 2017).
30. Robertson A, Sibley CG. Research Sampling: A Pragmatic Approach. In: Brough P, Occhipinti S, editors. Research methods for applied psychologists: design, analysis and reporting. Routledge; In press.

Eikenella corrodens retroperitoneal necrotising fasciitis post-endoscopic retrograde cholangio-pancreatography

Yee Sing Lin, Eva Susan Juhasz

Endoscopic retrograde cholangio-pancreatography (ERCP) is a common procedure for the removal of gallstones lodged in the biliary tract. Guidewires are often employed to reduce the risk of post-ERCP pancreatitis.[1]

This is the first reported case of a patient who developed retroperitoneal necrotising fasciitis as a result of a retained guidewire after ERCP. Fractured guidewires are a previously described rare complication of this common intervention.[2] It appears the guidewire was retained post-procedure and perforated the duodenum. The dominant organism isolated was an oral organism with well-documented ability to form biofilm. It was most likely introduced from the mouth during the passage of scope.

Case

A 49-year-old man presented with a two-day history of abdominal pain and spreading cellulitis of the abdomen as well as the appearance of bruising down his right leg. Communication was limited as he did not speak any English and had only recently come to New Zealand. Notes retrieved from the GP indicated that he had first presented with severe right hip pain and no fever a week prior. The history that could be elucidated was that he had undergone an endoscopic procedure for gallstones five months ago in Malaysia. He had no other medical conditions.

Admission blood tests showed that he appeared to be acidotic with respiratory compensation. He was afebrile with a temperature of 36.1 degrees Celsius. He had mildly raised white cell count (12,800/uL), normal neutrophil count (5,200/uL), elevated CRP (17mg/dL) as well as acute impairment of his renal function (creatinine at 1.40mg/dL). Blood cultures taken at the time demonstrated no growth on culture after five days. The patient was started on intravenous cefuroxime and metronidazole as per hospital protocol for abdominal infections.

A CT scan showed a metallic foreign body 20cm in length extending from the common hepatic duct, through the common bile duct and perforating the duodenum and into the retroperitoneum (Figure 1). There was extensive fluid and gaseous collections retroperitoneally around the duodenum and in the right pararenal space (greater on the right that the left); within the layers of the abdominal wall between internal and external oblique muscles; in the right iliac fossa overlying the iliacus muscle; further extension into the pelvis to surround the bladder; and the right anterior thigh (Figure 2).

Surgical findings were that there was contamination within the abdomen with infected fluid. Pus was present between the various layers of the abdominal wall with associated separation and destruction of the layers. There was also dissection of the fascia lower down into the groin region. All these areas looked grossly infected. On the right anterior thigh there was an area of bluish pigmentation consistent with ischaemia. After the abdomen had been explored an ellipse of tissue was taken from the anterior thigh and all the tissue from skin, subcutaneous fat and muscle

Figure 1: A-C, serial coronal sections demonstrating trajectory of guidewire (indicated by arrows) originating from the common hepatic duct confluence, through the inferior duodenal wall at D2/D3, and into the right iliac fossa.

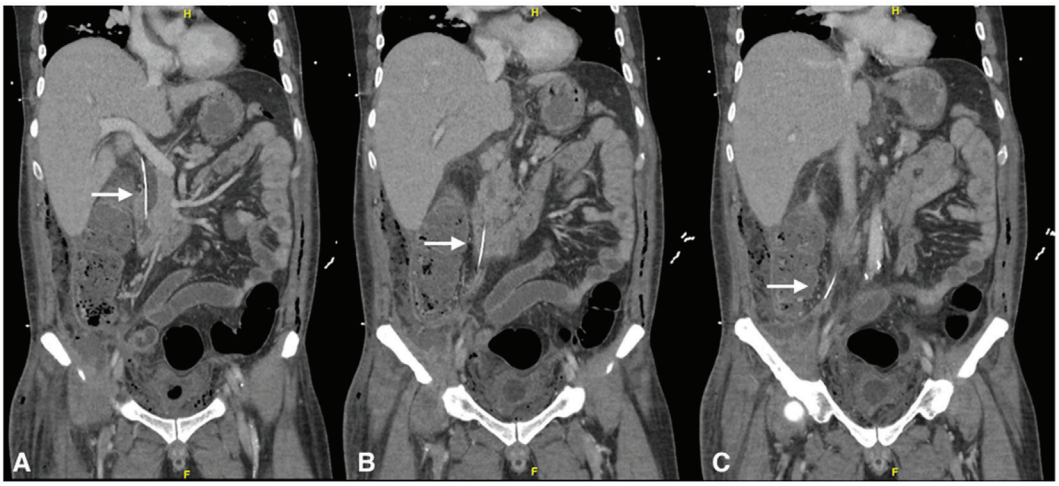
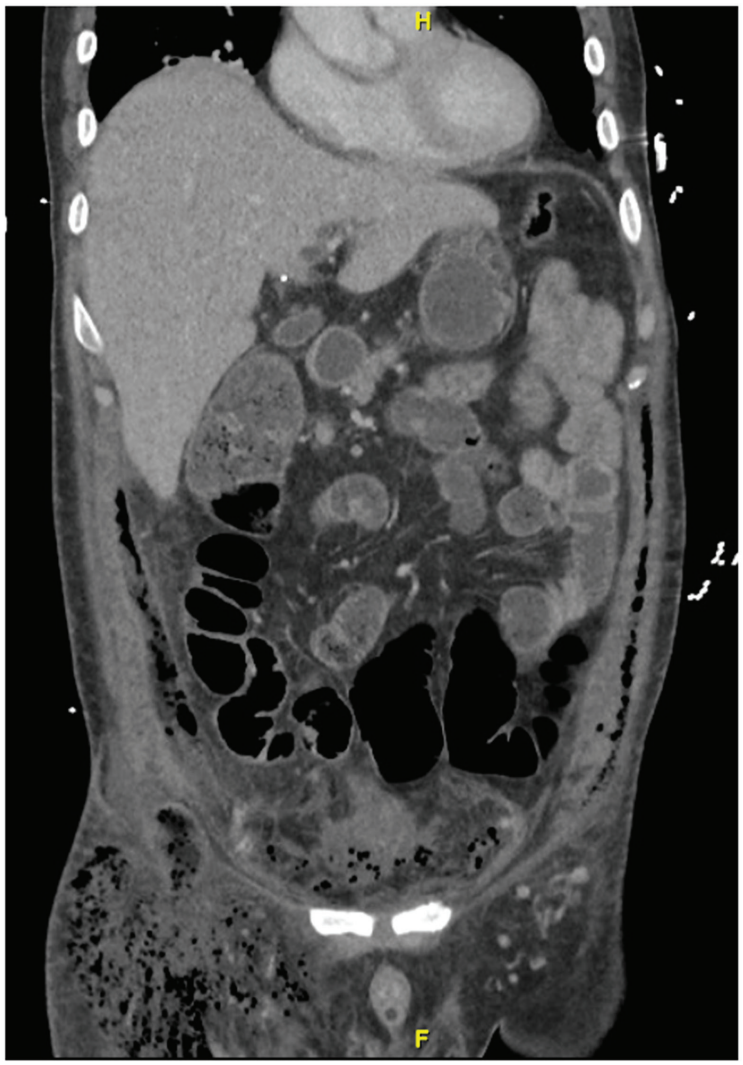


Figure 2: Coronal section demonstrating free air and fluid in the abdominal wall, pelvis and anterior right thigh.



was necrotic. There was a foul smelling discharge. Samples were sent for culture and microscopy.

After thorough exploration and assessment, it was deemed that this was not a survivable event. The decision was made to not proceed any further. The foreign body was not visualised and was therefore likely lodged retroperitoneally—removal would not have caused any improvement so was not pursued. The infection was so widespread that debridement was not feasible. His abdomen was closed and a dressing was applied to the anterior thigh. He was referred through to ICU for palliative management. Over the next 24 hours he continued to deteriorate and died during the following day. Subsequent microscopy of specimens confirmed a mixture of gram positive and negative bacteria, aerobic and anaerobic flora; Eikenella corrodens was isolated.

Discussion

The risk of serious complication following ERCP is less than 2% and includes pancreatitis; bleeding; cholecystitis; cholangitis; sepsis; perforation; myocardial infarction; death.[3] Basket trapping has also been reported.[3] Although rare, reports of fractured and retained guidewires have previously been described occurring due to excessive manipulation,[4] extracorporeal shock wave lithotripsy, sphincterotomy formation and during formation of a pancreaticoduodenostomy tract.[2] Wires usually remain in the hepatic ducts, duodenal wall or pancreatic duct.[2] In most cases, patients are asymptomatic and have no long-term complications. Removal of retained wires has been previously achieved using balloon catheters,[5] wire guided forceps and basket,[6] or surgically via a Whipple's procedure.[4] One case of wire migration has been recently described where a patient presented with right leg and back pain two weeks after ERCP. A 26cm wire was seen on CT in the retroperitoneum along the right iliopsoas muscle extending into the vastus intermedius to penetrate the common and deep femoral veins. Extensive infection was not seen. In this case, the wire was removed by interventional radiology through a transjugular approach.[2]

Eikenella corrodens is a gram-negative bacillus with biofilm capability, which colonises the oral cavity and is commonly associated with periodontal infections.[7] It has also been implicated in infections of the skin, chest, abdomen, blood, heart, central nervous system, thyroid gland, extremities and bone.[7] Eikenella corrodens has also been identified as a causative agent in another case of necrotising fasciitis, reported to have occurred after elective inguinal hernia repair.[8] Despite the wide variety of sites of infection, infection usually originates from the oral cavity. Many E. corrodens infections of the hand are associated with bite marks.[8] Previous case reports have demonstrated that it is typically resistant to cefuroxime and metronidazole[9] as well as clindamycin.[7] The majority of infections involving E. corrodens also tend to be polymicrobial, with the most common concurrent isolate being streptococci.[9] In a previous review of 43 patients infected by E. corrodens, malignancy was the most common underlying condition.[9]

Necrotising fasciitis is a soft tissue infection characterised by necrosis of the fascia and subcutaneous tissue. Management involves prompt resuscitation, initiation of antibiotics and aggressive debridement. Retroperitoneal necrotising fasciitis has been described secondary to appendicitis;[10] pancreatitis;[11] pelvic infection;[12] diverticulitis;[13] malignancy of the colon[14] and post-partum.[15] There has been one other case described post-ERCP.[16] Diagnosis is difficult due to absence of clinical signs in the early state. Even in the absence of comorbidity, successful treatment is difficult due to the anatomical extent of disease and the difficulty in effectively debriding the retroperitoneum, as evident in the present case. Surgical intervention [10–14,16] is required in most cases.

We conclude that a fractured guidewire was retained during the patient's previous endoscopic procedure and subsequently migrated into the retroperitoneum. The organism was most likely introduced during passage of the endoscope through the oral cavity and entered the retroperitoneum through the duodenal perforation. The retained wire likely facilitated the direct inoculation of this oral pathogen into the retroperitoneum by providing a surface which allowed biofilm formation. Subsequent super-infection by gut organisms

would have led to this clinically worsening condition. It is likely the infection spread initially from the retroperitoneum, through the layers of the abdominal wall, then into the soft tissues of the thighs. Biofilms are also known for their role in antibiotic tolerance.[17] Biofilm capable bacteria are able to evade the immune response, enabling spread of infection. The mechanisms by which biofilms are able to attenuate host immunity inhibiting macrophage activity;[18] inducing a fibrotic response;[19] down-regulation of virulence factors; and physical protection of bacteria from the host immune response, allowing unimpeded spread of infection.[17] This is the likely reason that he was afebrile with only mildly elevated inflammatory markers and white cells despite the extensive infection. Biofilms are also known for their role in antibiotic tolerance.[17]

Despite efforts, we were not able to contact the foreign institution at which the original procedure was completed and so do not know if retention of this foreign body was recognised. This case highlights the aggressive nature and difficulty in treatment of device-related infection and the contribution to this by the ability of biofilm capability. This potentially fatal complication needs to be brought to the attention of gastroenterologists performing ERCP and confirms the importance of removing this device post-procedure.

Competing interests:
Nil.

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https://www.nzma.org.nz/journal/read-the-journal/all-issues/2010-2019/2018/vol-131-no-1474-4-may-2018/7559

REFERENCES:

1. Cheung J, Tsoi KK, Quan WL, et al. Guidewire versus conventional contrast cannulation of the common bile duct for the prevention of post-ERCP pancreatitis: a systematic review and meta-analysis. Gastrointest Endosc. 2009; 70:1211–1219.
2. Pomeranz CB, Wehrli NE, Tyberg A, et al. Unusual migration of fractured ERCP guidewire: A case report. Clin Imaging. 2017; 43:93–96.
3. Masci E, Toti G, Mariani A, et al. Complications of diagnostic and therapeutic ERCP: a prospective multicenter study. Am J Gastroenterol. 2001; 96:417.
4. Pruitt A, Schutz SM, Baron T, McClendon D, et al. Fractured hydrophilic guidewire during ERCP: a case series. Gastrointestl endosc. 1998; 48:77–80.
5. Burdick JS, Schmalz MJ, Geenen JE. Guidewire fracture during endoscopic sphincterotomy. Endoscopy. 1993; 25:251–252.
6. Matsubayashi H, Sawai H, Tanaka M, Hotta K, et al. Endoscopic removal of foreign body from hepatic duct using wire guided forceps and basket. J interv gastroenterol. 2012; 2:86.
7. Chen CC, Wilson ME. Eikenella corrodens in human oral and non-oral infections: a review. J Periodontol. 1992; 63:941–953.
8. Miller AT, Byrn JC, Divino CM, et al. Eikenella corrodens causing necrotizing fasciitis after an elective inguinal hernia repair in

an adult: a case report and literature review. Am Surg. 2007; 73:876–879.

9. Sheng WS, Hsueh PR, Hung CC, et al. Clinical features of patients with invasive Eikenella corrodens infections and microbiological characteristics of the causative isolates. Eur J Clin Microbiol Infect Dis. 2001; 20:231–236
10. Hua J, Yao L, He ZG, et al. Necrotizing fasciitis caused by perforated appendicitis: a case report. Int J Clin Exp Path. 2015; 8:3334.
11. White NR, Fowler LL. Retroperitoneal and cutaneous necrotizing fasciitis secondary to necrotizing pancreatitis. J Emerg Med. 2014; 47:147–149.
12. Amaranathan A, Sahoo AK, Barathi D, et al. Retroperitoneal Necrotizing Fasciitis Masquerading as Perianal Abscess–Rare and Perilous. Cureus. 2017; 9.
13. Secil M, Topacoglu H. Retroperitoneal necrotizing fasciitis secondary to colonic diverticulitis. J Emerg Med. 2008; 34:95–97.
14. Takakura Y, Ikeda S, Yoshimitsu M, et al. Retroperitoneal abscess complicated with necrotizing fasciitis of the thigh in a patient with sigmoid colon cancer. World J Surg Oncol. 2009; 7:74.
15. Yagi H, Fukushima K, Satoh S, et al. Postpartum retroperitoneal fasciitis: a case report and review of literature. Am J Perinatol. 2005; 22:109–113.
16. Jong JH, Hong SL, Sung WJ, et al. Retroperitoneal necrotizing fasciitis after endoscopic retrograde cholangiopancreatography. Korean J Pancreas Biliary Tract. 2011; 16:169–174.
17. Scherr TD, Heim CE, Morrison JM, et al. Hiding in plain sight: interplay between staphylococcal biofilms and host immunity. Front immunol. 2014; 5:37.
18. Thurlow LR, Hanke ML, Fritz et al. Staphylococcus aureus biofilms prevent macrophage phagocytosis and attenuate inflammation in vivo. J Immunol. 2011; 186:6585–6596.
19. Hanke ML, Angle A, Kielian T. MyD88-dependent signaling influences fibrosis and alternative macrophage activation during Staphylococcus aureus biofilm infection. PloS one. 2012; 7:e42476.

Enteric duplication cyst as a cause for small bowel obstruction in adulthood

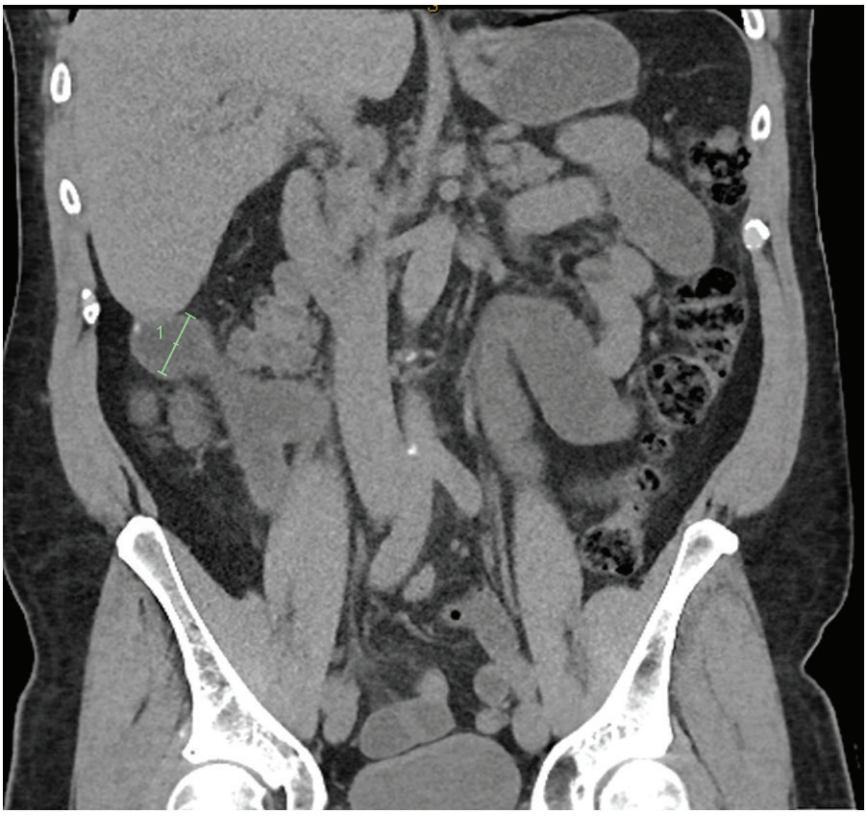
Joel D'souza, Simon Richards

ABSTRACT

We report a case of a patient presenting with small bowel obstruction secondary to an enteric ileal duplication cyst. Although common in infancy, they are rarely seen in adults. Radiologically they may be difficult to distinguish from a Meckel diverticulum and often the diagnosis is made retrospectively. Optimal management of the asymptomatic adult is unclear.

A 56-year-old male presented with a 24-hour history of colicky left upper quadrant abdominal pain and distension, with progression to nausea, vomiting and obstipation. He had no previous intra-abdominal surgery. An abdominal radiograph showed dilated loops of small bowel. A subsequent CT scan showed multiple loops of dilated small bowel proximal to a dilated tubular structure arising from small bowel in the right upper quadrant. This tubular structure appeared to be a Meckel diverticulum (MD) causing small bowel obstruction.

Figure 1: Coronal CT showing small bowel obstruction with an associated tubular structure in the right upper quadrant.



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The patient proceeded to a laparotomy where this tubular structure was noted to be arising from the mesenteric border of the mid-jejunum. This had caused a loop of small bowel to volve, resulting in subsequent small bowel obstruction. This and a margin of small bowel either side was resected using a linear stapler and a side to side anastomosis fashioned.

The macroscopic pathological findings of the specimen were of a 60mm blind ended tube lined by normal small bowel mucosa along with an adjacent non-communicating unilocular 10mm cyst. Microscopic findings were consistent with an intestinal duplication cyst with no evidence of malignancy or acute inflammation. The post-operative period was uncomplicated.

Discussion

Enteric duplication cysts (EDC) are rare congenital malformations with an estimated incidence of approximately 1 in 10,000. They may be present from mouth to anus, however, up to 50% of enteric duplications cysts are found in the small bowel, with the ileum being the most frequent site of origin.[1] They typically arise from the mesenteric margin of the bowel, and multiple duplications may be present.[1–4] They tend to share a common blood supply with the bowel segment of origin.

Over 80% are diagnosed in the paediatric population and they often present with obstruction or a palpable mass.[4] In adulthood, EDCs are often asymptomatic and diagnosed incidentally. The clinical presentation of symptomatic EDCs varies according to their location and proximity to adjacent structures, symptoms include abdominal pain, distention, mass and dysphagia.[2] They may also present secondary to complications such as haemorrhage, volvulus, perforation, obstruction and malignancy. Ultrasound and abdominal CT may be helpful in establishing a diagnosis, however, the lack of common clinical features and their rarity make pre-operative diagnosis a challenge. Multiple case reports describe the difficulty in differentiating an enteric duplication cyst from the more common MD due to similar clinical manifestations and complications.[5,6] This case report reaffirms this diagnostic challenge.

To date, there is no consensus on the management of asymptomatic cases. Surgery is recommended for symptomatic cases and in the setting of complications.[4] Malignant transformation is a rare but significant complication of EDC's.[7] A previous review reported that 23% of adult EDCs originating from the ileum had histological evidence of small bowel adenocarcinoma.[8] Therefore, the potential for malignancy should always be considered and incorporated into the decision-making process, particularly in the management of asymptomatic cases in adults.

Competing interests:
Nil.

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https://www.nzma.org.nz/journal/read-the-journal/all-issues/2010-2019/2018/vol-131-no-1474-4-may-2018/7560

REFERENCES:

1. Teeple EA, Conway MK. Enteric duplication cyst in a 33-year-old man. Am Surg. 2009; 75(4):350–2.
2. Otter MI, Marks CG, Cook MG. An unusual presentation of intestinal duplication with a literature review. Digestive Diseases and Sciences. 1996; 41(3):627–9.
3. Kim SK, Lim HK, Lee SJ, Park CK. Completely isolated enteric duplication cyst: Case report. Abdominal Imaging. 2003; 28(1):12–4.
4. Gumus M, Kapan M, Gumus H, Onder A, Girgin S. Unusual noncommunicating isolated enteric duplication cyst in adults. Gastroenterology Research and Practice. 2011;(no pagination)(323919).
5. Hamza AR, Bicaj BX, Kurshumliu FI, Zejnullahu VA, Sada FE, Krasniqi AS. Mesenteric Meckel's diverticulum or intestinal duplication cyst: A case report with review of literature. International Journal of Surgery Case Reports. 2016; 26:50–2.
6. Kim YS, Kim DJ, Bang SU, Park JJ. Intestinal Duplication Cyst Misdiagnosed as Meckel's Diverticulum. Chin Med J. 2016; 129(2):235–6.
7. Fletcher DJ, Goodfellow PB, Bardsley D. Metastatic adenocarcinoma arising from a small bowel duplication cyst. European Journal of Surgical Oncology. 2002; 28(1):93–4.
8. Fletcher DJ, Goodfellow PB, Bardsley D. Metastatic adenocarcinoma arising from a small bowel duplication cyst. European Journal of Surgical Oncology. 2002; 28(1):93–4.
9. Johnson JA, 3rd, Poole GV. Ileal duplications in adults. Presentation and treatment. Arch Surg. 1994; 129(6):659–61.

A case of skeletal fluorosis?

Michael Godfrey

A 79-year-old lady presented with a history of diffuse sero-negative arthritis dating from early adulthood. Numerous investigations and therapies had failed to provide any significant benefit and both knees and a hip had been replaced when initially seen a year ago. On questioning at that time, she admitted to daily drinking at least six cups of black tea since childhood. She lives in a retirement village where there has not been water fluoridation since 1994. However, her fasting fluoride results (Medlab) were elevated:

- Serum fluoride 2.5µmol/L (Ref. range 0.3–2.2)
- Urine fluoride 58µmol (Ref. range 0–31)
- Fluoride: creatinine ratio 13.5µmol (Ref. range 0–3.1)

She used a standard fluoridated toothpaste but was otherwise not on any fluoridated medications. However, given the fact that her preferred tea exceeded 3mg fluoride/L[1] it is possible that she has been unwittingly overdosing for many years. Skeletal fluorosis from tea has been identified.[2] Furthermore, excessive use of fluoridated toothpaste caused severe arthritis initially diagnosed as ankylosing spondylitis with full recovery after stopping exposure.[3] A year after stopping black tea drinking and changing to a herbal non-fluoridated toothpaste, this elderly woman's joint pain levels had markedly decreased with considerably improved mobility enabling her to have a long-awaited trip overseas.

Discussion

Fluoride exposures are pervasive. Traditionally, this country has been a major tea consumer and the consequences of fluoride in tea have recently been extensively covered with one cup of the most widely consumed tea brands supplying over 1mg of fluoride per teabag even without any added water fluoridation.[1] Absorption of fluoride from toothpaste at 1,000ppm are considerable and equivalent to, or more than from a cup of tea.[1,4] Fluoride is present in beverages, and in over 200 pharmaceuticals with some being given on a long-term daily basis, eg, atorvastatin, fluvastatin, fluticasone, celecoxib and fluoxetine.

Long-term accumulative exposures to fluoride even at low levels carries a risk of sub-clinical or stage-1 musculo-skeletal fluorosis presenting as joint pain or arthritis.[5] Notably, arthritis is a leading cause of disability with 647,000 now affected in this country and annual costs exceeding $3 billion.[6] Chronic pain was also reported in a New Zealand community study with the most common pain locations being lower back (59%), pelvis/abdomen (49%), joints (39%), neck (34%), muscle (31%) and headache (31%).[7] It would thus be logical to include possible fluorosis in the differential diagnosis of these patients with at least urine fluoride assessments. Notably, this woman's serum fluoride level was considerably higher than that of women in her age group living in a low fluoride area, with a mean serum level of 0.56µmol/l and 0.948µmol/l being the highest recorded with impaired renal function.[8]

Prescriptions for arthritis are among the highest on Pharmac lists with similar health problems being recorded in the Republic of Ireland, the heaviest tea-drinking nation and with long-term nationwide fluoridation. Notably, excessive tea consumption can cause skeletal fluorosis[2] as can toothpaste.[3] The accumulating evidence could suggest that the population is potentially being overdosed with fluoride and certainly exposed to far more than the initial well-intentioned dental hypothesis of 1mg/day for caries prevention proposed in the US 70 years ago.

The findings in this case would indicate that further primary health investigations are warranted and for those interested, Dr Susheela, a leading fluoride researcher, gives a useful diagnostic protocol.[9] Notably, the evidence presented here is but a fraction of the available peer-reviewed literature, demonstrating the potential for harm from this element as reviewed by Peckham and Awofeso.[10]

Competing interests:
Nil.
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REFERENCES:

1. Waugh DT, Godfrey M, Limeback H, Potter W. Black Tea Source, Production, and Consumption: Assessment of Health Risks of Fluoride Intake in New Zealand. J Environ Public Health (2017) 5120504. doi: 10.1155/2017/5120504. http://www.ncbi.nlm.nih.gov/pubmed/28713433
2. Kakumanu N, Sudhaker D, Rao SD. Skeletal Fluorosis Due to Excessive Tea Drinking. N Engl J Med 2013; 368:1140 DOI: 10.1056/NEJMicm1200995.
3. Kurland ES, Schulman RC, Zerwekhm JE, Reinus WR, et al. Recovery from skeletal fluorosis (an enigmatic, American case). J Bone Miner Res. 2007 Jan; 22(1):163–70.
4. Ekstrand J, Koch G, Petersson LG. Plasma fluoride concentrations in pre-school children after ingestion of fluoride tablets and toothpaste. Caries Research. 1983; 17(4):379–384. doi: 10.1159/000260691. [PubMed] [Cross Ref
5. Fluoride in Drinking Water: A Scientific Review of EPA's Standards Chapter 5 Musculoskeletal Effects. ISBN 978-0-309-10128-8 | DOI 10.17226/11571
6. www.arthritis.org.nz (accessed January 2018).
7. Swain N, Johnson M. Chronic pain in New Zealand: a community sample. The New Zealand Medical Journal. 2014; 127(1388):21–30. [PubMed]
8. Itai K, Onoda T, Nohara M, Ohsawa M, et al. Serum ionic fluoride concentrations are related to renal function and menopause status but not to age in a Japanese general population. Clinica Chimica Acta 411 2010; 263–266.
9. Susheela AK. Fluorosis and Associated Health Issues Indian Journal of Practical Pediatrics 2015; 17(2):138.
10. Peckham S, Awafeso N. Water fluoridation: A critical review of the physiological effects of ingested fluoride as a public health intervention. The Scientific World Journal (2014) Volume 2014, Article ID 293019, 10 pp. http://dx.doi.org/10.1155/2014/293019

Considering the issue of euthanasia

Grant Gillett

This journal has recently published a critique of the report on euthanasia that I authored for consideration and discussion by the NZMA.[1] That report took a very pro-life and anti-euthanasia position. It did so in the light of major changes in medicine and patient education, some of which have been highlighted by the critique. It is true we now work with a much more informed and empowered patient body who, by and large, have a clearer understanding of their illnesses than what used to be the case in the past. It is also true that patients' voices are increasingly being heard and acknowledged as an important part of treatment planning. Those voices seem to range across the spectrum on this issue and, where legislation has been carefully drafted, it should endorse controlled and life-affirming care in dying by recommending a policy that does not lightly give away a hard-won respect for and valuation of life in conditions of great personal loss and despair. That reaffirms the profession's traditional stance on this issue and seems commendably to put a high value of human life even where the person whose life it is has lost sight of that. It is informed, in part by a recognition of the soft and sometimes fuzzy divide between unbearable suffering which cannot be relieved and despair at one's own end-of-life prospects. That mix is not easily discerned or negotiated with the skill required in risky clinical dilemmas, and opening the door, however cautiously, to assisted dying is a policy fraught with dangers. If doctors find such situations hard, then the distress, despair and unbearability of suffering must be even harder for those who do not have an educated and experienced grip on the value of life in the extremes to which disease can take us. A chink of an opening can easily become a point of fixation for a suffering person and intensify the felt need to escape by ending it all. That can make life-affirming care in dying near impossible to hold on to as one contemplates the fact that it is another who is suffering and who one is asking to bear it with whatever help one can give.

Many of the points in the recent appraisal of the NZMA document are cogent and require our respect and attention in the interest of most adequately dealing with our patients in extremis. It is true that a doctor does not have the experience that his or her suffering patient is having to endure and that medical professionals are heavily inclined towards treatment and life, even (sometimes) to the point where all realise it is no longer kind and caring to force that journey to continue or to impede the way to its inevitable end. Those of us in acute and extreme neurological care have had to absorb that painful and deeply challenging lesson. It is also true that suffering which cannot be endured and which should not be allowed to continue is difficult to assess with objectivity or any medical certainty; at that point empathy and appreciation of the ordeal of the patient are qualities which must inform terminal care. Therefore the conduct of VAD (voluntary assisted dying) practice in Belgium, the Netherlands, Canada and Oregon and its relationship to palliative services deserves the most careful consideration. The Australian statement does not really engage with the distress of one's own imminent death despite its endorsing the need for quality hospice care. "The major patient advocacy groups" may, however, not include the most abject and vulnerable among us. The apparently innocuous statement that "for the individual, life is precious only when it is worthwhile" admits of many interpretations especially when we consider the tangled mix of self-evaluation and quasi-objective considerations that may shape a sense of one's own worthwhileness or the value of one's life.

One must commend the move in legislation that mandates referral to hospice or palliative care, as this is bound to improve quality of care and expertise available for those who are inclined to think that their only viable option going forward is to hasten their own death. It is heartening to know that the situation in Belgium is less worrying than initially seemed to be the case and a comprehensive end-of-life care referral process is to be commended.

Irrational suicide may have a different clinical profile from VAD but the sense that life has nothing worthwhile left to offer remains a point of convergence (mitigated of course by the possibility of a multi-faceted referral in a wrap-around end of life service and the deeply supportive values informing hospice care. Any move which makes that more likely and accessible ought to be encouraged. The deeply taxing end-of-life journey for those who must share it through their commitment to the patient, and particularly for a compassionate doctor is a welcome note to strike when one considers the distress that those who care for the person at its centre must either face in person or witness.

I am not a doctor who champions a commitment to prolong life at all costs and indeed have championed a more nuanced position in severe head injury where the values of patient care and compassion espoused by the CMA might lead to a limitation of life-extending treatment. The NZMA should be constructively involved if there is to be a new legal framework for compassionate ethical and medical responses to the difficult issues surrounding death and dying. It is important that these are responsive to the considered voice of the New Zealand community and that its law-givers are informed by the values that as ethicists we strive to uphold on behalf of doctors and we ought to encourage respectful dialogue with patients. We should however, remain wary about conflating what is intolerable to a patient with what we, as clinicians, are inclined to regard as intolerable. The latter is as difficult to endure as it is to succinctly outline but the difficulties of making the case should not open the door to doctors killing their patients, even where the patient requests that. What may be done only rarely if ever can become an accepted part of our professional culture, especially when the considerations against it cannot succinctly or easily be stated but lie deep within an ethos that is foundational to medical values.

Competing interests:
Nil.

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https://www.nzma.org.nz/journal/read-the-journal/all-issues/2010-2019/2018/vol-131-no-1474-4-may-2018/7562

REFERENCES:

1. Havill J, Smales L, Williams M, Kueppers F. Evaluation of the Report on Euthanasia for the New Zealand Medical Association by Grant Gillett. 2018; 131(1468):85–88.

A New Zealand osteoarthritis model of care in South Canterbury, New Zealand

Sharon K Peck, Janice E Mueller, Jennifer L Murphy

We read with interest the Viewpoint article by Baldwin and colleagues published in the December edition of the NZMJ, advocating for a model of care for osteoarthritis for New Zealand.[1] While such models have not been systematised across New Zealand, there are successful local models such as our community-based osteoarthritis programme in South Canterbury, the Physiotherapy Primary Intervention Group (PPIG), which targets adults with mild to moderate hip and knee arthritis.

The PPIG was formed in 2011 by seven physiotherapists in response to an identified need and service gap regarding the management of osteoarthritis in the South Canterbury (SC) region; minimal services were available to manage arthritis prior to joint arthroplasty. Treatment was disparate, episodic and siloed, with large numbers of the community disadvantaged by their rurality (50% of the region's population lives rurally) and lower-than-average economic status. Furthermore, SC's percentage of older adults over 60 years (28.6%) is higher than the national average (20.8%).[2]

The PPIG model of care

PPIG looked at the multifactorial aspects of the disease's impact on the patient and local and national health services, and recognised that an interdisciplinary collaboration was required to address the disease impact factors that were identified in the published evidence. By engaging patients in an early, conservative intervention, it was hoped that benefits would be seen with a reduction in pain, disability and indirect costs, such as hospital service involvement and loss of productivity.

Following a successful pilot of 24 patients in 2011, PPIG was contracted by South Canterbury District Health Board (SCDHB) to deliver a physiotherapy-led, community-based osteoarthritis self-management and exercise programme. As recommended by many authors, PPIG modelled their programme on international guidelines, existing models of care and contemporary evidence.[3–8] The programme is standardised for all groups of participants to ensure consistent data collection.

The programme itself encourages self-management through education, community involvement and a 12-week series of one-hour group exercise and education classes for six to eight participants, using a wellness approach. After assessment, participants receive an individualised exercise programme recognising their personal goals, problems and locality, run by specially-trained local physiotherapists. The extended multidisciplinary team available to participants includes dietitians, occupational therapists, orthopaedic surgeons, mental health services, pharmacists, smoke-free facilitators, general practitioners, clinical nurse specialists and podiatrists. The physiotherapy-led classes are held in local community gymnasiums, with a strong emphasis on deep joint stability, posture, functional performance, self-care and pain management, using exercises that are reproducible at home. By negotiating subsidised gym memberships and encouraging swimming and walking groups, the participants are encouraged to continue exercising once the programme has finished. Additionally, regular follow-ups with each group over three years following completion of the classes, engenders a greater confidence in self-management and compliance with exercises, and provides support throughout their arthritis journey.

Our results

Between 2011 and 2016, 196 participants (293 joints) were treated. The median age was 63 years, with a 96% programme completion rate. The largest referral sources were orthopaedic surgeons (50%), general practitioners (33%) and other physiotherapists (10%).

The range of outcome measures used included the Western Ontario McMasters Universities Arthritis Index (WOMAC), Stanford Chronic Disease Efficacy and Exercise Behaviour questionnaires, and the Six-Minute Walk Test. All outcome measures showed statistically significant improvements between the start and end of the programme with maintenance of the improvement in 80% of participants at three-year follow up. For most measures, the effect sizes showed improvements in the large to very large range.

The PPIG programme is cost effective in reducing the number of joint arthroplasties required by participants, compared with expectations prior to programme involvement. For those patients who subsequently still required a joint replacement, post-surgical rehabilitation was enhanced.

Community engagement

The SCDHB website has a link to PPIG information for consumers and referrers via HealthInfo.[9] Steps have also been taken to support involvement with Māori consumers through engagement with local Māori healthcare providers.

In 2017, PPIG were successful in bidding for a Ministry of Health contract under Tranche 1 of the Mobility Action Programme (MAP) funding[10] to deliver additional classes to rural communities in South Canterbury. We would welcome a strong public policy approach that addresses New Zealand's increasing osteoarthritis burden as our population ages.

Competing interests:
PPIG holds a contract with SCDHB to deliver this community-based exercise programme.

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https://www.nzma.org.nz/journal/read-the-journal/all-issues/2010-2019/2018/vol-131-no-1474-4-may-2018/7563

REFERENCES:

1. Baldwin J, Briggs A, Bagg W, Lamer P. An oseoarthritis model of care should be a national priority for New Zealand. N Z Med J 2017; 130(1467):78–86.
2. Population of South Canterbury DHB [internet]. Ministry of Health NZ; 2018 [cited 18 March 2018]. Available from: http://www.health.govt.nz/new-zealand-health-system/my-dhb/south-canterbury-dhb/population-south-canterbury-dhb
3. Zhang W, Moskowitz RW, Nuki G, et al. OARSI recommendations for the management of hip and knee osteoarthritis, Part II: OARSI evidence-based, expert consensus guidelines. Osteoarthritis and Cartilage 2008; 16(12):1585.
4. NICE. Osteoarthritis: the care and management of osteoarthritis in adults. NICE clinical guideline 177. United Kingdom: London; 2014. Available from: http://www.nice.org.uk/guidance/cg177
5. Royal Australian College of General Practitioners. Guideline for the non-surgical management of hip and knee osteoarthritis.

2009. Available from: http://www.racgp.org.au/download/documents/Guidelines/Musculoskeletal/racgp_oa_guideline.pdf

6. Ottawa Panel Evidence-Based Clinical Practice Guidelines for Therapeutic Exercises for Manual Therapy in the Management of Osteoarthritis. Physical Therapy. 2005; 85:907–971.
7. McAlindon T, Bannuru R, Sullivan M, Arden N, Berenbaum F, Bierma-Zeinstra S et al. OARSI guidelines for the non-surgical management of knee osteoarthritis. Osteoarthritis and Cartilage. 2014; 22(3):363–388. Available from: http://dx.doi.org/10.1016/j.joca.2014.01.003
8. Larmer PJ, Reay ND, Aubert ER, et al. Systematic review of guidelines for the physical management of osteoarthritis. Arch Phys Med Rehabil 2014; 95(2):375–89.
9. Health Info Aoraki//South Canterbury [Internet]. [Cited 14 March 2018]. Available from: http://www.healthinfo.org.nz/Aoraki/
10. Mobility Action Programme Projects [internet]. Ministry of Health NZ; 2018 [cited 14 March 2018]. Available from: http://www.health.govt.nz/our-work/preventative-health-wellness/mobility-action-programme/mobility-action-programme-projects

Rivaroxaban with or without aspirin in patients with stable coronary artery disease

Coronary artery disease is a major cause of morbidity and mortality worldwide, and is a consequence of acute thrombotic events involving activation of platelets and coagulation proteins. Factor Xa inhibitors and aspirin each reduce thrombotic events but have not yet been tested in combination or against each other in patients with stable coronary artery disease.

This trial involved 24,824 appropriate patients who were randomly assigned to receive rivaroxaban (2.5mg orally twice a day) plus aspirin (100mg once a day), rivaroxaban alone (5mg orally twice a day) or aspirin alone (100mg orally once a day). The primary outcome sought was myocardial infarction, stroke or cardiovascular death.

The investigators report that in patients with stable coronary artery disease, addition of rivaroxaban to aspirin lowered major vascular events, but increased major bleeding. There was no significant increase in intracranial bleeding or other critical organ bleeding. There was also a significant net benefit in favour of rivaroxaban plus aspirin and deaths were reduced by 23%. Thus, addition of rivaroxaban to aspirin has the potential to substantially reduce morbidity and mortality from coronary artery disease worldwide.

***Lancet* 2018; 391:205–18**

Trial of prazosin for post-traumatic stress disorder in military veterans

In randomised trials, prazosin, an α1-adrenoreceptor antagonist, has been effective in alleviating nightmares associated with post-traumatic stress disorder (PTSD) in military veterans. This trial was undertaken to elucidate as the previous trials included smaller number of participants and a briefer follow-up period.

Half of the 304 participants were assigned to prazosin and the other half received placebo for 26 weeks. The dose of prazosin was escalated over the first five weeks to a daily maximum of 20mgms in men and 12mgms in women.

The conclusion reached was that in this trial involving military veterans who had chronic PTSD, prazosin did not alleviate distressing dreams or improve sleep quality over 10 or 26 weeks.

N Engl J Med 2018; 378:507–17

Use of electronic cigarettes

This interesting paper is a comprehensive review of the use of e-cigarettes in Australia. Apparently 1.2% of Australians aged 14 years or older use them. The younger people try them out of curiosity and the older as a less harmful alternative to tobacco smoking.

There is strong evidence that they are effective in reducing the incidence of tobacco smoking. There appears to be no harm in the short term, apart from irritation of the mouth and dry cough. However, the long-term effects are not yet known. It has been suggested the use of e-cigarettes may entice the young to smoke tobacco—the so-called gateway effect.

The author concludes that there is substantial evidence that the use of e-cigarettes is effective in helping smokers to cease using tobacco. Although not completely harmless they are substantially less harmful than smoking tobacco.

Internal Medicine Journal 2018; 48:391–396

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The (Protopathic) Sensory Nerve Areas of the Hand

By Arthur S Herbert, Major, N.Z.M.C., P.M.O., Rotorua Military Hospital

Gunshot wound of the arm, owing to the frequency with which the nerve trunks are involved, has made most of us revise our anatomy. Of course, in the majority of cases a glance at the resultant deformity of the hand makes it obvious at once which of the main nerve trunks is involved; but when more than one nerve is affected the matter is not always as simple, and it becomes important to map out accurately the anaesthetic areas. Before the war we all realised in a general sort of way that the ulnar nerve supplied the little and half the ring finger; that the median and radial supplied the other half of the ring finger, the middle and fore fingers, and most of the thumb; and that the radial branch of the musculo-spiral supplied the back of the base of the thumb: the present frequency of nerve lesions has made us appreciate more accurately the distribution of these nerves and caused us to modify our ideas of the unalterable nature of their distribution.

Of the four nerves supplying the hand, the ulnar is the most constant in its distribution, and vagaries of area are quite rare. Occasionally, however, there is no branch to the ring finger and the whole of this finger is supplied by the median nerve. I have only met this latter condition twice amongst all my cases, and the phenomenon would appear to be due to conduction via the communicating filaments from the radial and median nerves.

One fallacy has to be guarded against: the case may be examined when in a recovering condition, and the ulnar nerve tends to recover in a definite sequence of areas. Thus sensation returns first either on the ulnar edge of the hand or on the ulnar surface of the first phalanx of the ring finger. The little finger, and especially the distal phalanx of the little finger, may continue anaesthetic for months after the other areas have recovered, and a hand examined at this stage may give apparently abnormal results.

The remaining area of the hand is much more variable in nerve-distribution, owing, apparently, to the varying degree of anastomosis of the nerves concerned, the median, radial branch of the musculo-spiral, and the musculo-cutaneous, so that there is, except in two areas, a debatable “no man’s land.”

These two areas are the dorsum of the two distal phalanges of the fore and mid fingers, which is claimed to be the exclusive territory of the median nerve, and a pear-shaped area on the dorsum of the hand between the metacarpals of the thumb and forefinger, which is supplied by the radial branch of the musculo-spiral alone. With a view to defining this latter area, highly important from a diagnostic point of view, I mapped it out in a large number of uncomplicated cases of complete musculo-spiral paralysis. The diagram Fig. I. shows the results in four consecutive cases. It will be noted that, while the area varies widely in every case, yet a certain pear-shaped area, shown shaded, remains common to all.

Figs II. and III. show the areas of anaesthesia in two cases of median nerve injury, uncomplicated by injury of the other nerves.

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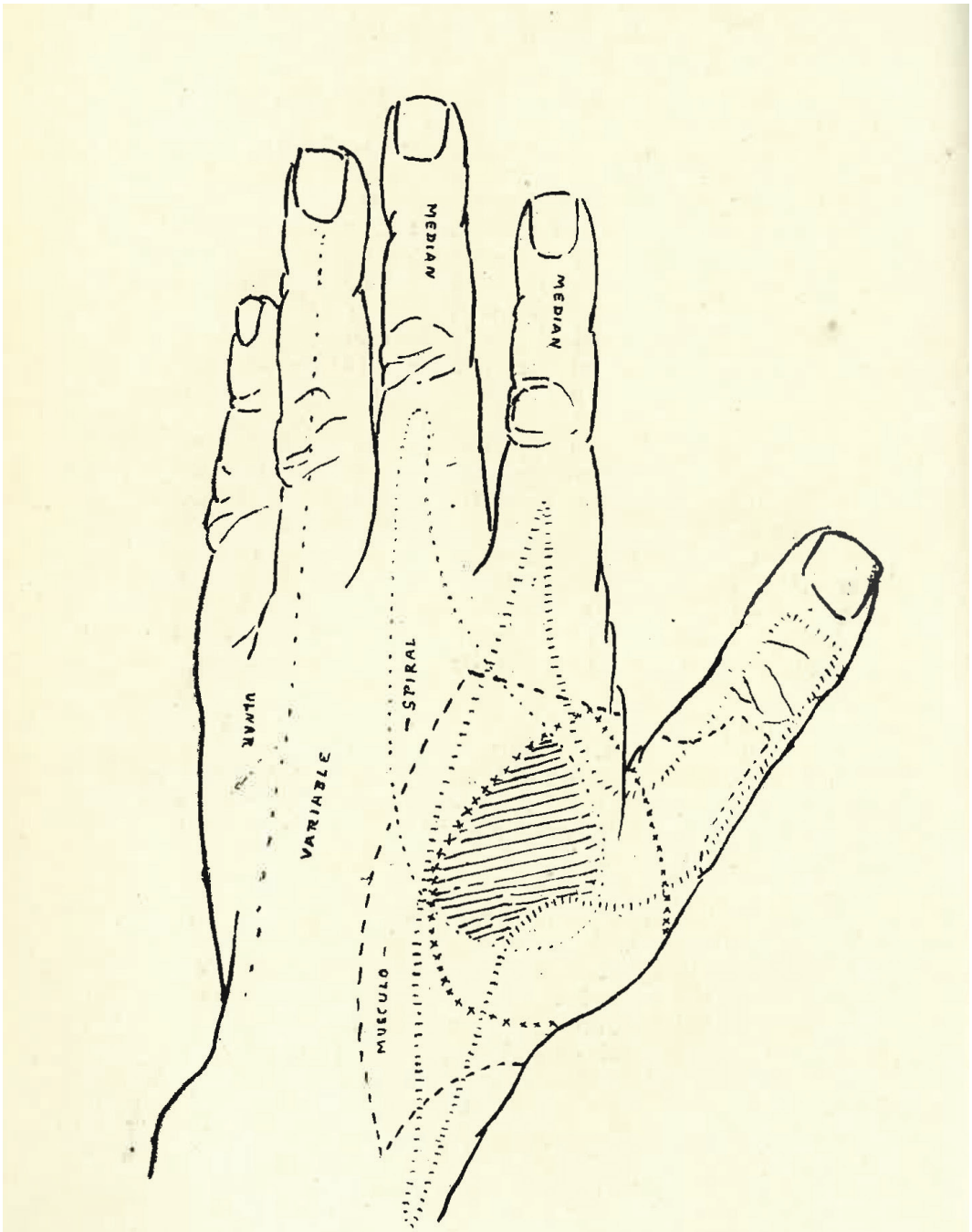

FIG. I.

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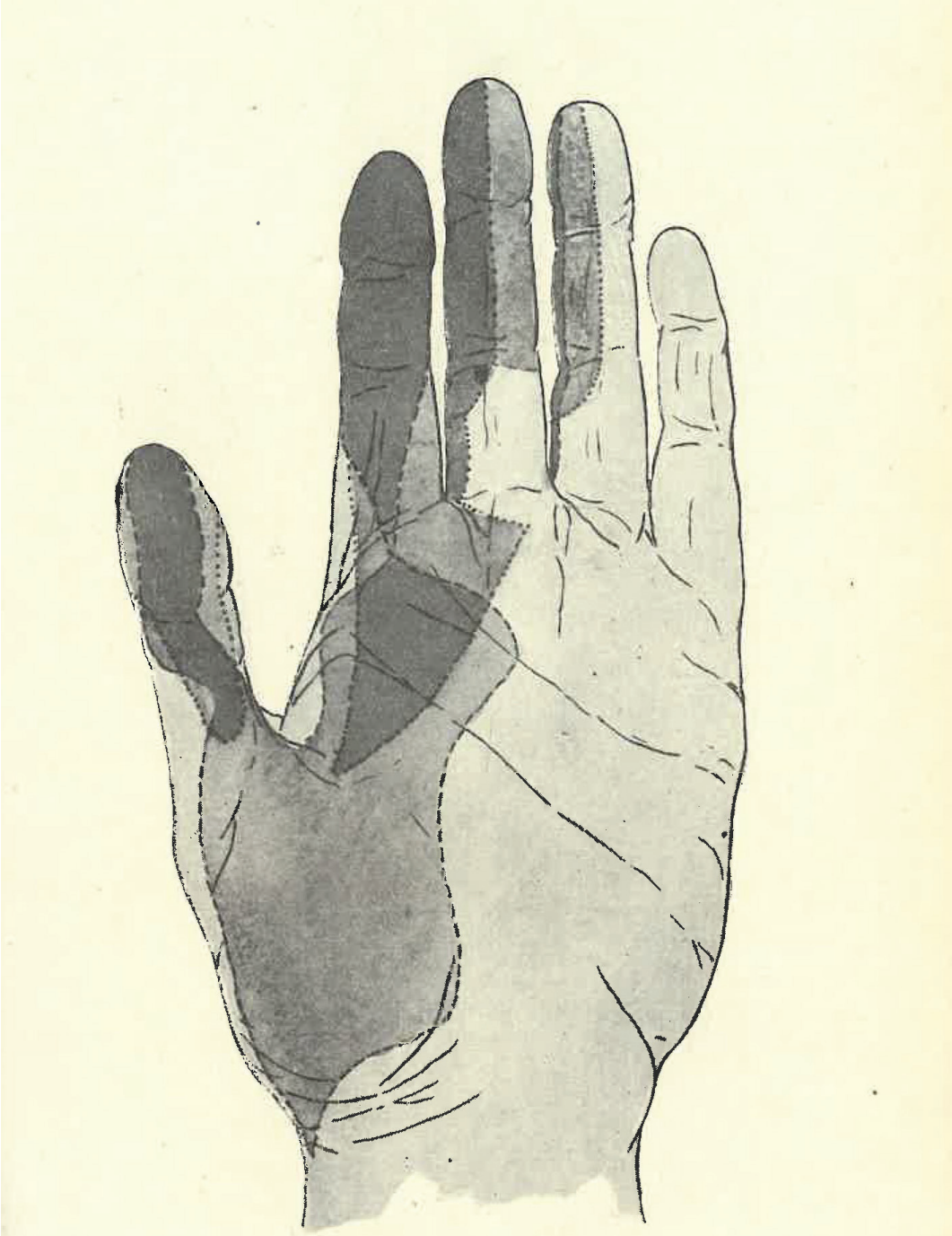

FIG. II. MEDIAN I.

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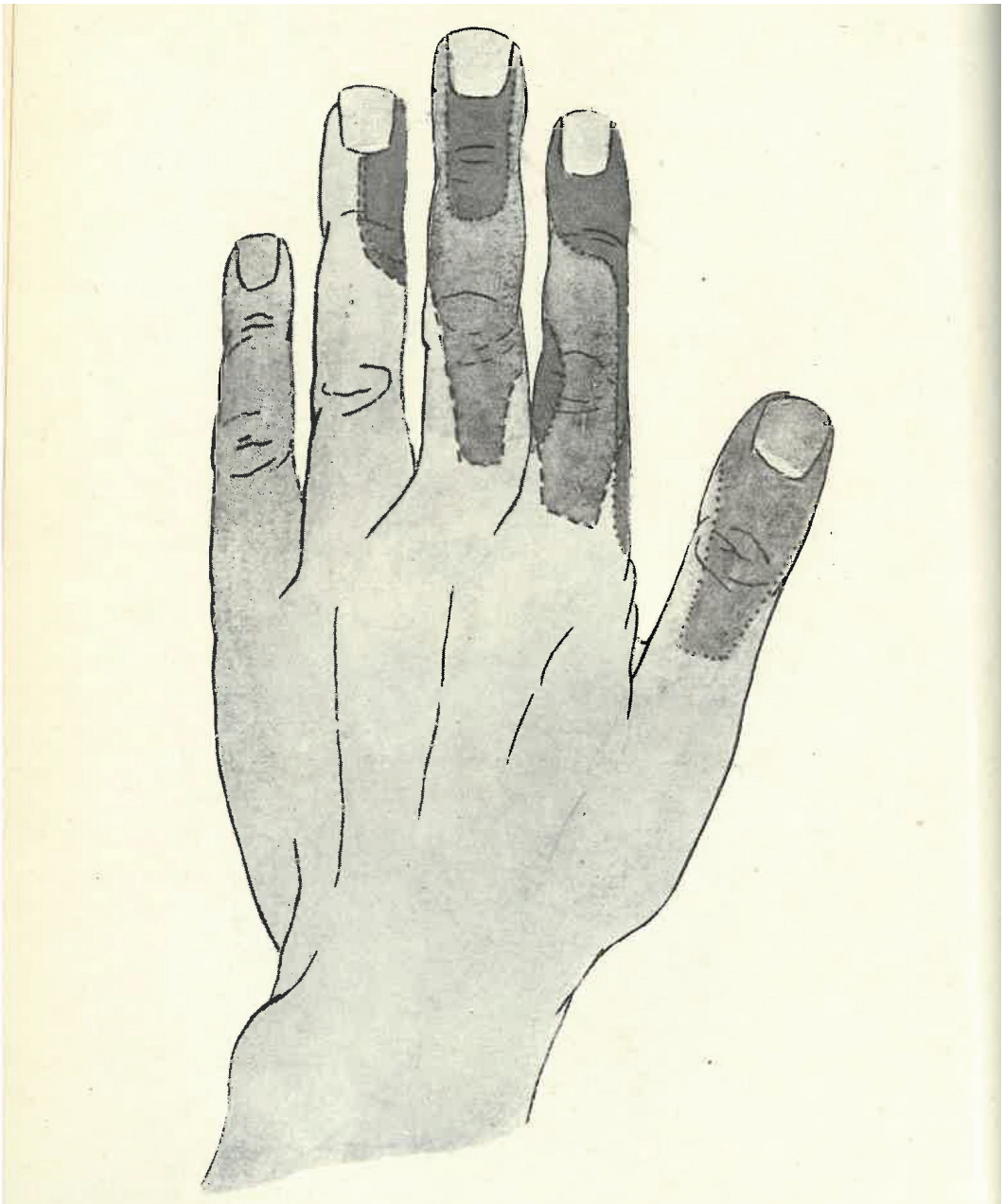

FIG. III. MEDIAN II.

MEDIAN NERVE ANAESTHESIA.

The dotted lines outline the area of anæsthesia in Case I., the broken lines the area in Case II.
The darkest areas show the territory common to both cases.

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