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Target CLAB Zero: A national improvement collaborative to reduce central line-associated bacteraemia in New Zealand intensive care units

Jonathon Gray, Suzanne Proudfoot, Maxine Power, Brandon Bennett, Sue Wells, Mary Seddon

The use of central line catheters (catheters inserted into blood vessels near the heart) to deliver treatment into a patient's blood stream and monitor their progress is common practice in New Zealand ICUs. However, the process creates a potential entry point for infection. Such infections are known as central line associated bacteraemia (CLAB). Target CLAB Zero was a national campaign led by Ko Awatea that reduced the incidence of CLAB in intensive care units to one-tenth of its previous level, saving much harm and about $0.5 million per annum. It was the first quality improvement campaign to bring together all New Zealand district health boards in collaboration.

Randomised controlled trials cited in pharmaceutical advertisements targeting New Zealand health professionals: do they support the advertising claims and what is the risk of bias?

Alison Ma, Lianne Parkin

Randomised controlled trials (RCTs) are the best way to determine whether one treatment works better than another (or no treatment) – providing they are done well. Pharmaceutical (drug) advertisements are commonly found in publications which are read by health professionals. Internationally, there is concern that the therapeutic claims made in some advertisements are not supported by good evidence and might have a negative impact on what doctors prescribe. We systematically examined the advertisements in two publications directed at New Zealand health professionals and found that only 35% of therapeutic claims referred to an RCT as supporting evidence. Moreover, in 19% of cases the RCT did not support the claim, and in only 8% of cases was the claim supported by an RCT with a low risk of bias.

Hospital admissions for non-cystic fibrosis bronchiectasis in New Zealand

Susan Bibby, Richard Milne, Richard Beasley

Bronchiectasis is a chronic lung condition, usually caused by damage to the lungs from a serious childhood infection, and leading to in recurrent lung infections. Here we show that there is a significant burden for New Zealanders and the New Zealand health system due to bronchiectasis. People admitted to hospital due to this condition are much more likely to be of Maori and Pacific descent, and more likely to be young children and elderly people, from low socioeconomic areas. There is a seasonal variation, suggesting that the cold and damp in winter and spring makes this condition more likely to flare up. We recommend that further research is done into why this disease is more common in these populations, and what can be done to better treat and prevent it.

Understanding administrative coding of emergency department visits for unspecified acute allergic reactions

Colleen McMilin, Carlos Camargo Jr, Susan Morton, Cameron Grant

In many countries increasing numbers of children are being reported as being affected by food allergy. The most severe allergic reactions to food can be life threatening and can require the child to attend the hospital emergency department. We reviewed paediatric emergency department visits to Auckland City Hospital from 1988 to 2011. We showed that that hospital emergency department presentations for food-related allergic reactions have increased over time in Auckland.

What have five years of the shorter stays in the emergency department health target done to us?

Michael Ardagh

This paper reviews the first five years of the Shorter Stays in the Emergency Department national health target – its genesis, implementation and impact. Five years of the target have seen a maturing 'whole of system' collaboration leading to better patient care. However, there is still much to do and demand continues to increase. Assisted by the 'Quality framework and suite of quality measures for the Emergency Department phase of acute patient care in New Zealand,' a good structure and methodology driving improvement, and a patient centred focus, this work must continue.

Regulating our emergency care paramedics

Bronwyn Tunnage, Andrew Swain, David Waters

Patients have a right to know that the people who care for them are fully qualified, up to date, and practising safely. In New Zealand the law requires a wide range of healthcare professionals to be registered in order to monitor standards. However, even though ambulance paramedics care for over 450,000 patients each year and perform advanced medical skills, in New Zealand they are not registered healthcare professionals.

Partnership and rigor in improving patient care

Alan F Merry, Richard Hamblin

The Health Quality and Safety Commission (HQSC) was created in 2010 to promote improvement in health and disability services for all New Zealanders. One way to improve outcomes for patients is through implementing evidence-based guidelines to reduce inappropriate variation in practice. Unfortunately this is notoriously difficult to do.[1-3] In this edition of the Journal, Gray et al report the latest episode in a story about such an endeavour that has been a notable success—first overseas, then in Counties Manukau and now in New Zealand nationally.[4]

The story began just over fifteen years ago at Johns Hopkins Hospital in Baltimore, where Peter Pronovost (an intensivist) led the successful implementation of an infection control guideline to reduce central line associated bacteraemia (CLAB)—a problem previously held to be integral to the use of central venous lines (CVLs).[5] Pronovost's team used a novel improvement model that drew from principles in the human factors literature and also addressed barriers to the uptake of guidelines identified by Cabana et al.[1] The model included four relatively generic interventions to improve the sterile insertion of a CVL.

1. Education: about the problem and the solution.
2. Facilitation of compliance: in this case, creating a catheter insertion cart to provide everything needed to follow the guidelines.
3. A checklist: to avoid missing key elements of the guidelines.
4. Insistence on compliance: empowerment of nurses to stop the procedure if the guidelines were not followed.

It is relevant that the elements of the guideline on CVL insertion itself (hand hygiene, chlorhexidine skin antisepsis, maximal barrier precautions, optimal catheter site selection) were supported by evidence.[6] A further evidence-based element was implemented as a fifth, less generic, intervention:

5. Asking daily (in the ICU or on the ward) whether the inserted central venous catheters could be removed and prompt removal when no longer needed.

The median rate of CLAB per 1,000 catheter days decreased from 11.3 infections in the first quarter of 1998 to zero in the last quarter of 2002. It was estimated that 43 CLABs, eight deaths, and USD 1,945,922 had been saved. In the now famous Keystone Project, Pronovost and his team then implemented this "bundle" in 108 ICUs in the state of Michigan (103 reported data). The mean rate of CLAB per 1,000 catheter-days decreased from 7.7 infections at baseline to 1.4 a year and a half later.

Dr Mary Seddon, in her role as Clinical Director of the Quality Improvement Unit at Counties Manukau District Health Board, noticed this work and engaged senior ICU clinicians at Middlemore Hospital in discussions on its merits. She gained agreement to adopt four out of five of the elements of the bundle (subclavian placement being the exception). This group reduced the mean CLAB rate in their intensive care unit (ICU) per 1,000 line days from 6.6 in 2008 to 0.9 in 2010. They estimated cost savings at NZD 200,000 in 2009 and NZD 260,000 in 2010.[6] They then extended this initiative to the rest of Middlemore Hospital, and decreased the hospital-wide rate of CLAB per 1,000 days from 7.04 to 1.37.[7]

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It has been alleged that New Zealand's 20 DHBs often fail to learn from each other. Not so this time. These extraordinary gains in patient safety have now been extended to the whole country. The national average rate of CLAB per 1,000 line days has been reduced from 3.32 at baseline to 0.28 in March 2013. Between April 2012 and March 2013, an estimated 90 incidents of CLAB were prevented with a savings of NZD 1.8 million. More importantly, much suffering and some loss of life has been averted. Furthermore, the changes in practice that have brought about this substantial improvement in patient safety appear to have become embedded in New Zealand practice. Data from the HQSC show that the reduction in CLAB rate has been maintained, with fewer than 0.5 CLABs per 1,000 line days since March 2013. There were only 28 instances of CLAB in the entire country between April 2013 and December 2014, 160 fewer than would have been expected had the baseline rate continued. HQSC have calculated that by December 2014, the savings generated by avoided CLABs were in excess of NZD 5 million.

If this story can go from Hopkins, to Michigan, to Middlemore, to New Zealand… is the next step The World? Possibly not. There are many other places where the CLAB bundle has been successfully adopted and implemented (Gray et al provide examples), but the national success reported here would be difficult to replicate in some countries. It is worth reflecting on some of the factors that facilitated this success in New Zealand. In this respect, Gray et al outline several elements of the improvement method as applied by the "CLAB Zero" team more than a decade after the first work at Hopkins. We would like to expand on some of these points and add one or two others.

Foremost to add is the leadership of Mary Seddon in this matter. To have followed the literature, understood its implications and then mobilised support for adopting its messages at Middlemore is impressive enough. In addition, the understanding of the importance of measuring the impact of the practice changes at Middlemore and publishing the results was masterful: the Middlemore data were critical to taking the CLAB Zero campaign nation wide. People seem more compelled by local data than by data from overseas. In part this may reflect something emotive in one's response to information from various sources, but there is also a legitimate question of context. It is not a given that findings from different countries will apply in the particular healthcare setting that pertains in New Zealand. It was worth demonstrating that the problem was as real here as anywhere else and that the solution could be applied here with as much success as in the US. Following root causes (in this case of positive events), one step further back in the chain leads to Geraint Martin, CEO at Counties Manukau. This CEO established or fostered the infrastructure and environment at Counties Manakau that enabled these efforts to succeed—the Quality Improvement Unit directed by Dr Seddon, and the Centre for Health System Innovation (Ko Awatea) directed by Professor Gray. Engagement of senior hospital administrators in the quality of the services their organisations provide is essential for high standards of quality and safety to flourish, and is becoming increasingly apparent in New Zealand. Similarly, the Government, in establishing the HQSC, created a national agency with an explicit focus on improving quality, and therefore was ready, willing and able to partner with, support and fund the team from Ko Awatea in extending this initiative to the whole country. The overall culture of healthcare in New Zealand also deserves credit. The collaborative methodology used in this project will have found fertile ground in our workforce. Our health professionals are highly networked and are already in the habit of working together, inter-professionally, to solve problems. Gray et al mention the peer-led nature of the campaign (Dr Shawn Sturland was the clinical lead), and we agree with the importance of this, both in making the initial change and in ensuring that improvement is sustained and embedded by the time the program concludes. We note that a focus on clinical leads, respected by their colleagues, underpins all the work of the HQSC. Flexibility is also mentioned, and again we agree. Notably, insufficient flexibility to concede on the question of the optimal site of CVL insertion would probably have been a deal breaker.[6] Also, the latter parts of the campaign were probably helped

considerably by the introduction and open publication of a relevant quality and safety marker by the HQSC—this was a novel element of the New Zealand campaign, not seen in previous initiatives or elsewhere, and not necessarily an approach that all who espouse quality improvement over quality assurance would find entirely comfortable. This is to some extent understandable: the potential perverse effects of ill-conceived accountability regimes are well known.[8] However, well-conceived and clinically relevant measures can support quality improvement efforts. It is notable that compliance with the insertion bundle increased even further from 80 to 95% following the introduction of the Quality and Safety Marker.[9] In our opinion, there are many ways to skin a cat, and the worn term "multifaceted approach" has currency.

One of the challenges in improving patient safety is obtaining convincing evidence of success. This raises an interesting question: in the context of healthcare, is there a fundamental difference between quality improvement and research? In the US, this very question was asked about the Keystone Project, and generated an interesting debate in the literature, summarised by Savel et al.[10] One aspect to consider is the question of equipoise and risk to patients. Even in the first chapter of the story, at Hopkins, there was neither equipoise nor risk: the intervention amounted to asking clinical staff to do what everyone agreed they ought to be doing anyway, on the basis of a synthesis of the best available evidence. What was at stake was simply whether clinicians could be persuaded to adopt best practice. This is one distinction that does separate many quality improvement initiatives from more traditional research. However, there are many ways in which good ideas can go astray, and we do not think that this difference reduces the need for the public to be able to rely on the results claimed by those who seek to improve the quality and safety of our health services (Ko Awatea and the HQSC included). Many of the approaches advocated in what is often called "safety science" are aimed at accelerating the process of improvement, for example through the use of iterative plan, do, study, act cycles as seen in this New Zealand project. This accelerated and flexible approach may at times raise questions of rigor when it comes to evaluating results. The Agency for Healthcare Research and Quality recently convened a panel to consider how to improve the conduct and reporting of interventions to improve patient safety.[11] It turns out that there is little difference between the underlying principles of any clinical research and those recommended for robust initiatives to show demonstrable improvement in patient safety. Perhaps after all there is only "science". The starting point should always be a sound theoretical construct—a clear reason why the proposed intervention is likely to produce a particular improvement. The intervention should be described in sufficient detail to allow others to repeat it. Context is critical, and must be adequately described. The process of implementation must also be adequately described, including details of how the intervention changed over time (if it did). Outcomes need to be meaningful. Possible unexpected effects should be reported or discussed. And the health economic implications of the intervention should be considered. In our view, the paper by Gray et al is a good model for a quality improvement initiative that meets these expectations, and we have confidence that the improvements claimed are both real and worthwhile.

It is a great credit to all concerned, most particularly the doctors and nurses who care for patients who need CVLs, that the CLAB bundle is now so embedded in practice in New Zealand that the HQSC has been able to stop monitoring this problem and move its limited resources on to other important priorities for improving the health services of New Zealand. This, perhaps, is the hallmark of worthwhile quality improvement: improvement that has become sustained because a return to former, lower quality approaches has become unthinkable.

Competing interests:
Professor Merry is Chair of the Health Quality & Safety Commission New Zealand (HQSC).

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The art and science of marketing medications

Les Toop, Dee Mangin

The paper by Ma and Parkin[1] highlights, yet again, that we should assume the majority of claims in advertising materials, both to prescribers and to the public, will generally extend well beyond the published scientific evidence cited to justify them. Similar findings have been demonstrated in older and contemporary New Zealand contexts and in other jurisdictions.

We should not be surprised. Advertising is primarily designed for the purpose of selling products. Partial truth and hype is the advertiser's stock-in-trade, misinformation is common and the exaggeration of benefits and minimisation of harm well defined.

The question here is "Why does misleading advertising matter?"

It matters because it has a negative influence on prescribing quality.[2] Poor prescribing adversely influences both health outcomes that matter to patients and increases the costs to the health care system.

There is little regulatory control to counter these influences. The self-governing Advertising Standards Authority in New Zealand, and the self-monitoring codes of practice—designed and policed by industry—are both lax, and complaints and sanctions rarely applied. Penalties for breaches, even if identified, are absent or minimal.[3] In the US, very large (multimillion dollar) fines are often levied for misleading advertising. Given the vast profits from the sale of blockbuster drugs, even fines of this magnitude and out-of-court settlements (with no culpability admitted) are simply seen and accepted as an affordable cost of doing business and often do not prevent repeat offending.

Given the widespread publicity around misleading marketing, it might be hoped readers of the magazines containing these advertisements would pay little or no attention to them. However, the industry's market research suggests otherwise, as do studies of the negative influences of marketing on prescribers.[2] Without a demonstrable positive return on investment, this type of advertising simply would not continue.

It would be impractical in a country the size of New Zealand to centrally vet all advertising claims against even the cited "evidence", and without having access to the complete trial data, it is—and would remain—very difficult to ensure that claims are both evidence-informed and balanced.

Instead, the solution surely lies with prescribers voluntarily distancing themselves from biased industry sources of information, and for regulators, professional bodies, medical journals and academic funding institutions to support and incentivise this distancing. There is a growing chorus of consumer demand and pressure for the profession to disentangle itself from the harmful influence of industry.[4] These influences, of course, extend well beyond colourful advertisements in magazines. For those interested in reading more about the extent of the influence of the pharmaceutical industry, it is well summarised in the extensive UK parliamentary health select committee report.[5] Education of medical graduates is largely lacking in any training of how to recognise and deal with the 'hidden curriculum' of acculturation to industry influence. To assist, the WHO has published a practical training manual for health professionals on the subject.[6]

The public has little understanding of citations and references, and consumer advertisements are full of claims such as "clinically or scientifically proven". Many

mistakenly trust that 'someone' is vetting information with their interests to the fore. In reality, much of the pre-vetting is done by the larger manufacturers themselves.[7] Unfortunately, without scientific training and skepticism, the public are likely to be more vulnerable than clinicians to the beguiling effects of partial, exaggerated, misleading and often emotionally charged "information" that is the hallmark of direct-to-consumer advertising (DTCA).New Zealand remains out on a limb, joined only by the US, in allowing DTCA—a practice which most authorities and clinicians around the globe have decided is of net harm to public health and prohibit it. So effective is DTCA, the European pharmaceutical industry is constantly pushing to allow its legalisation in the European Union, a pressure which has been so far resisted.

Professional colleges and organisations can and should shoulder responsibility and provide leadership by declining industry sponsorship for education, and removing trade stands from their scientific conferences and meetings. There have been encouraging precedents—the RNZCGP has, in recent years, diminished pharmaceutical industry sponsorship to minimal levels. Regrettably the NZMA has moved in the opposite direction with its national CME meetings. It is often said "there is no such thing as a free lunch", and there should be no prescribers so poor they cannot afford to buy their own.

A partnership between consumers and prescribers is necessary to advocate for replacing biased and misleading advertising with independent information that is based on access to all study and trial information.

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Target CLAB Zero: A national improvement collaborative to reduce central line-associated bacteraemia in New Zealand intensive care units

Jonathon Gray, Suzanne Proudfoot, Maxine Power, Brandon Bennett, Sue Wells, Mary Seddon

ABSTRACT

AIM: Central line-associated bacteraemia (CLAB) is a preventable cause of patient morbidity and mortality in intensive care units. Target CLAB Zero was a national campaign that ran from October 2011 to March 2013 across all New Zealand ICUs (intensive care units). The campaign aimed to reduce the national CLAB rate to less than one incident per 1,000 line days and to establish a national measurement system for CLAB.

METHOD: We used Institute for Healthcare Improvement (IHI) Breakthrough Series methodology to structure the campaign. IHI bundles of care for catheter insertion and maintenance were implemented across 25 New Zealand ICUs. We collected monthly data on line days, CLAB infections and compliance with the bundles. Data were analysed using run charts.

RESULTS: The rate of CLAB per 1,000 line days fell from 3.32 at baseline to an average of 0.28 between April 2012 and March 2013. In the final 3-month period, January to March 2013, average insertion bundle compliance was 80% and average maintenance bundle compliance was 75%. All ICUs participated in the collaborative. Over 90% of those invited attended all three national learning sessions and bi-monthly regional learning sessions.

CONCLUSION: National collaboratives can effect improvement and shared learning in New Zealand. International evidence combined with New Zealand experience, a supportive methodology, partnership, clinical respect and an effective communication plan were keys to successful engagement.

Central line-associated bacteraemia (CLAB) in intensive care units (ICUs) is associated with a mortality rate of between 10% and 50% and a significant burden of morbidity.[1-3] The cost is estimated at around NZ$20,000 per CLAB infection.[4]

CLAB rates can be reduced effectively by aseptic insertion, use of an insertion checklist, monitoring of line days, standardised management and early catheter removal.[5-7] Quality improvement collaboratives to implement these interventions in the US and New South Wales, Australia, achieved reductions of CLAB incidence between 60% and 74%.[6,8,9]

In 2008, Counties Manukau Health used Institute for Healthcare Improvement (IHI) insertion and maintenance care bundles in a local improvement programme in the Critical Care Complex at Middlemore Hospital, Auckland. The incidence of CLAB dropped from 6.6 cases per 1,000 line days to 0.9 cases.[5] This compares to a drop in the mean incidence of CLAB from 3.73 to 0.97 per 1,000 line days in Rhode Island, from 1.5 to 0.6 in Hawaii, and from 3.0 to 1.2 in New South Wales.[6,8,9]

This successful local programme, combined with the weight of research evidence and an encouraging policy environment, created a powerful case for action across New Zealand ICUs.

The Target CLAB Zero campaign commenced in October 2011. The campaign was a national collaborative of New Zealand ICUs. Ko Awatea, the health system

innovation and improvement centre at Counties Manukau Health, led the campaign and the Health Quality & Safety Commission (HQSC) funded it. The campaign's objective was to reduce the rate of CLAB in New Zealand ICUs to less than one incident per 1,000 line days by the end of March 2013, and to establish a national measurement system for CLAB.

We report on the results of the collaborative and the lessons learnt from its development and implementation.

Context

At the time of the study, healthcare in New Zealand was configured into 20 district health boards (DHB) covering four regions. There were 24 adult and one paediatric ICUs, which collectively admitted around 19,000 patients per year.[5]

Intensive care services are configured as ICUs, high dependency units (HDUs) or mixed ICU/HDU units. Considerable variation exists in size, access to specialist services, and staff and patient mix.

Patients in smaller ICUs requiring specialist care are often transferred to hospitals with larger units. The patient mix is therefore broader, and acuity higher, in the larger units. As a result, CLAB rates at the beginning of the collaborative ranged from zero to six incidents per month, and were higher in the larger units.

We identified key challenges. Firstly, because of New Zealand's geography and varying population density, some ICUs are geographically isolated and there was considerable variation in the experience of CLAB. Furthermore, there was no mechanism for shared learning and improvement. Additionally, New Zealand lacked a national surveillance system for CLAB to establish an accurate baseline incidence rate. Finally, definitions of CLAB and data collected were inconsistent across ICUs.

We used two methods to obtain a baseline:

1. We extrapolated from data collected from a local improvement programme in the Auckland Region. The programme covered four of the largest ICUs in New Zealand, which collectively serve a third of the country's population. The region had three to six CLAB infections per month, giving a regional annual extrapolated rate of 48 to 72 CLAB infections.
2. We also conducted a 12-month retrospective audit of clinical notes from all patients admitted to all New Zealand ICUs who had a central line inserted from November 2010 to December 2011 against the Centers for Disease Control and Prevention (CDC) definition of central line-associated bloodstream infection (Table 1). The audit was completed at each site by a person who understood the criteria and had training in the audit process. The person nominated was the project leader, a registered nurse or an infection prevention control nurse.

Method

Faculty and stakeholders

Ko Awatea assembled a national project team and a steering group to lead the collaborative. The project team comprised a national project manager, a clinical leader and an improvement advisor. The steering group included clinicians, experts in improvement science from Ko Awatea and IHI, and representation from the HQSC. An expert group and a measurement group, comprising intensivists, microbiologists and infectious disease specialists, provided overall clinical leadership and guidance to support the project team and steering group. Each participating site had a clinical leader (ICU physician, anaesthetist or clinical head) and a project leader. In addition, there were four regional clinical leaders (ICU clinical director or consultant).

We secured the support of key DHB stakeholders (chief executive, operating and medical officers; directors of nursing and ICU management) with a targeted invitation letter and background document. A follow-up letter acknowledged those who had committed to take part and encouraged those yet to respond to do so. All ICUs agreed to participate.

The intervention

IHI bundles of care for the insertion and maintenance of central lines used in the 2008 CLAB reduction programme at Middlemore Hospital, Auckland, were adopted for Target CLAB Zero (Table 1).[10]

Due to the wide variation among ICUs, teams at each site adapted implementation of the bundles to suit their local context.

Teams were trained in IHI Breakthrough Series Collaborative Model (BTS) methodology to support adoption of the bundles.[11] The clinical leader and project leader from each site were sponsored to attend two 3-day training programmes in improvement science and BTS methodology.

We structured the BTS model as three national learning sessions interspersed with action periods. The first learning session, in November 2011, covered how to implement the insertion and maintenance bundles, collect data and interpret operational definitions. A guide developed from the 2008 programme at Middlemore Hospital was provided. The second learning session, in November 2012, focused on testing the validity and reliability of data and overcoming barriers to collection of bundle compliance data. The third, in March 2013, addressed how to sustain the improvements achieved. Clinical leaders were sponsored to attend sessions.

Regional meetings and WebEx online conferencing supplemented learning sessions. These provided additional coaching in improvement methods and measurement, and support from peers and the project team.

Teams applied learning during the action periods, using the Model for Improvement.[12] This model required teams to set specific aims and measures, then develop and test change ideas using plan, do, study, act cycles.

A communication plan supported the intervention. A website enabled participants to access resources, report progress and interact through a discussion forum. We added a dedicated blog to the Ko Awatea website and produced a quarterly newsletter. Each ICU received promotional resources and displayed a progress board.

Measures

We collected two outcome measures—incidence of CLAB (O1) and a count of central venous line days (O2). We used these to calculate our primary outcome measure, the national rate of CLAB per 1,000 line days (O3) (Table 1).

We also collected two composite process measures—compliance with the insertion bundle (P1) and compliance with the maintenance bundle (P2). These comprised three and four process measures respectively. The rate of compliance with the insertion and maintenance bundles was calculated by dividing the number of patients who had all elements of a bundle correctly executed by the number of checklists completed. Patients admitted to ICUs with a central line from operating theatres were included in the data, as staff were trained in the use of the insertion and maintenance bundles and were able to check insertion compliance. Operational definitions were agreed for all measures (Table 1).

To judge the degree of engagement with the collaborative, we measured attendance at learning sessions, regional meetings and WebEx sessions. We also monitored monthly data submissions.

Data collection and analysis

A national web-based database was established for collecting data. Each ICU entered data monthly from January 2012 to March 2013. Following March 2013, the HQSC took over the data collection and reporting. Data were checked for completeness 10 working days after the end of the month. Follow-up contact was made with teams who had incomplete data and/or data anomalies. Data were then extracted from the database into an Excel spreadsheet.

Monthly progress reports were fed back to teams. Project managers and clinical leads reported monthly data to DHB stakeholders from January 2012.

Estimates of effect were determined using random and non-random variation flags on run charts.

Results

The collaborative ran from October 2011 to March 2013. Data are reported on 23 units—one unit had no line days for the duration of the campaign, and one unit implemented the insertion and maintenance bundles, but had not determined a method for data collection on the three key measures.

CLAB rates

The estimated baseline CLAB rate for the 12 months prior to the project was 3.32 per 1,000 line days. The period January to March 2012 provided data gathered against

Table 1: Operational definitions for outcome and process measures

Outcome measures
O1 (CLAB): An infection associated with central venous catheters which meets the CDC criteria and is independently confirmed by a qualified third party (microbiologist, intensive care consultant). **CDC technical description:** i. Presence of a recognised pathogen cultured from one or more blood cultures and organism cultured from blood not related to infection at another site. *OR* ii. Fever (>38°C), chills, or hypotension *and* organism cultured from blood is not related to infection at another site *and* presence of at least one of the following: • Common skin contaminant (eg, diphtheroids, bacillus species, propionibacterium species, coagulase negative staphylococci or micrococci) cultured from two or more blood samples drawn on separate occasions. • Common skin contaminant cultured from at least one blood culture in a sample from a patient with an intravascular catheter. • Positive antigen test on blood (eg, haemophilus influenzae, streptococcus pneumoniae, neisseria meningitidis, or group B streptococcus).
O2 (Count of central venous line days): A count of the number of central venous catheters inserted in a great vessel (eg, superior vena cava).
O3 (Rate of CLAB/1,000 line days): The rate of CLAB per 1,000 line days, calculated by dividing the number of confirmed cases of CLAB (numerator) by the number of central line days per month (denominator) and multiplying the result by 1,000.
Process measures for insertion and management of the line
P1 (Compliance with insertion bundle): 1. *Hand hygiene:* Appropriate hand hygiene prior to handling the insertion pack. 2. *Chlorhexidine skin antisepsis:* Chlorhexidine skin preparation completed appropriately prior to insertion of the line. 3. *Maximum barrier precautions*: The inserter is to wear a cap, mask, sterile gown and sterile gloves, and make appropriate use of a full body drape for the patient, including the area around the site.
P2 (Compliance with maintenance bundle): 1. *Daily necessity review*: The line is reviewed by a qualified member of staff to determine if it is still required, and the need to retain the line is documented on the maintenance checklist. 2. *Dedicated port for TPN*: The total parenteral nutrition line is always separate from the central venous line. 3. *Daily site check*: The insertion site is checked for redness, pain and swelling. This is documented on the maintenance checklist. 4. *Chlorhexidine prior to each access*: Documented evidence of chlorhexidine scrubbing of the hub prior to each site access.

a defined, consistent standard (Table 1). During this period, CLAB rates were between 1.6 and 2.7 per 1,000 line days. By April 2012, all ICUs had implemented both the insertion and maintenance bundles. The CLAB rate fell immediately to 0.28 per 1,000 line days and was sustained throughout the collaborative period (Figure 1). This represented a relative reduction of 90% from the baseline of 3.32.

Between January 2012 and June 2012, New Zealand experienced an average of 4.6 days between CLAB infections. This rose to 13 days after June 2012 (Figure 2).

Process compliance

The first 3 months of the collaborative (January–March 2012) were spent establishing consensus on how to measure compliance with the insertion and maintenance bundles. By April 2012, all but one unit had set up measurement systems and were reporting compliance rates. By the final 3-month period, January to March 2013, average compliance with the insertion bundle was 80%, and with the maintenance bundle 75%.

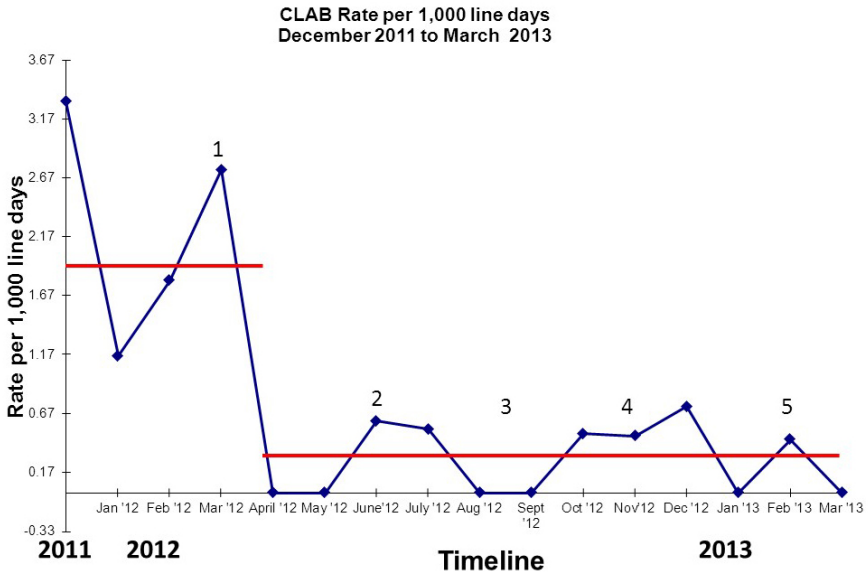
Collaborative participation

Participation in the collaborative was high. Over 90% of those invited attended all three national learning sessions and the meetings held in each of the four regions (Table 2). All sites submitted data and posted reports each month.

Discussion

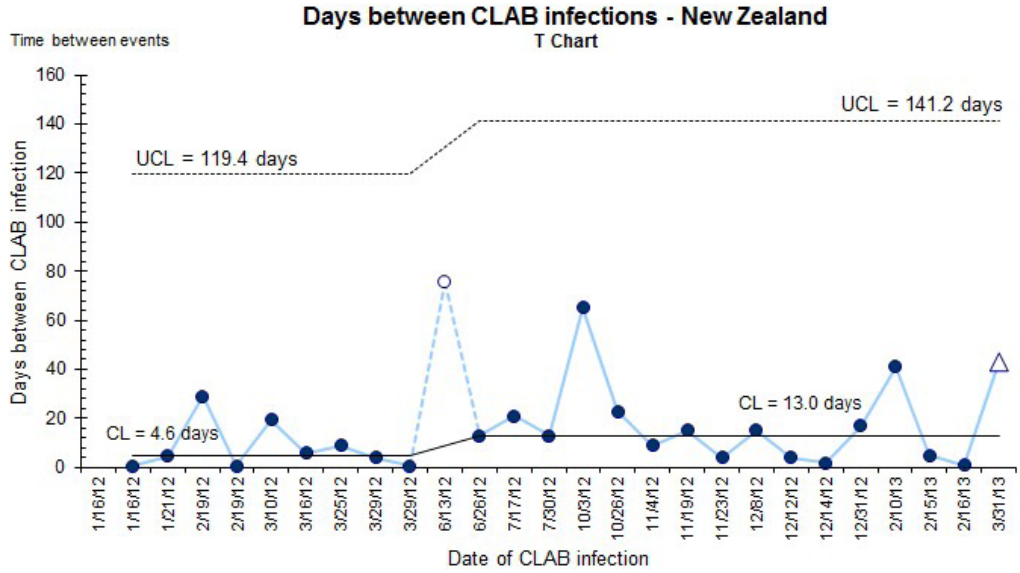
CLAB rates were significantly reduced, and participation in the collaborative and process compliance was high. This

Figure 1: CLAB rate per 1,000 line days (all ICUs)



1. End of the implementation period
2. Learning session 2
3. Regional workshops
4. Christmas period
5. Learning session 3

Figure 2: Days between CLAB infections



improvement in the CLAB rate and engagement with the collaborative occurred despite differences in ICU size, staff and patient mix, population and geographic location among participating DHBs.

Our results reinforce existing studies that demonstrate the effectiveness of hand hygiene, aseptic skin preparation, barrier precautions and removing unnecessary catheters for reducing CLAB.[6,7,8] Burrell et al. report a drop in the rate of CLAB from 3.0 to 1.2 in a quality improvement collaborative across 37 ICUs in New South Wales (NSW) using comparable bundles of care.[6] An initiative covering 45 states in the US, On the Cusp: Stop BSI, reported a baseline rate of 1.87 CLAB infections per 1,000 central line days for units that began participating in the project in 2009 and 2010. After 10–12 months of participation, this rate decreased to 1.25.[13] Target CLAB Zero covered all New Zealand ICUs and achieved a decrease in the average rate of CLAB from 3.32 to 0.28. However, the NSW and US projects were considerably larger in scale than the New Zealand project. New Zealand's small size, and centralised public health service, made a national approach feasible and contributed to the high participation throughout the collaborative.

Collaborative methodology was used in New South Wales, Rhode Island and Hawaii to successfully implement evidence-based best practices for CLAB reduction.[6,8,9] To our knowledge, Target CLAB Zero is the first nationwide improvement collaborative in

Table 2: Characteristics of New Zealand ICUs, bed numbers, participation, and compliance with reporting and quarterly line days

Regions	Unit	Level	Size (beds)	Number of learning session attendees			Number of data submissions by unit/ number of possible submissions		Number of central venous line days				
				LS1	LS2	LS3	(Jan 2012–June 2012)	(July '12–March '13)	Jan –Mar '12	April – June '12	July –Sept '12	Oct –Dec '12	Jan – Mar '13
Northern	A1	2	6	2	1	2	6/6 (100%)	90 (100%)	107	153	181	168	111
	A2	2	14	4	3	5	6/6 (100%)	9/9(100%)	247	316	328	369	327
	A3	3	20	2	1	2	6/6(100%)	9/9 (100%)	951	1190	1080	1014	920
	A4	3	24	2	1	2	6/6(100%)	9/9(100%)	577	630	655	664	685
	A5	3	22	2	0	1	6/6(100%)	9/9(100%)	628	698	800	715	768
	A6	3	20	5	8	10	6/6(100%)	9/9(100%)	528	572	442	395	401
Central	B1	1	6	0	1	2	6/6(100%)	9/9(100%)	30	120	138	115	128
	B2	1	4	3	5	5	6/6(100%)	9/9(100%)	64	88	94	118	72
	B3	2	6	2	1	1	6/6(100%)	9/9(100%)	407	429	520	462	471
	B4	2	6	2	3	3	6/6(100%)	9/9(100%)	201	197	201	230	238
	B5	3	18	4	4	4	6/6(100%)	9/9(100%)	762	917	964	870	820
Southern	C1	1	2	0	0	2	4/6 (67%)	9/9 (100%)	12	85	45	37	90
	C2	2	7	1	1	1	6/6(100%)	9/9(100%)	60	90	45	59	82
	C3	2	12	4	3	3	6/6(100%)	9/9(100%)	307	341	394	321	326
	C4	3	16	4	4	5	6/6(100%)	9/9(100%)	609	613	747	720	733
Midland	D1	1	4	(3)	(3)	(3)	6/6(100%)	9/9(100%)	14	32	37	41	31
	D2	1	3	1	2	1	6/6(100%)	9/9(100%)	70	66	180	122	187
	D3	2	12	3	3	3	6/6(100%)	9/9(100%)	201	242	426	270	298
	D4	2	4	1	1	1	4/6 (67%)	9/9 (100%)	36	189	279	170	164
Total			**221**	**52**	**50**	**56**			**6,692**	**7,912**	**10,837**	**7,746**	**7,869**

the New Zealand healthcare context.

Carter et al. identify accounting for context, setting realistic goals, providing sufficient time and resources, and careful management of collaboratives as factors that mitigate over-competitiveness, inertia, conflicting organisational pressures and free-riding in collective action.[14] We found that the flexibility of the BTS methodology gave frontline staff the tools, knowledge and direction to adapt the change package according to local context. This enabled Target CLAB Zero to work effectively across ICUs of varied size, patient mix and degree of specialism. The national project team avoided being prescriptive about how the bundles were implemented. Instead, the focus was on agreed definitions and guiding principles, and on building improvement capability and capacity through a learning network. The emphasis was on measurement for improvement rather than performance imperatives. Competitiveness was apparent without resultant hostility or inertia.

Our results are likely to be accompanied by a reduced mortality rate, shorter lengths of stay in hospital, and a reduction in the economic burden of CLAB. Although our data finish in March 2013, when HQSC took over data collection and reporting, data available from HQSC show that the improvements have been sustained.[15]

The cost per CLAB infection is approximately NZD 20,000.[4] The implied monthly incidence of CLAB at the baseline level was up to 8.9 per month (3.3/1,000 * 2,700). Extrapolating to the post set-up period (April 2012

to March 2013), we would have expected up to 105 incidents of CLAB had no corrective action been taken. There were 15 incidents of CLAB during this period. This represents potential savings of NZD 1.8 million.

Other benefits of the campaign were:

- development and agreement on process flow for obtaining blood cultures
- an agreed national approach to determining a CLAB from a positive blood stream infection
- establishment and development of four regional reusable networks
- increase in staff awareness and commitment to reducing CLAB
- increased health sector capacity and capability in using IHI improvement methodology
- reduction in patient harm.

Target CLAB Zero achieved high national participation. We identified six key facilitators of participation:

1. The existence of strong international evidence for the effectiveness of the intervention.[6-9,16-18]
2. The existence of a proven example of international evidence being successfully applied in the New Zealand context.[5]
3. The flexibility of BTS methodology.
4. The peer-led nature of the campaign. The ability to attract influential clinicians to leading roles was important. Clinical respect was leveraged within and across DHBs.
5. The involvement of HQSC. HQSC sponsored attendance at learning sessions and lent weight to the campaign as a national initiative.
6. An effective communication plan. Targeted messages secured engagement from key stakeholders. The communication plan, and the use of regional and virtual meetings, also enabled participants to connect despite the geographical isolation of some units.

Limitations

The lack of an existing CLAB surveillance system using standard definitions of CLAB presented challenges in establishing an accurate baseline rate. The retrospective audit conducted to establish the baseline depended upon information in clinical notes that were not compiled according to a consistent standard. Counting mechanisms for line days were still under development at the time the baseline data were collected. Furthermore, the definition of a CLAB infection used during the collaborative required two positive blood cultures, but this standard was not in place during the baseline period. The baseline may therefore under- or over-represent the national CLAB rate at the beginning of the collaborative.

The period from January to March 2012 is probably more indicative of the true national baseline, even though some ICUs began implementing the intervention from January 2012. It is also possible that the Northern regional ICUs “drove” the bulk of the CLAB incidence. Therefore the early focus by clinical staff in this region was already resulting in service improvements that were quickly realised and sustained by the collaborative process and the national monthly surveillance system.

Conclusion

Target CLAB Zero exceeded its aim of reducing the rate of CLAB in New Zealand ICUs to less than one CLAB incident per 1,000 line days, and established a national measurement system for CLAB. The project demonstrates that national improvement collaboratives are feasible in New Zealand. Barriers of geographical isolation and variation in the size and characteristics of participants can be overcome by effective communication and the use of an improvement methodology that accommodates differences in local context. The lessons learned from the Target CLAB Zero experience would inform successful development and implementation of improvement collaboratives aimed at addressing other deficiencies in quality of health care, where a strong evidence base exists to support definable best practice. The Enhanced Recovery after Surgery (ERAS) collaborative, which was launched in 18 DHBs in November 2013 to improve care for orthopaedics patients, provides one such example.[19,20]

Competing interests:
We declare that Ko Awatea was funded by HQSC to deliver the Target CLAB Zero collaborative improvement programme. Sue Wells reports grants from the Stevenson Foundation during the conduct of the study, and grants from Health Research Council of New Zealand, Roche Diagnostics Ltd, National Heart Foundation of New Zealand and from University of Auckland, outside the submitted work. Jonathon Gray is Director of Ko Awatea, The Centre for Improvement & Innovation at Counties Manukau District Health Board. He is employed part-time by both CMDHB and Victoria University of Wellington.

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Randomised controlled trials cited in pharmaceutical advertisements targeting New Zealand health professionals: do they support the advertising claims and what is the risk of bias?

Alison Ma, Lianne Parkin

ABSTRACT

AIMS: To determine whether pharmaceutical advertisement claims targeting health professionals were supported by the randomised controlled trials (RCTs) cited in the advertisements, and to assess the risk of bias in those trials.

METHODS: Pharmaceutical advertisements were obtained from *New Zealand Doctor* and *Pharmacy Today* for the period July 2013 to June 2014. All claims made regarding efficacy, safety, and indications were identified and RCTs cited to substantiate these claims were examined. A claim was defined as supported by an RCT if the conclusions drawn in the paper were consistent with the claim. The quality of the RCT was assessed separately, using the Cochrane Risk of Bias Assessment Tool.

RESULTS: In 25 (19%) of the 133 instances in which an RCT was cited, the published paper did not support the promotional claim. Moreover, there were only 10 (8%) instances in which the claim was supported by an RCT with a low risk of bias. Of the 78 cited RCTs, only 14% had a low risk of bias, while 49% had an unclear risk and 37% had a high risk.

CONCLUSIONS: A high proportion of advertisements failed to meet New Zealand regulatory requirements that claims "are valid and have been substantiated".

Pharmaceutical advertisements are commonly found in publications aimed at health professionals and provide a significant source of income for the journals.[1] While some commentators have argued that advertisements have an educational value in informing prescribers about currently available products, others have expressed concern about the accuracy of therapeutic claims and negative influences on prescribing practices.[1]

Investigators in diverse settings (including Australia,[2] Finland,[3] Sweden, the Netherlands,[4] Switzerland,[5] Spain,[6] Russia,[7] and the US[8]) have documented misleading and unsupported pharmaceutical advertising claims in national medical publications. Similar findings have been reported for advertisements in high-impact general medical journals and a range of specialty journals.[9-15]

In parallel with an increasing focus on evidence-based medicine, there has been an increasing move to cite randomised controlled trials (RCTs) in advertisements.[6] However, while RCTs are the gold standard for testing the effectiveness of treatments, they are not immune to bias. For example, researchers in the Netherlands recently used a modified instrument, based on the Chalmers' score, to assess the quality of RCTs cited in pharmaceutical advertisements and found that only 55% had a high quality score.[13]

Poor quality pharmaceutical advertisements are a matter of concern, as exposure to such advertising material can sometimes lead to inappropriate prescribing and higher costs to the healthcare system.[9,16,17]

In New Zealand, therapeutic product advertising is governed by the Medicines

Act 1981, the Medicines Regulations 1984, and the Misuse of Drugs Regulations 1977, as well as self-regulation through the Advertising Standards Authority (ASA) and industry codes of practice.[18] The Therapeutic Products Advertising Code states that advertising directed to healthcare practitioners "must contain truthful and balanced representations and claims that are valid and have been substantiated", and "must not encourage, or be likely to encourage, inappropriate or excessive use".[19] Information about how well pharmaceutical advertisements in New Zealand comply with these regulations is very limited. A narrative account of misleading advertising in four publications read by New Zealand doctors was published in 2002,[20] but there have been no subsequent systematic investigations.

The aims of the present study were to determine whether pharmaceutical advertising claims in two publications that target New Zealand health professionals were supported by the RCTs they cited, and to assess the risk of bias in those trials.

Methods

Unique pharmaceutical advertisements for medicines and medical devices, in the period July 2013 to June 2014, were obtained from two publications targeting New Zealand health professionals: *Pharmacy Today* (hospital and community pharmacists) and *New Zealand Doctor* (general practitioners and other health sector workers). Advertisements were considered unique if they differed in product, claim, or cited studies. Each advertisement was assessed for claims regarding efficacy, safety, and indications. Any material cited to substantiate claims was classified in terms of type. All advertisements which included a claim and cited at least one RCT were included in the study.

Full-text copies of the cited RCTs were accessed digitally via Medline. Some articles could not be found immediately on Medline as insufficient information was provided in the citation, thus a general search was performed in Google in order to obtain the name of the article and other relevant information. Eight articles, which could not be found or accessed via Medline, were sourced using the Interloans Service of the University of Otago Medical Library.

Claims were classified as supported or unsupported. A claim was defined as supported if the findings of the cited RCT were consistent with the advertising claim, irrespective of the quality of the study. Claims were classified as unsupported if the subject of the claim was not examined in the RCT, the claim exaggerated the benefits of the drug, the study population was different to that for which claims were made, or the claim was contradicted by the findings of the RCT.

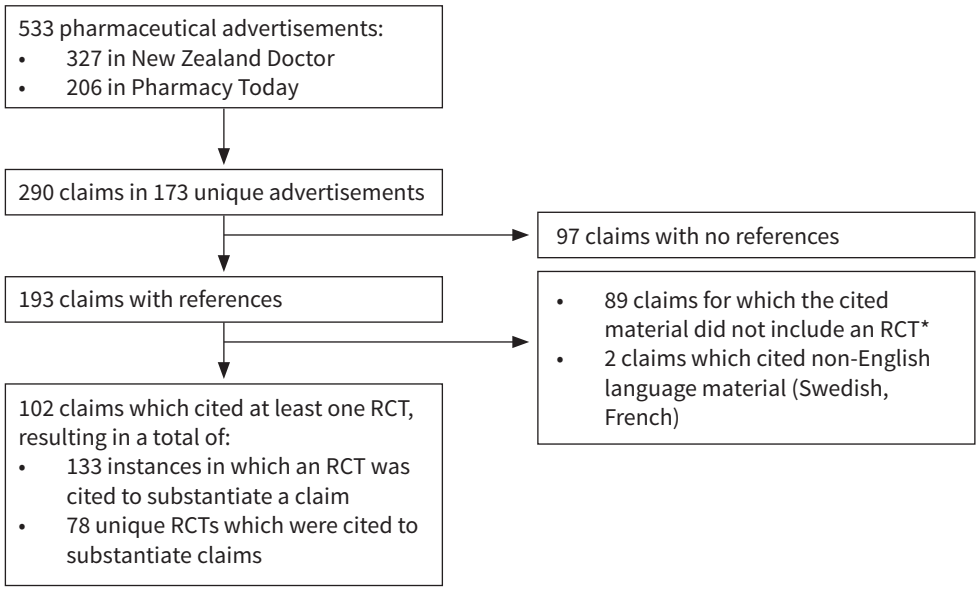
The risk of bias in each RCT was assessed using the Cochrane Risk of Bias Assessment Tool, a standardised instrument which systematically evaluates potential bias in six domains (sequence generation; allocation concealment; blinding of participants, personnel and outcome assessors; incomplete outcome data; selective outcome reporting; and other sources of bias) and provides an overall summary assessment (low risk of bias, unclear risk of bias, and high-risk of bias) for each study.[21,22] Both the published paper and any available protocols or trial registration data (if links to protocols, and/or trial registration numbers, were provided by the journal) were examined. The funding source (pharmaceutical industry, non-industry) was also noted.

To standardise the application of the assessment tool, three RCTs which were cited in pharmaceutical advertisements before July 2013 (and therefore were not included in this study) were independently assessed by both investigators. Findings were compared and any inconsistencies were resolved through discussion. The primary investigator (AM) subsequently assessed all of the study RCTs and sought an independent opinion from the second investigator when required.

Results

Figure 1 shows the number of pharmaceutical advertisements published in *Pharmacy Today* and *New Zealand Doctor* during the study period, the number of unique advertisements, the number of claims with and without references, and the number of claims which cited RCTs. Ninety-seven (33%) claims cited no supporting evidence, 89 (31%) cited material other than RCTs, two (<1%) cited non-English language material (Swedish, French), and only

Figure 1: Flow diagram showing the number of advertisements, claims, and RCTs cited in *New Zealand Doctor* and *Pharmacy Today*, July 2013 to June 2014



* The most commonly cited material was drug data sheets. Other material included uncontrolled intervention studies, narrative reviews, observational studies, conference posters, 'data on file', drug reference handbooks, summaries of pharmacological studies, and reports from Ministries of Health and drug regulators. In only six instances were systematic reviews and meta-analyses cited.

102 (35%) cited one or more RCTs. Some claims cited more than one RCT and some RCTs were cited for more than one claim. Therefore, in relation to the 102 claims which cited at least one RCT, there were 133 instances in which an RCT was cited to support a claim and 78 unique RCTs which were cited.

In 25 (19%) of the 133 instances in which an RCT was cited, the published paper did not support the promotional claim in the pharmaceutical advertisement: in 11 instances the subject of the claim was not examined in the cited RCT; in nine, the claim exaggerated the benefits of the drug; in four, the study population was different to that for which claims were made; and in one, the claim was contradicted by the cited RCT.

Of the 78 RCTs cited, 24 (31%) provided trial registration details in the published paper and 12 (15%) provided access to protocols via the journal webpage. The risk of bias for each RCT is shown in Figure 2. In terms of sequence generation, 39 (50%) RCTs had a low risk of bias, 37 (47%) had an unclear risk and 2 (3%) had a high risk (Figure 3). The corresponding figures (low, unclear, high risk) for the other five domains were: allocation concealment, 34 (44%), 39 (50%) and 5 (6%); blinding of participants, personnel and outcome assessors, 36 (46%), 32 (41%) and 10 (13%); incomplete outcome data, 46 (59%), 24 (31%) and 8 (10%); selective outcome reporting 28 (36%), 46 (59%), 4 (5%); and other sources of bias 43 (55%), 29 (37%) and 6 (8%). The overall risk of bias was low in 11 (14%) RCTs, unclear in 38 (49%) and high in 29 (37%).

Of the 133 instances in which an RCT was cited to substantiate an advertising claim, there were only 10 (8%) in which the claim was supported by an RCT with a low risk of bias. In a further 98, the claim was supported by an RCT with an unclear (55 [41%]) or high (43 [32%]) risk of bias.

The risk of bias, according to whether an RCT was sponsored by a pharmaceutical company, is shown in Table 1. Sixty-one (78%) trials were industry funded. A higher proportion of sponsored trials had a high risk of bias (41%) as compared with those which were not sponsored (24%); conversely, the proportion with an unclear risk of bias was higher in the unsponsored trials (59% versus 46%). For both sponsored and unsponsored studies, the proportion of trials with a low risk of bias was low (13% and 18%, respectively).

Figure 2: RCTs (n=78) according to risk of bias, citing publication, sponsorship by pharmaceutical company, and whether a protocol and trial registration information was available. Green, yellow and red circles indicate low, unclear and high risk of bias respectively. (Full list of references available on request from authors)

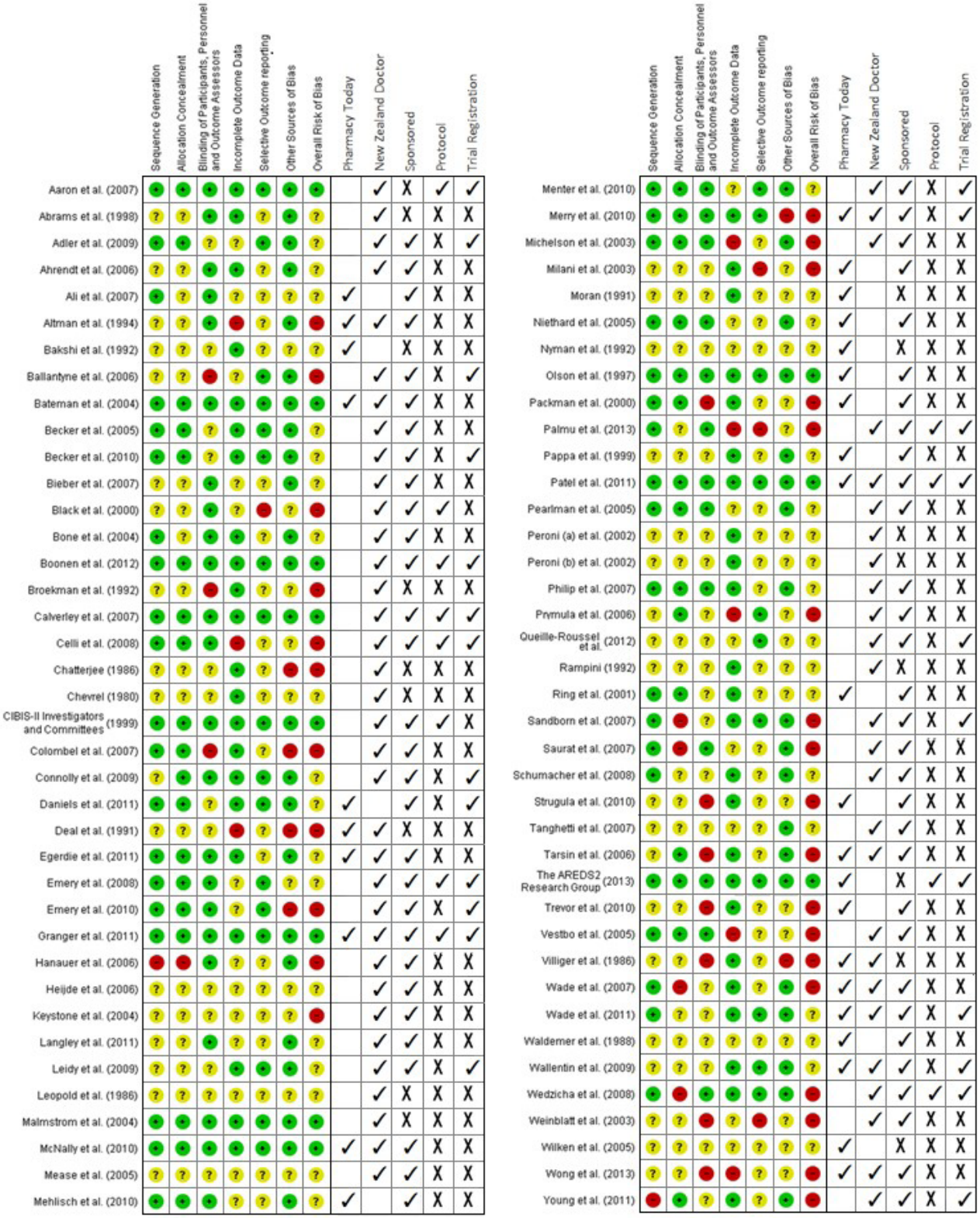


Figure 3: Summary of the risk of bias in each domain, and overall, in the 78 RCTs assessed

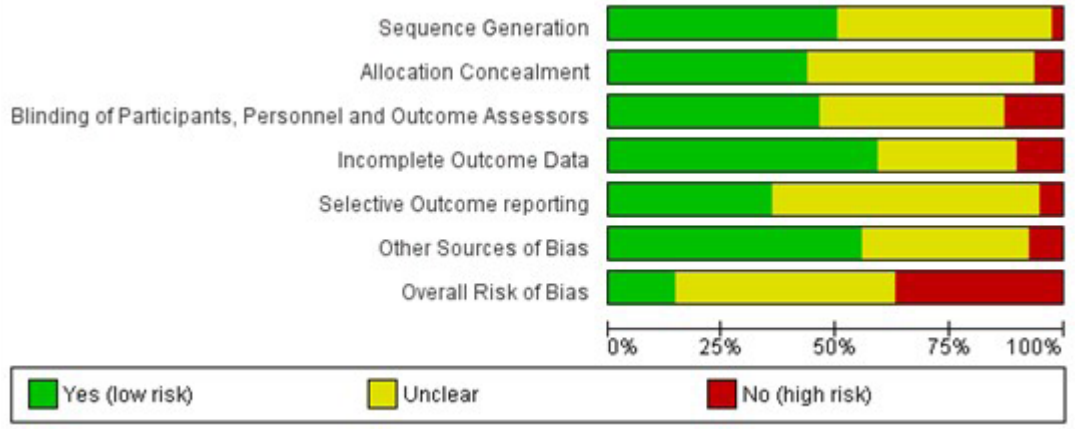


Table 1: Overall risk of bias according to whether RCT sponsored by a pharmaceutical company

Overall risk of bias	Sponsored (no. [%])	Not sponsored (no. [%])	Total (no. [%])
Low	8 (13)	3 (18)	11 (14)
Unclear	28 (46)	10 (59)	38 (49)
High	25 (41)	4 (24)	29 (37)
Total	61	17	78

Discussion

This review of pharmaceutical advertisements published in *New Zealand Doctor* and *Pharmacy Today* between July 2013 and June 2014 found that 33% of advertising claims cited no supporting evidence and only 35% cited at least one RCT. In 108 (81%) of the 133 instances in which an RCT was cited to support a claim, the RCT drew conclusions which were consistent with that claim. However, only 14% of the 78 cited unique RCTs had a low risk bias and 37% had a high risk; in the remaining 49% insufficient information was reported in order to come to a justified decision. Moreover, in only 10 (8%) of 133 instances was the claim supported by an RCT with a low risk of bias. Conversely, there were 43 (32%) instances in which the RCT that apparently supported a claim had a high risk of bias.

This study had several strengths. First, a systematic approach was taken to collect advertisements; all unique advertisements published over the course of a year were examined to ascertain eligibility for inclusion in the study. Second, the 12-month study period enabled the assessment of advertisements for a range of medicines, including those whose use varies by season (such as drugs for hay fever). Third, a validated instrument, the Cochrane Risk of Bias Assessment Tool, was used to assess the risk of bias in each of the RCTs. Fourth, trial registration information and study protocols, if found, were also examined to enable a thorough assessment.

There were also some limitations. First, one researcher assessed all of the RCTs; in ideal circumstances, the second investigator would have independently assessed the same trials. However, an independent assessment of RCTs cited in advertisements published outside the study period was undertaken for training purposes before the study RCTs were reviewed. The investigators also met regularly to discuss progress and to resolve any uncertainties. Second, vague advertising claims were considered supported as long as the advertised drug was reported to be significantly superior to the comparison drug or placebo. However, the fact that the results were statistically significant does not mean that the findings were clinically important.

Our findings are consistent with previous research in that not all pharmaceutical advertising claims cited material to support the claim; not all claims were supported by the documents they cited; few systematic reviews and meta-analyses were cited; and observational studies, product sheets, 'data on file', and conference abstracts were commonly cited as supporting evidence.[2-6,8-11,13,14,20]

Only two other investigations have systematically assessed the quality of the studies cited to support advertising claims aimed at health professionals. A Swiss study found that 32% of claims were based on potentially biased evidence—defined as RCTs with at least three of the following: no evidence of concealment of allocation, open-label studies, loss-to-follow-up >10%, unexplained drop-outs, selective reporting of positive outcomes, no intention-to-treat analysis; abstracts of RCTs which had not undergone peer-review; observational studies; studies in which non-responders and those experiencing side-effects were excluded in the run-in phase; post-hoc analyses; and narrative, rather than systematic, reviews.[5] A Dutch study, like the present investigation, focussed on the quality of RCTs which were cited to support advertising claims. Using a different tool, a modified version of the Chalmers' score, the researchers found that only 55% of the RCTs had a high quality score, and even fewer (39%) had both a high quality score and provided support for the claim for which they were cited.[6]

Several findings of this study warrant further discussion. Overall, 49% of the RCTs examined were classified as having an unclear risk of bias because of incomplete reporting of methods. While reporting improved progressively by decade, and recent publications were more likely to describe the methods clearly and to provide trial registration details and protocols, a considerable proportion (40%) of the trials published in the 2010s still provided insufficient information to enable an assessment of the risk of bias. It will be interesting to see whether this situation improves in the wake of the AllTrials campaign, which calls for all past and present clinical trials to be registered and their full methods and summary results to be published.[23]

RCTs are the optimal design to study treatment effects and a reference to an RCT in an advertisement may lead some readers to assume that the advertising claim is supported by strong evidence. However, as the present study demonstrates, this cannot be confirmed without critically appraising the relevant RCT. While we located all but one of the cited studies (a study of unknown design which was cited alongside RCTs to support two claims), this took considerable effort and involved the use of the library resources at the University of Otago, especially the Interloans Service which provided material that could not be found through Medline. Many practising physicians and pharmacists are unlikely to have the time and resources to locate the original source material cited in pharmaceutical advertisements. A further barrier is language: although *New Zealand Doctor* and *Pharmacy Today* are English language publications, two advertisements referred to non-English language (Swedish, French) studies to support their claims.

Of the 78 RCTS cited to support advertising claims, 78% were sponsored by the pharmaceutical industry and it is possible that the true proportion was even higher, as funding sources may not have been disclosed in earlier publications. In this highly selected sample of RCTs, we found that the cited industry-sponsored trials were more likely to have had a high risk of bias than the RCTs without industry funding. The impact that pharmaceutical industry funding might have on research findings and the prescribing practices of doctors with financial ties to the industry is a matter of increasing concern nationally and internationally.[24] In line with many earlier publications, a recent Cochrane Review found that industry-sponsored trials reported greater benefits, fewer harms, more favourable overall conclusions, and were more likely to draw conclusions which were inconsistent with the actual results of the research than non-industry-sponsored studies.[25] The authors concluded that these differences were not explained by the sources of bias included in standard risk of bias assessment tools (but might be attributable to the choice of comparators, dosage and timing of comparisons, selective analyses, and selective reporting)

and they called for industry sponsorship to be viewed as a factor which increases the risk of bias. Such an approach obviously requires that funding sources are fully reported. There have also been calls in New Zealand for disclosure of industry payments to doctors.[24]

To conclude, we found that a high proportion of pharmaceutical advertisements failed to meet New Zealand regulatory requirements that claims "are valid and have been substantiated". About a third of claims had no references, only 35% of claims cited at least one RCT, and a very small proportion of those claims were supported by an RCT with a low risk of bias. We focussed on two publications and therefore cannot comment on the quality of any advertising material in other New Zealand health professional journals. Nonetheless, our findings do suggest a need for greater monitoring of pharmaceutical advertising in New Zealand.

Competing interests:
Alison Ma received a Summer Research Scholarship from the Division of Health Sciences, University of Otago, to undertake this work.

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Hospital admissions for non-cystic fibrosis bronchiectasis in New Zealand

Susan Bibby, Richard Milne, Richard Beasley

ABSTRACT

AIM: To investigate hospital admissions for non-cystic fibrosis bronchiectasis during July 1, 2008 to June 30, 2013; and to describe their distribution and annual cost in New Zealand.

METHODS: Admissions with a principal diagnosis of bronchiectasis (ICD10 J47), excluding cystic fibrosis, and length of stay <90 days were analysed by age, sex, ethnicity, socioeconomic deprivation, DHB, re-admissions and seasonality.

RESULTS: There were 5,494 admissions with a mean annual rate of 25.7 (age adjusted rate 20.4) per 100,000. Admission rates peaked in childhood and in the elderly, and increased steeply with socioeconomic deprivation. Age-adjusted rates were 38% higher for women, 4.9-fold higher for Māori and 9.1-fold higher for Pacific peoples. Counties Manukau had the highest unadjusted rate for any DHB (49.4 per 100,000). The overall 30 day readmission rate was 12.4%. Admissions peaked in winter and spring. The estimated cost in financial year 2012/13 was NZD 5.34M.

CONCLUSION: Hospital admissions for bronchiectasis are concentrated in socioeconomically disadvantaged young and elderly Māori and Pacific peoples; are more common in winter and spring, and incur a high annual cost. Evidence- based interventions to reduce the disproportionate burden of bronchiectasis in Māori and Pacific children and the elderly is a public health priority.

Bronchiectasis, a condition characterised by dilated, thick-walled bronchi, is associated with recurrent respiratory tract infection,[1] chronic cough, sputum production, dyspnoea and progressive loss of lung function.[2] Treatable, but rarely curable, management revolves around preventing or slowing progression by regular clearance of airway secretions and prompt treatment of lung infections.[3] It places a large burden on the healthcare system, as it is a chronic disease that may require not only hospital admissions, but also frequent outpatient visits, physiotherapy, and antibiotic use.[3]

While there is a general belief that the incidence of bronchiectasis has fallen since the introduction of antibiotics, its prevalence in the US is reportedly increasing, with one study showing an annual increase of 8.7% from 2000 to 2007.[4] This could represent a true increase in prevalence, and/or improved survival, and/or increased diagnosis due to more frequent use of high resolution computed tomography (HRCT).[4] The true incidence and prevalence are likely to be underestimated due to under-diagnosis.[3,5] There is also a wide variation in prevalence and incidence between and within populations.[1,2]

Bronchiectasis is considered a serious health issue for the indigenous and disadvantaged populations of the US, Australia and New Zealand.[1,6] Prevalence rates are consistently higher for indigenous populations in all these countries: 52 per 100,000 overall in the US, but 1,100–2,000 per 100,000 in southwest Alaskan native children;[7] and 1,470 per 100,000 in Australian Aboriginal children.[5] Another study estimated the point prevalence of bronchiectasis solely in Auckland (in 1998–2000) as 17 per 100,000; further breakdown by ethnicity gave values of 24 per 100,000 for Māori and 53 per 100,000 for Pacific children, compared to 4 per 100,000 for Europeans.[8]

Another New Zealand study also reported that the incidence of bronchiectasis varies with ethnicity: a rate of 3.7 per 100,000 children per year in 2001–2, breakdown by ethnicity of 17.8 for Pacific peoples, 4.8 for Māori and 1.5 per 100,000 per year for the European population.[1]

The main purpose of this study was to analyse national hospital admissions for bronchiectasis over a recent 5-year period, in order to estimate the burden of moderate or severe bronchiectasis, and the distribution by age, ethnicity, socio- economic status, geographical location and other variables. A secondary purpose was to estimate the budget impact of these admissions.

Methods

A nation-wide data set of anonymised publicly funded hospital admissions with a principal clinical diagnosis of bronchiectasis (ICD10 J47; which includes bronchiolectasis but excludes cystic fibrosis and congenital and tubercular bronchiectasis) was obtained from the Ministry of Health, for the period July 1, 2008 to June 30, 2013 (financial years (FY) 2008/09 to 2012/13). Admissions with a length of stay >89 days were excluded in an attempt to avoid biasing the mean costs and the average length of stay (LOS). The data included age, sex, prioritised ethnicity, District Health Board (DHB), length of stay, deprivation index (NZDep06), patient complication and morbidity level (PCCL), Australian Refined Diagnosis Related Group (AR-DRG) version 6.0, case weight and seasonality.

Multiple ethnic groups were prioritised using the following hierarchy: Māori; Pacific; European/Other. Population denominators were obtained from the 2013 census (Statistics NZ). An index admission in 2012/13 was defined as an admission for a patient who had not been admitted over the previous 4 years—which in some cases might have been a re-admission from earlier years. The time to a repeat admission was defined as the number of days from the date of discharge from an admission to the date of the next admission, excluding same day readmissions and transfers between hospitals. Age-adjustment by sex and ethnicity was by the direct method, with 'male' and 'European/other' as the references. Age-standardisation was not attempted for DHBs because of the small numbers of admissions.

Australian Refined Diagnosis Related Groups (AR-DRGs) are a patient classification system used by the New Zealand Ministry of Health to structure episodes of care into groups that are clinically similar both in terms of patient characteristics and health interventions, and that are therefore anticipated to consume comparable levels of hospital resources.

The 'NZDep' is a small, geographical area-based index of socioeconomic deprivation calculated from each 5-yearly census based on the following variables: income; employment; communication; transportation support; educational and other qualifications; home ownership and household crowding. It is arranged in 10 (approximately equal) deciles, with '1' representing the least disadvantaged and '10' representing the most disadvantaged. Higher decile groups tend to have higher proportions of Māori and Pacific peoples. Individuals were assigned a domicile code based on their home address at the time of admission, which was then mapped to the NZDep for 2006 (NZDep06).[9]

Admission costs were estimated using admission-specific diagnosis related group (DRG) cost weights applied to financial year 2012/13, multiplied by the mean national price for all types of hospital admission (NZ4614; NZ Ministry of Health). These costs take into account resource consumption, which reflects the intensity of care and length of stay. More detailed costings could be obtained hospital by hospital, but that would be beyond the scope of this study.

No attempt was made to obtain numbers of patient presentations or costs for Outpatient Clinic or Emergency Department visits because this information is not specific to the indications under study.

Analyses were conducted using Stata v.12 and a spreadsheet.

Results

Admissions by age, ethnicity and socioeconomic status

There were 5,519 admissions with a principal diagnosis of bronchiectasis in financial

Figure 1: Admission rates by age group, sex and ethnicity in FY 2008/09 to 2012/13

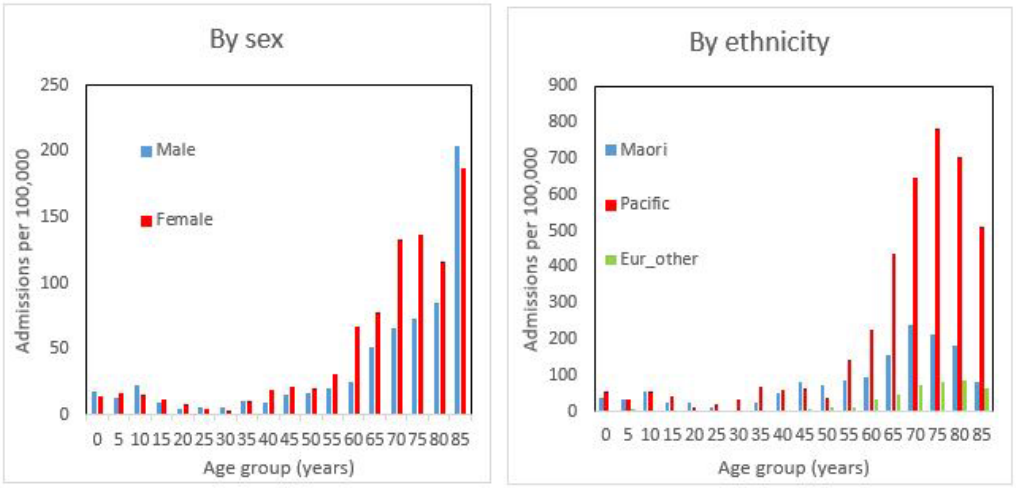
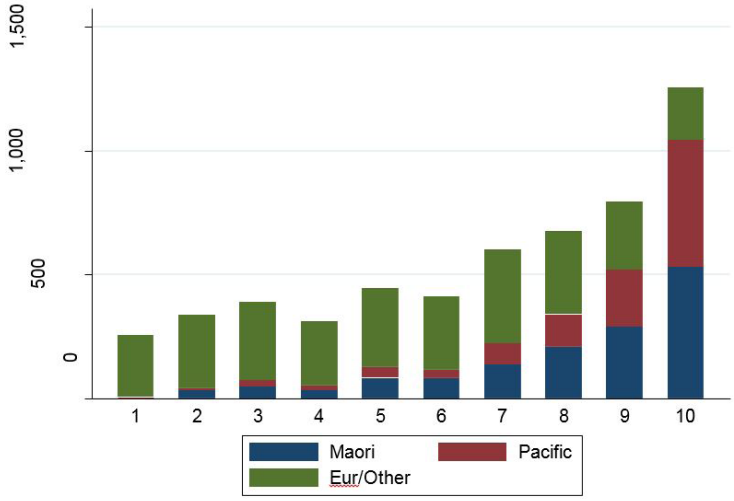


Table 1: Average length of stay in FY 2008–2012 by ethnic group

	Number of admissions	ALOS in days (±95% CI)
Māori	1,448	5.78 (5.51, 6.05)
Pacific	1,095	5.60 (5.26, 5.94)
European/Other	2,951	5.50 (5.25, 5.74)
Total	5,494	5.59 (5.43, 5.76)

ALOS = average length of stay

Figure 2: Admissions in FY 2008–2012 by ethnicity and socioeconomic deprivation



Abscissa: NZDep2006

years 2008/09 to 2012/13. Twenty-five admissions had a length of stay greater than 89 days, leaving 5,494 admissions for analysis. The annual number of admissions was stable across the 5-year period, despite an ageing population, with a mean of 1,100 admissions per annum.

By age group, admissions had a double peak which centred on children less than 15 years of age and older adults. Admission rates for children were markedly higher for Māori and Pacific peoples than for European/other children. Adult admission rates for older adults were higher for women than men, and also for Māori and Pacific than for European/others (Figure 1).

The average length of stay did not differ statistically across the 3 main ethnic groups (Table 1).

Admissions varied substantially with the level of socioeconomic deprivation. The total number of admissions for those patients residing in NZDep06 decile 10 was approximately five-fold higher than those in decile 1: when broken down by ethnicity, this was largely accounted for by the

Table 2: Admission rates by sex and by the major ethnic groups in FY 2012/13

	Number	Crude rate[a]	Age adjusted rate	Rate ratio[b]
By sex				
Females	3,402	30.9	23.5	1.38
Males	2,092	20.2	17.0	1.00
Total	5,494	25.7	20.4	
By ethnicity				
Māori	1,448	51.2	54.3	4.93
Pacific	1,095	78.4	100.0	9.09
European/other	2,951	17.2	11.0	1.00
Total	**5,494**	**25.7**	**20.4**	

[a]Per 100,000 population
[b]Relative to males or relative to European/Other (age adjusted)

Table 3: Hospital admissions in FY 2008/09 to 2012/13 by DHB

DHB	Māori	Pacific	Eur/Other	Total	Crude rate/100K[a]	% of M/P admissions	30 day readmissions	Cost ($m)
Counties Manukau	338	537	285	1160	49.4	75%	13.0%	$5.49
Auckland	109	214	354	677	31.0	48%	13.1%	$3.59
Lakes	111	3	38	152	31.0	75%	12.5%	$0.71
Hutt Valley	83	36	82	201	29.1	59%	15.4%	$0.93
Bay of Plenty	80	3	214	297	28.8	28%	6.7%	$1.06
Canterbury	55	32	578	665	27.6	13%	10.7%	$3.09
Northland	136	1	70	207	27.3	66%	22.2%	$0.87
Tairawhiti	38	0	19	57	26.1	67%	8.8%	$0.27
Waitemata	101	164	367	632	24.1	42%	13.9%	$2.86
Waikato	184	18	184	386	21.5	52%	8.5%	$1.71
Capital & Coast	48	49	170	267	18.8	36%	12.4%	$1.50
Nelson Marlborough	16	5	105	126	18.4	17%	6.3%	$0.46
Hawkes Bay	49	11	77	137	18.1	44%	14.6%	$0.59
West Coast	1	0	25	26	16.2	na	19.2%	$0.11
Whanganui	18	0	30	48	16.0	38%	14.6%	$0.28
Southern	18	4	212	234	15.7	9%	12.4%	$1.07
MidCentral	37	13	52	102	12.5	49%	14.7%	$0.49
Taranaki	19	0	47	66	12.0	29%	15.2%	$0.28
South Canterbury	1	0	23	24	8.6	na	12.5%	$0.09
Wairarapa	4	0	5	9	4.4	na	na	$0.05
Total or mean[a, b]	1,446	1,090	2,937	5,473	100.0%	40% (mean)	12.5% (mean)	$25.50

Na = small numbers and uncertain conclusions; M/P = Māori or Pacific peoples
[a]2013 census populations were used to calculate rates
[b]Totals and means for New Zealand differ slightly from those expressed elsewhere because of missing DHB allocations

Figure 3: Time to readmission for patients who were readmitted within 12 months of discharge

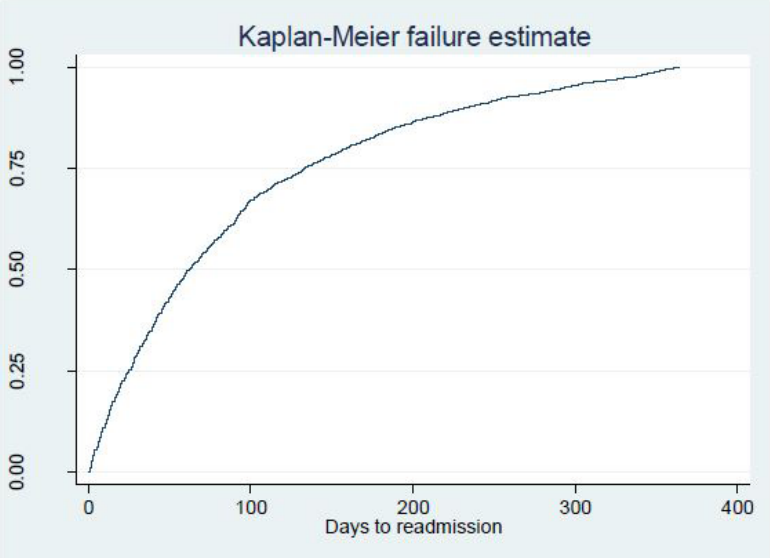
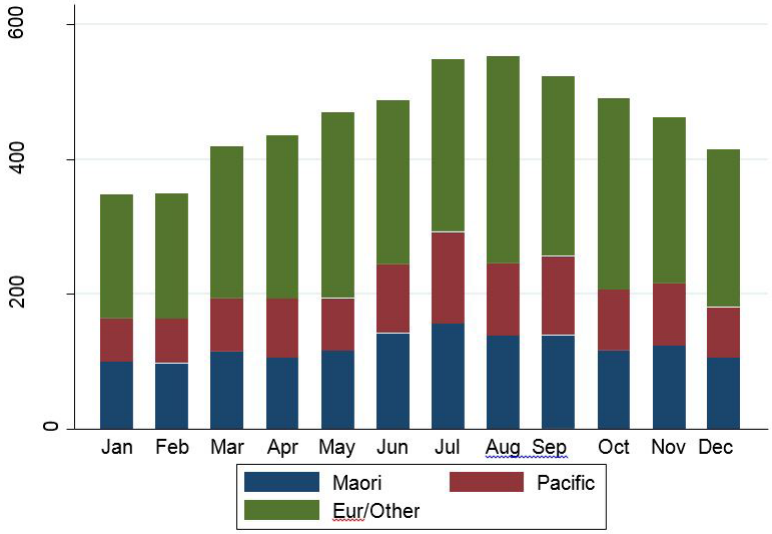


Figure 4: Season of admissions for bronchiectasis



proportions of admissions for Māori/Pacific peoples increasing steeply with socioeconomic deprivation (Figure 2).

Age adjusted mean admission rates over the 5-year period were 38% higher for women than men; and 4.9-fold higher for Māori and 9.1-fold higher for Pacific peoples than for European/other ethnicities (Table 2). The overall crude rate was 25.7 and age-adjusted rate 20.4 admissions per 100,000 population.

Admissions by DHB

Admissions were distributed unevenly across the 20 DHBs (Table 3).

Re-admissions

In the 12-month period July 1, 2012 to June 30, 2013 there were 1,172 admissions, 227 re-admissions (19%) within 90 days, and 115 re-admissions within 30 days. Over the entire 5-year study period, the 30 day re-admission rate was 12.4%, and 2,364 patients out of 5,494 (43%) were re-admitted within 12 months: the time to re-admission of those 43% is shown in Figure 3. Time to re-admission was independent of ethnicity and socioeconomic deprivation.

Season of admissions

Hospital admissions were more common in winter and spring than summer or autumn (Figure 4).

Budget impact

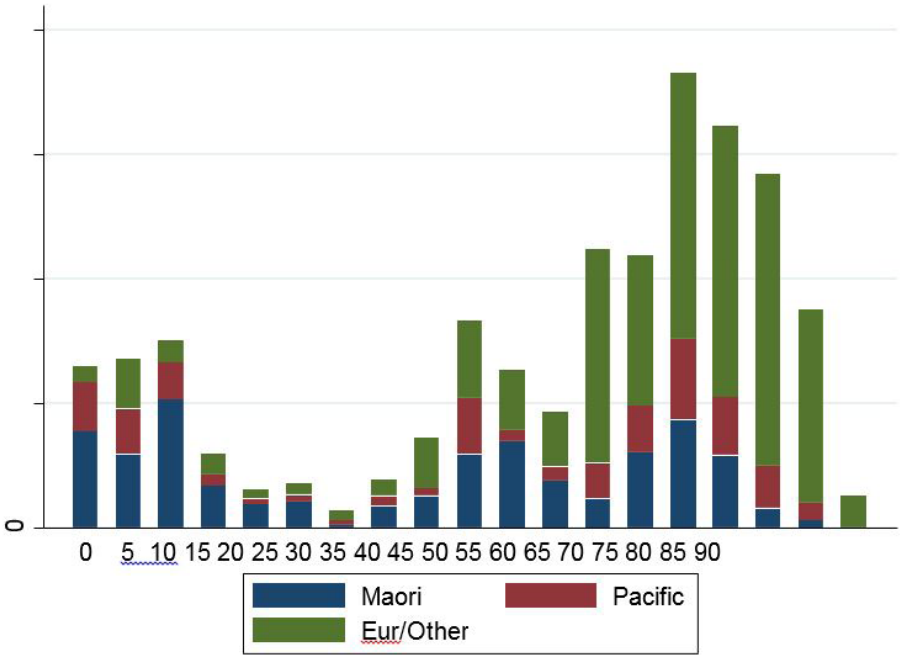
Over the 5-year period there were 5,494 admissions at an estimated cost of NZD 25.6M. There was no evidence of a statistically significant difference in mean cost across years (Table 4). In financial year 2012/13, the mean cost per admission for bronchiectasis was NZD 4,555, and the total cost was NZD 5.34 million. Corresponding to admissions, most of the cost was for the elderly, with NZD 0.95 million (18%) for

Table 4: Admissions and their estimated budget impact in FY 2008/09 to 2012/13

Financial year	Admissions	Mean cost (±95% CI)	Total cost ($m)
2008/09	1,028	4,616 (4,486, 4,745)	4.74
2009/10	1,078	4,714 (4,589, 4,838)	5.08
2010/11	1,083	4,618 (4,495, 4,741)	5.00
2011/12	1,133	4,806 (4,686, 4,926)	5.45
2012/13	1,172	4,555 (4,442, 4,668)	5.34
Total	5,494	4,662 (4,637, 4,686)	25.61

All costs are in 2012/13 New Zealand dollars (NZD)

Figure 5: Budget impact by age and ethnicity in FY 2012/13 (NZD)



Abscissa: 5-year age group (years)

children and youth less than 20 years of age and a disproportionally high cost for Māori children (Figure 5).

Discussion

This analysis shows that there is a substantial burden of bronchiectasis in New Zealand occurring from hospital admissions for moderate to severe exacerbations. There is a double peak of hospital admissions for bronchiectasis by age, occurring in children less than 10 years of age, and the over-65s, with adult admissions being higher for women than men, higher in Māori and Pacific communities, and increasing with the standard index of socioeconomic deprivation.

After adjustment for age, admission rates are raised by 5-fold in Māori and by 9- fold for Pacific populations compared to others. Previous reports also highlight the difference in rates of hospital admissions for bronchiectasis between ethnic groups: admissions in 2003–2005 were 3.6 times higher for Māori compared to non-Māori, with the difference rising with age from double the rate for the paediatric population to nearly 6 times the rate at ages 45–64 years.[6] The high prevalence in Māori and Pacific communities is likely to be related, at least in part, to socioeconomic deprivation: here, we found that admission rates increased markedly with decreasing socioeconomic status, as also found previously in studies that focused on the wider Auckland area,[8,10] which has the highest rate of admissions in the country. In a retrospective study of adults hospitalised with bronchiectasis in Middlemore Hospital during 2002,[10] 27% were Māori

and 41% Pacific peoples. Another study, of paediatric outpatients with bronchiectasis in Auckland, showed that 25% of outpatient visits were by Māori and 55% were by Pacific patients.[8] This contrasts with the census population of this area, where only 18% and 17% of children were Māori and Pacific respectively.[8] Similarly to our national data, these studies show admission rates in Auckland also increasing with decreasing socioeconomic status: 77% of adult inpatients[10] and 67% of paediatric outpatients[8] lived in areas categorised as the 30% most deprived in New Zealand, where just 49% of adults reportedly reside.[10] Substandard housing, malnutrition, barriers to medical care and inadequate education are all likely to impact on the occurrence and outcome of bronchiectasis.[6] Low immunisation rates in these communities may also be a factor, as infant vaccination against diseases such as whooping cough are important in childhood prevention.[6] In New Zealand, half of the cases in children and adults with a known aetiology were caused by childhood infection,[8,10] underlying the importance of prompt treatment of respiratory infections. Vaccinations against influenza and pneumococcal diseases are also important parts of the management of bronchiectasis.[6]

The rate of admissions in different DHBs varied substantially, with Counties Manukau having much a higher admission rate than other DHBs, and thus the highest 5-year cost. With the exception of Canterbury, those DHBs with the highest rates generally had the highest proportions of Māori and Pacific peoples admitted. The overall percentage of cases which were in people of Maori and Pacific Island descent, 40%, is over twice that reported in the last census (19.6%).

The impact of sex on adult admissions seen here has been noted previously: an analysis of Medicare beneficiaries in the US showed that women 65–85 years had a prevalence 1.3 to 1.6-fold higher than men of the same age group.[4] At Middlemore Hospital, 59% of patients admitted with bronchiectasis were women, despite an almost equal male/female balance in census data for Counties Manukau DHB.[10] Bronchiectasis was reported in 1994 to be the 6th most common cause of death for Pacific women over 65 years of age, but was not listed in the top eight causes for men of the same age and ethnic group; it did however have almost equal ranking as a cause of admissions.[11] The imbalance between the sexes in our study is unlikely to be due to relative longevity because age-specific admission rates were higher for women 40–80 years of age.

The estimated costs corresponding to admissions reported in this analysis are likely to be a gross underestimate of the real disease burden. Admissions with other principal diagnoses, such as chronic obstructive pulmonary disease (COPD), asthma or pneumonia, that could have been due to, complicated and/or prolonged by a comorbidity of bronchiectasis were excluded from the analysis, as we did not assess admissions in which bronchiectasis was a secondary diagnosis. However, we suspect that bronchiectasis may be a contributing factor in other respiratory admissions, as previous studies have reported comorbidities in 80% of adults admitted with bronchiectasis (most commonly COPD or asthma),[10] while 37% of children with bronchiectasis had a clinical history of asthma.[8]

Hospital admission is an indicator of disease severity,[12] with prior research showing that 21% of adults admitted with bronchiectasis died within 12 months of admission: that study, on adult inpatients over a 12-month period, showed a readmission rate of 46%.[10] Here we found a similar rate of 43% having a repeat admission within 12 months of the index admission over this 5-year period. We did not find ethnic or socioeconomic differences in the time to readmission. Other predictors of disease prevalence thus presumably influence the reports of different mortality rates in different ethnic groups (in 2000–2004 the overall mortality rate from bronchiectasis was 6.7 times higher in Māori than Non- Māori).[6]

Bronchiectasis also comprises a costly respiratory disease, with 1,172 hospital admissions in 2012/13, costing the DHBs an estimated NZD 5.34 million (giving a mean cost per admission for bronchiectasis of $4,555). This figure is likely to be an underestimate, as it was based on casemix cost weights rather than detailed patient-level assessment. This estimate is also conser-

vative due to the exclusion of outpatient and GP appointments, emergency care, community pharmaceuticals and admissions with a length of stay greater than 90 days. These will all contribute to care of these patients, but were outside the scope of this study. Non-medical costs also include disability care and loss of earnings by patients. In the US, it was estimated that total medical-care expenditures for the year 2001 were on average $5,681 higher for those individuals with bronchiectasis than without.[13] While the annual cost is much less than that due to COPD in New Zealand,[14] community interventions to prevent or treat bronchiectasis and reduce admissions could have an important impact on the healthcare budget. The disproportionately high cost for Māori children that we see here is also a concern.

Interventions that may help reduce the burden of bronchiectasis include increasing immunisation rates;[6] improvements in housing (overcrowding has been shown to increase risk of other diseases in New Zealand[15]); treatment of exacerbations with antibiotics—IV when indicated, and long-term when appropriate[3]—and sputum clearance techniques.[3] Novel medical therapies are now also becoming available, such as long term humidification therapy, which may also help decrease the frequency and duration of exacerbations; although this study did not separate bronchiectasis from COPD.[16]

In conclusion, hospital admissions for bronchiectasis peak in both the young and the older adult by age, and are concentrated in socioeconomically disadvantaged Māori and Pacific peoples. Admissions are more common for women than for men, and for colder months of the year: and they incur a high cost. Effective community interventions that are targeted to disadvantaged communities, high-risk ethnic groups and perhaps tailored to season could greatly reduce the human and economic burden of respiratory illness.

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Understanding administrative coding of emergency department visits for unspecified acute allergic reactions

Colleen McMilin, Carlos Camargo Jr, Susan Morton, Cameron Grant

ABSTRACT

AIM: Emergency department (ED) visits for food-related acute allergic reactions enable estimation of temporal trends in food allergy prevalence. To use this approach in New Zealand requires an understanding of the proportion of ED visits coded as 'anaphylaxis, unspecified' or 'allergy, unspecified' that are food-related allergic reactions.

METHOD: We reviewed all ED presentations of children, coded as 'anaphylaxis, unspecified' or 'allergy, unspecified', from 1988–2011 to the Auckland City Hospital ED. Charts were reviewed independently by two investigators to determine agreement on categorisation of presentations as being food-related acute allergic reactions. We compared ED presentation rates in different time intervals using rate ratios (RR) and 95% confidence intervals (CI).

RESULTS: Sixty-five (29%) of the 221 ED presentations given a discharge code of 'anaphylaxis, unspecified' or 'allergy, unspecified', were a food-related allergic reaction. Inter-observer agreement was very good (kappa >0.80). The ED presentation rate with food-related allergic reactions in 2004-2011 was 98% higher than in 1988–1995 (RR=1.98, 95%CI 1.10–3.72). By contrast, ED presentation rates for non-food-related allergic reactions did not change over these years.

CONCLUSION: ED presentations for food-related allergic reactions are identifiable from within ED presentations coded as 'anaphylaxis, unspecified' or 'allergy, unspecified'. ED presentations for food-related allergic reactions have increased over time in Auckland.

Worldwide, food allergies have been the subject of much debate in recent decades due to what many observe as a dramatic increase in childhood food allergy prevalence, incidence, and severity.[1–5] Despite New Zealand having one of the highest prevalences of asthma worldwide, the epidemiology of other atopic diseases, including food allergy, has been poorly characterised.[6–8]

Due to difficulties inherent with the establishment of stable and repeatable measures of food allergy prevalence in the community or in primary care settings, hospital emergency department (ED) presentations for food-related acute allergic reactions have been used in other countries to estimate temporal trends.[9–12] Such an approach would seem particularly appropriate in New Zealand given that acute hospital-based secondary care services are free, the hospital presentation data is stored and accessible at both a national and regional level, and each person having contact with health services in New Zealand is assigned a unique identifier: the national health index (NHI) number.

While hospital event data only describes food-related allergic reactions at the severe end of the clinical spectrum, these data do allow for a measure of disease burden that is less subject to bias than those based upon self-report, or in the case of children, parental report. Rates of IgE-mediated food allergy can easily be overestimated as people confuse IgE-mediated food allergy

with other, non-IgE-mediated, food intolerances. Rate estimates based on studies that use self-reported data are often based on broad questions, for example "do you (or your child) have a food allergy?"[13] A systematic review of studies published from 1988 to 2009 showed that the prevalence of food allergy estimated from self-report data is much higher than that estimated when diagnosis is based upon skin prick testing, food specific IgE determinations or food challenges.[14] For example, based on the inclusion of 51 relevant studies, the pooled estimate for cow's milk allergy prevalence from self-report was 3.5%, and from the other three methods was between 0.6% and 0.9%.[14] Population estimates of food allergy prevalence based upon self-reported data also vary widely between studies, ranging from 1.2% to 17% for milk, 0.2% to 7% for egg, 0% to 2% for peanuts and fish, 0% to 10% for shellfish, and 3% to 35% for any food.[15]

Episodes of acute allergic reactions that result in ED presentations are identified by administrative codes based on the International Classification of Diseases (ICD) system. These codes include both those specific to food-related allergic reactions (eg, contact dermatitis due to food in contact with skin, dermatitis due to food taken internally, anaphylactic shock due to peanuts) and those that are more generic (eg, anaphylaxis unspecified, allergy unspecified).

Inconsistent code assignment and lack of a universally-accepted clinical definition for anaphylaxis have required that investigation of ED presentations for food-related allergic reaction presentations consider both visits coded as being food-related and visits coded as being due to an anaphylactic or allergic reaction not further specified.[9,12,16–18] In a study conducted across multiple US EDs, relying solely on food specific ICD-9-CM codes resulted in identification of only 53% of patients presenting to the ED with a food-related allergic reaction, whereas 87% of patients presenting with insect sting-related allergic reactions were identified by the codes specific to insect sting-related reactions.[17] In another multi-site ED study from the US—specifically of ED visits for food-related allergic reactions—57% of patients were identified by using food-related allergic reaction codes and an additional 43% were identified from within less specific ICD-9 codes.[16] Hence, the inclusion of only patients who are identified by ICD codes specific to food-related allergic reactions results in an underestimation of the true frequency of ED presentations.[11,17]

To describe temporal trends in food-related allergic reactions in New Zealand requires a more comprehensive understanding of the application of the commonly used administrative codes (ie, ICD-9-CM-II and ICD-10-AM). Specifically, it is necessary to determine for what proportion of ED visits coded as ICD-9 codes 995.0 (ICD-10 T78.2) (anaphylaxis, unspecified) and 995.3 (ICD-10 T78.4) (allergy, unspecified) is the ED presentation due to a food-related allergic reaction?

Our objective was to complete a review of the ED presentations of children who presented to a public hospital ED between 1988 and 2011 with allergic reactions that were coded as either 'anaphylaxis, unspecified' and/or 'allergy, unspecified'. From this review we sought to establish the proportion of children with an ED presentation, identified by the aforementioned ICD-9 and ICD-10 codes, in whom the presentation was caused by a food-related allergic reaction. Knowledge of this proportion is necessary before being able to utilise national ED presentation data to determine if there have been increases in food-related allergic reaction hospital presentations in New Zealand in recent decades.

Method

We completed a chart review of all presentations from 1988 to 2011 of children (0–14 years old) to the public hospital ED in the Auckland District Health Board (ADHB) region, for which the ICD codes for 'anaphylaxis, unspecified' or 'allergy, unspecified', were assigned. Although these codes only capture a subset of acute allergic reaction presentations, it is important to focus on these unspecified codes as they account for the majority of ED presentations that are not identified by food specific ICD codes. We chose this time period because it is the same as that for which data are available nationally. The ADHB operates New Zealand's largest public hospital, with almost two million patient contacts

Table 1: Definitions used to categorise hospital presentations identified by ICD codes 'anaphylaxis, unspecified'* and 'allergy, unspecified'† in children (0–14 years).

Food-related allergic reaction category	Features used to assign hospital emergency department visits to each category
Food-related	• History of atopic disease and generalised reaction shortly after consuming specified food *Or* • A previous episode of food-related allergic reaction with the reaction occurring in a location where food supervision was potentially not stringent and the history indicated timing in association with food consumption *Or* • A generalised reaction in association with food without documentation that exposure to a new food had occurred
Not food-related	• Non-food allergen identified • Localised reaction eg, digit or eye
Unknown cause	• Generalised reaction not related to meal • No known allergen exposure or no allergen exposure documented • No past history of food-related allergic reaction

* Anaphylaxis, unspecified = ICD-9 code 995.0 or ICD-10 code T78.2

† Allergy, unspecified = ICD-9 code 995.3 or ICD-10 code T78.4

annually, serving more than 30% of the Auckland population.[19] The demographics of the ADHB population are broadly generalisable to the national population. Population estimates were based upon the national five-yearly census and intercensal estimates.[20] Ethical and institutional approval for the project was granted by the ADHB Research Review Committee (Approval number A+ 6133).

Patient record data at ADHB is predominantly electronic. Once identified, patient charts were obtained from the ADHB. We reviewed these charts and extracted data to describe demographics and determine whether the hospital presentation was due to a food-related allergic reaction. Presentations were categorised as food-related, not food-related or due to an unknown cause (Table 1).

To ensure that data extraction was complete and allergic reaction categorisation was consistent, the two reviewers (CM and CCG) independently reviewed all of the patient charts and assigned each ED presentation as being due to a food-related allergic reaction, non-food-related allergic reaction or due to a reaction for which the cause was unknown. We then determined inter-observer agreement for this categorisation.

Statistical analyses

Agreement between investigators was calculated using a Kappa (κ) statistic. Kappa scores and 95%CI were calculated using SAS SAS-PC version 9.3 software. Kappa scores were defined as showing poor (κ ≤0.2), fair (κ >0.2 to ≤0.4), moderate (κ >0.4 to ≤0.6), good (κ >0.6 to ≤0.8) or very good (κ >0.8 to ≤1.0) agreement.[21]

We compared the age of those for whom the ED presentation was or was not a food-related allergic reaction using the Wilcoxon Rank-Sum test. We described the number of individuals in each year with an ED presentation that was food-related, not food-related or of unknown cause and determined whether the annual number of presentations in each of these three categories changed over time. We assumed that, in addition to being infrequent, presentations to the ED in each of these categories occurred independently of each other and at a constant rate.[22]

In view of the small number of ED presentations per year in each of the three categories (food-related, not food-related or unknown cause) and large year-to-year variability we grouped cases into eight-year intervals (ie, 1988–1995, 1996–2003, and 2004–2011), and described the number of presentations per person-year in each interval. Using the first time interval as the reference period, we then determined if ED presentation rate in the other two subsequent eight-year time intervals differed from this baseline interval, using rate ratios (RR) and 95% CIs. Because anaphylaxis is only identified in a proportion of patients

Table 2: Categorisation of children aged 0 to 14 years presenting to the hospital emergency department with 'anaphylaxis, unspecified'* and 'allergy, unspecified'† from 1988 to 2011.

			Categorisation by investigator one n(%)		
	Food-related allergic reaction category	Food-related	Not food-related	Reaction to unknown cause	Total
Categorisation by investigator two n(%)	Food-related	58 (26)	2 (1)	3 (1)	63 (29)
	Not food-related	5 (2)	125 (57)	13 (6)	143 (65)
	Unknown cause	2 (1)	3 (1)	10 (4)	15 (7)
	Total	65 (29)	130 (59)	26 (12)	221 (100)

* Anaphylaxis, unspecified= ICD-9 code 995.0 or ICD-10 code T78.2
† Allergy, unspecified = ICD-9 code 995.3 or ICD-10 code T78.4

Table 3: Agreement between researchers in categorising of hospital presentations

Categories	Kappa score* (κ)	95% CI
Food-related vs. not food-related or unknown	0.87‡	0.80-0.94
Food-related vs. not food-related	0.92‡	0.85-0.98

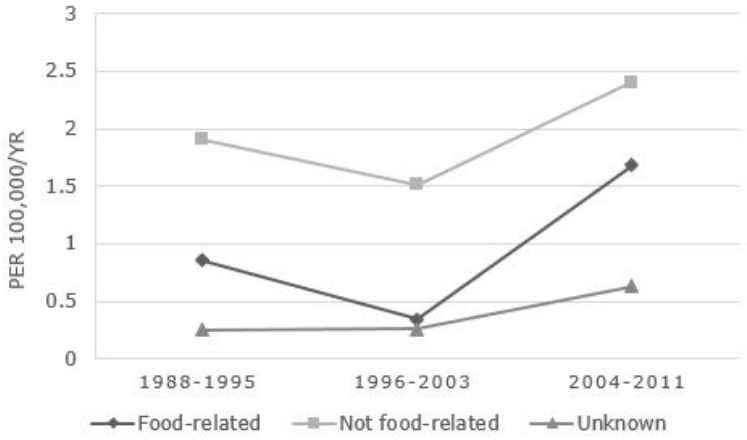
* Inter-observer agreement classification: Poor (κ ≤ 0.2), fair (κ >0.2 to ≤0.4),moderate (κ >0.4 to ≤0.6), good (κ >0.6 to ≤0.8) or very good (κ >0.8 to ≤1.0) agreement.
‡ Simple kappa

Table 4: Comparison of rate of hospital presentations due to acute allergic reactions in Auckland that were coded as 'anaphylaxis, unspecified'* and 'allergy unspecified'†: 1996–2003 and 2004–2011 versus 1988 to 1995.

Time interval	Average population per year	Number of ED presentations	Rate ratio vs. 1988–95 (95% CI)‡	P value
Food-related				
1988–95	249,270	17	1.00	---
1996–03	289,047	8	0.41 (0.15–0.99)	0.03
2004–11	296,841	40	1.98 (1.10–3.72)	0.02
Not food-related				
1988–95	249,270	38	1.00	---
1996–03	289,047	35	0.79 (0.49–1.29)	0.32
2004–11	296,841	57	1.26 (0.82–1.95)	0.27
Unknown				
1988–95	249,270	5	1.00	---
1996–03	289,047	6	1.03 (0.26–4.29)	0.95
2004–11	296,841	15	2.52 (0.87–8.86)	0.06

Abbreviation: ED, emergency department.
* Anaphylaxis, unspecified = ICD-9 code 995.0 or ICD-10 code T78.2
† Allergy, unspecified = ICD-9 code 995.3 or ICD-10 code T78.4
‡ CI = confidence interval

Figure 1: Trends in hospital presentations due to acute allergic reactions that were coded as 'anaphylaxis, unspecified'* and 'allergy, unspecified'†



* Anaphylaxis, unspecified = ICD-9 code 995.0 or ICD-10 code T78.2
† Allergy, unspecified = ICD-9 code 995.3 or ICD-10 code T78.4

making an ED presentation with anaphylaxis we combined ED presentations for which the code identified or did not identify the presence of anaphylaxis.[18]

Results

Of the 248 records that met the inclusion criteria, 226 were reviewed by both reviewers. We included 221 (89%) in the analysis, with the five excluded being duplicate presentations; we only counted the first event for the individuals who presented twice. None of the five presentations excluded were food-related acute allergic reactions. Of these 221 presentations, 120 (54%) were coded as 'anaphylaxis, unspecified', and 101 (46%) as 'allergy, unspecified'. Records reviewed by both investigators were categorised with respect to the probability of the allergic reaction being due to a food allergen (Table 2).

Inter-observer agreement was very good for categorisation into a food-related allergic reaction versus all other visits (κ=0.87) or only an allergic reaction not due to food (κ=0.92) (Table 3).

Sixty-five (29%, 95%CI 24–36%) of the 221 hospital presentations with a discharge code of 'anaphylaxis, unspecified' or 'allergy, unspecified', were identified as food-related allergic reactions. Of these 65 presentations, 43 (19%) were coded as 'anaphylaxis, unspecified', and 22 (10%) as 'allergy, unspecified'. Of the remaining presentations, 130 (59%, 95%CI 52–65%) were not due to a food-related allergen, and 26 (12%, 95%CI 8–17%) were due to an unknown allergen. Median age at presentation of those with a food-related allergic reaction (2.0 years) was less than those for whom the allergic reaction was not food-related (7.0 years, p<0.001) or was due to an unknown allergen (8.5 years, p=0.02).

Change over time was evident for the rate of hospital presentations for food-related allergic reactions, but not for reactions that were non-food-related or for which the allergen was unknown (Figure 1). In comparison to the 1988–1995 time interval (average annual rate 0.85/100,000), the rate of presentation with food-related allergic reactions was lower from 1996–2003 (0.35/100,000, RR=0.41) and higher from 2004–2011 (1.68/100,000, RR=1.98) (Table 4).

The proportion of presentations that were due to a food-related allergic reaction varies slightly between the three time intervals (p=0.04), however not in any directional way. Upon further investigation in which the proportions were grouped into six four-yearly time intervals, random variance is present, as there is no statistically significant directional trend (p=0.07). The distribution of food-related allergic reactions and their proportion of all presentations across the four-year period was 7 (29%) in 1988–1991, 10 (28%) in 1992–1995, 1 (6%) in 1996–1999, 7 (21%) in 2000–2003, 9 (23%) in 2004–2007 and 31 (42%) in 2008–2011.

Discussion

Food-related acute allergic reactions account for 29% of hospital presentations that were assigned a discharge code for 'anaphylaxis, unspecified' or 'allergy, unspecified'. Identification of these cases permitted us to have a more complete picture of ED visits for unspecified acute allergic reactions. In comparison with

1988–95, the ED presentation rate for food-related allergic reactions decreased during 1996–03 and then increased during 2004–11, with the average annual rate from 2004–11 being almost twice as high as it had been from 1988–95. In contrast, there was no significant change over time in the hospital presentation rates for 'anaphylaxis, unspecified' or 'allergy, unspecified' ED presentations that were not food-related or for which the allergen was unknown.

An unanticipated finding from this study was the decrease in food-related allergic reaction presentations during the time period 1996–03. A similar, but non-significant, reduction was also seen during this time interval in hospital presentation rates for acute allergic reactions that were not food-related. In July of 1995 (the start of the 1995/96 New Zealand financial year), New Zealand changed from using ICD-9-CM to ICD-9-CM-A discharge coding systems. As part of this change the National Coding Standards were introduced, including a coding standard for allergic reactions. These standards were introduced to improve consistency in applying the classifications across the hospital and health services of New Zealand. This change may have resulted in a more strict application of the ICD codes investigated in this study, potentially leading to a decrease in the number of ED presentations assigned these codes. Another factor that may potentially explain the decrease in ED presentations during this time period is that it was a period when the New Zealand health care system experienced some major structural changes which included the temporary introduction of part charges for public hospital presentations.[23]

Based on the data obtained from the ADHB, the code 'anaphylaxis, unspecified' (19%) was used for a larger proportion of the hospital presentations than was reported from a large US study of ED presentations for acute allergic reactions where <1% of all ED visits were coded as anaphylaxis.[18] Based on other work by the authors of this US study,[16,24] which shows that approximately 51% of food-related allergic reactions and 31% of venom-related allergic reactions result in anaphylaxis, this very low proportion of ED presentations that were coded as anaphylaxis implies these codes cannot be used to reliably identify all ED presentations where anaphylaxis has occurred. Due to the variable documentation of presenting symptoms and signs in the Auckland records, we cannot determine from our study if the rate of hospital presentation with true anaphylaxis differs in New Zealand from that reported in the US.

Our study represents the first attempt to estimate the frequency of hospital ED presentations of food-related allergic reactions in New Zealand. We have validated the methodology for identifying, at a national level, the food-related proportion of hospital presentations assigned a discharge code for 'anaphylaxis, unspecified' or 'allergy, unspecified'. Our data suggest that, consistent with observations reported from Australia and the US, the rate of such presentations has increased in New Zealand in recent years.[11,12]

In comparison with other causes of ED presentations, food-related acute allergic reactions are relatively rare events. Our study only included a subset of these food-related allergic reactions, as we were only investigating those ED presentations that were coded as 'anaphylaxis, unspecified' and 'allergy, unspecified'. Because of these small numbers it was necessary to combine years to allow for temporal trends to be determined. As a result it was difficult to identify the true impact of events such as the 1995 change from using ICD-9-CM to ICD-9-CM-A codes. Nor were we able to determine if there has been a plateauing in the rate of hospital presentations for food-related allergic reactions as has been reported recently from the US.[9] A subsequent larger national study is likely to overcome the issues described, as it will allow for the inclusion of the unspecified and specific food-related allergic reaction codes.

We showed very good inter-observer reliability in our assignment of ED presentations to the different food-related categories and to the food versus not-food related categories. No trend over time was observed in our estimate of the food-related proportion of hospital presentations coded as 'anaphylaxis, unspecified' or 'allergy, unspecified'. Thus it appears reasonable to infer that these observations are likely to apply to national data over the same time interval. It

is important though to remain aware of the potential for the quality of such clinical data to change over time. For example, in 1992 the number of diagnosis codes for an event that were included in National Minimum Dataset reporting expanded from 4 to 25. Since this time they have been expanded even further to 99 codes which could lead to an increase in the number of codes used per event, and thus potentially inflate the overall total number of presentations for which a food-related code was included.

Our study provides insight into the use of two unspecified ICD codes in one large New Zealand hospital ED and sets the foundation for future work on the epidemiology of food allergy and food allergy-related allergic reactions in New Zealand. We can now justify including a proportion of presentations from both ICD codes 'allergy, unspecified' and 'anaphylaxis, unspecified' in a national study of ED presentations of food-related allergic reactions. This will enable us to describe this aspect of food allergy epidemiology in a manner that will enable comparison with other countries.

Competing interests: Nil

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What have five years of the shorter stays in the emergency department health target done to us?

Michael Ardagh, Lynette Drew

ABSTRACT

This paper reviews the first five years of the shorter stays in the emergency department national health target—its genesis, implementation and impact. Five years of the target have seen a maturing 'whole-of-system' collaboration leading to better patient care. However, there is still much to do and demand continues to increase. Assisted by the *Quality framework and suite of quality measures for the Emergency Department phase of acute patient care in New Zealand*, a good structure and methodology driving improvement, and a patient centred focus, this work must continue.

In May 2009, the Minister of Health announced six national health targets for New Zealand, including the 'Shorter stays in Emergency Departments' health target (the target), defined as '95% of patients will be admitted, discharged or transferred from an emergency department (ED) within six hours of presentation.' District Health Boards have been required to aspire to the target since 1 July 2009. After 5 years of this aspiration what have we achieved? This paper will briefly discuss this before suggesting future challenges and directions.

A new health target

The target was a very significant development in acute care in New Zealand, being the first and only high-level accountability measure specifically examining the timeliness of the whole system of care for acute (unplanned and urgent) illness and injury. The absence of any specific accountability measure for acute care prior to the target had allowed worsening overcrowding of EDs and hospitals and the associated high levels of adverse events, complaints, and negative media attention.[1]

The target's origins came from the advocation of clinicians over a number of years and led to a seminal workshop on ED overcrowding in Wellington in early 2008. A concluding consensus was that a time-based health target should be 'worked up'. This culminated in the presentation of a document to the Minister of Health in late 2008 called: *The Report of the Working Group for Achieving Quality in Emergency Departments*. The report included a thorough examination of the current state of ED and acute care, a summary of the literature and international precedents regarding ED overcrowding and a number of recommendations. The principle recommendation was the adoption of a high-level health target based around length of stay for patients in the ED.

As a result of the report's recommendations, the Minister appointed a National Clinical Director of Emergency Department Services—a position also known as the 'Target Champion'—endorsed the establishment of a National ED Advisory Group (the Group), consisting mostly of doctors and nurses from throughout New Zealand, and agreed to an ED length of stay health target.

While the ED phase of acute care is only one part, it was appreciated that prolonged ED length of stay, and by association ED overcrowding, were manifestations of defi-

ciencies throughout the acute care system (the Minister described ED length of stay as a 'barometer' for the whole system). For this reason, and for its ease of measurement and comparison, an ED length of stay target was chosen as the most appropriate single, high-level measure of performance of the acute care system.

The English experience

However, an ED length of stay target was not a new concept. The English National Health Service (NHS) had entertained one for the previous several years. The views in England regarding the success of their 4-hour ED length of stay target were mixed,[2] with both praise for its influence on reducing ED overcrowding and suggestions that it caused more harm than good.[3] With an understanding of the NHS experience and initiatives to improve acute patient care (particularly patient flow through the hospital system) using methodologies such as Lean Thinking, the New Zealand target was defined and implemented.

Quality versus compliance[4]

An important contrasting feature of the New Zealand target was the formative involvement of clinicians in its genesis, definition and ongoing implementation. Clinicians were aware that it was possible to achieve the target without resolving important contributors to patients staying longer in EDs, and without getting patients more quickly to the care they should be receiving.

It is possible to achieve compliance without improving quality—hitting the target, but missing the point. Awareness of this, and particularly perceptions that compliance and not quality drove a number of initiatives in NHS hospitals, was (and still is, to a lesser degree), a barrier to acceptance of the target by many clinicians. A second barrier is the unfortunate but unavoidable focus on the ED in the target's title, suggesting to many non-ED clinicians that the target was not their concern.

Without embedding genuine quality there are two possible adverse effects of the target; gaming the target, and shifting the problem.

Gaming the target may include delays to starting the clock, (eg, by keeping patients in ambulances), and premature stopping of the clock, (eg, by calling patients in the corridor admitted 'observation patients'). If patients are moved out of the ED to hospital wards, without adequate provision for this work, the problem currently manifest in the ED will surface elsewhere (shifting the problem).

From the beginning, pursuit of the target in New Zealand has been prefaced with the proviso that the target must drive quality and not blinkered compliance (the clock must not trump clinical decisions). In addition to the Ministry of Health scrutinising activities, there is a commitment from the clinical community to 'police' activities towards the target and to stand against any attempts to achieve the target by gaming or shifting the problem. While this has been successful it is important to reiterate the importance of not gaming or shifting the problem.

The solutions are 'whole-of-system'—attention to this principle is a pre-requisite for success. To achieve 'whole-of- system' commitment to this work requires the willing engagement of all clinicians throughout the system. Gaming the target or shifting the problem will inevitably disengage clinicians, in addition to being bad for our patients. False gains achieved in this way ultimately will undermine target performance as clinicians disengage.

Consequently, underpinning the implementation of the target in New Zealand has been the realisation that achieving the target by any means other than genuine improvements in the quality of care will result in the 'double whammy' of poorer care for our patients and, ultimately, failure to achieve the target.

Why does it matter?

First, it matters to the patient. Second, it matters because, by staying longer in the ED and in hospital, it obstructs access for others seeking these resources. Third, it causes the accumulation of patients in the ED—the flow coming in is unabated, but the flow out is obstructed.

The ED becomes overcrowded and ED overcrowding matters. It is associated with delays to care, longer total hospital length of stay, decreased satisfaction, adverse outcomes and, most significantly, increased mortality.[5-10]

Among the patient population who have gone through an overcrowded ED, there are about one-third more deaths over the 10 days following admission. In Australia this equates to a death rate equivalent to the road toll. In New Zealand this would translate to more than 300 deaths each year. How applicable these figures are to New Zealand is open to debate—there might have been relatively fewer or more deaths in New Zealand. However, the least plausible argument is that these figures have no relevance to New Zealand. There is no doubt that ED overcrowding was causing death and other harms in this country.

Achieving the target

The target, like any other intervention in health care, has the potential to benefit, to harm, or to achieve nothing at all. We accept, in relation to medications in particular, the concept of a therapeutic window; too little and nothing is achieved, too much and the adverse effects outweigh the benefits, just right and the benefits predominate. In astronomy, a planet close enough, but not too close, to a star so that the temperature allows a potentially inhabitable context, is described as being in 'the Goldilocks Zone'—not too hot, not too cold, but just right.

Those who argue that targets of this sort are bad have some merit in their argument. So do those who argue that targets of this sort are good. Six hours and 95% were chosen for a variety of reasons, but among them was the thought that these were less likely to drive blinkered compliance than 4 hours and 98%. That is, we would be better able to keep in the therapeutic window, or Goldilocks Zone, thereby maximising the utility of the target. Similarly, it was appreciated that achieving the target across New Zealand, if we were to do it through genuine quality improvements, would take at least four to five years. Perhaps the most significant challenge for the implementation of this target has been to push it hard enough but not too hard.

Local solutions

Another contrast between the New Zealand and NHS approaches is that New Zealand has seen much less central (Ministry) input into the specifics of the activities undertaken locally. The Ministry devoted a resource to this target of a two-tenths full-time equivalent Target Champion, and one full-time equivalent Senior Advisor. Much of this resource is consumed dealing with the 'summative' requirements of measuring and reporting target performance, leaving limited resource for 'formative' assistance with activities towards the target. In contrast, the NHS devoted dozens of staff, analysed data on behalf of local Trusts, and came back with specific advice as to what should be done. The New Zealand approach from the Ministry resource has been a supportive and advisory one, with an expectation that solutions, although more generally informed, will be locally derived and implemented. In retrospect, this is a strength of the New Zealand approach. Locally derived solutions are more likely to be successful and success is more likely to be sustained.

The context for change

Although the specifics of the activities undertaken are locally derived, it is expected that these activities occur on a foundation consisting of these layers:

1. Understanding what the problem is and what solving the problem would look like.
2. Having a structure with all the components necessary to address the problem.
3. Constructing a plan, based on a good methodology, which is comprehensive, but prioritises what should be done and in what order.
4. Implementing the components of the plan.

Space in this paper limits opportunity to discuss this context for change at length, and more detail can be found in other publications.[4,11] However, suffice it to say, a recipe for failure is to take ideas, activities, or projects 'off the shelf' (step 4) and expect

Table 1: Top 10 challenges for DHBs in pursuit of the target.

Top 10 challenges for DHBs in pursuit of the target	
1=	Access to hospital beds
1=	Access to diagnostic tests
1=	In-patient registrar delays
4	Increased demand for ED services
5=	ED facility deficiencies
5=	ED staff deficiencies
7	Delays to discharge of inpatients
8	Difficulty engaging hospital clinical staff in changes
9	Difficulty accessing aged care beds
10	Nights and weekends

them to work without the foundation of the prior steps. An analogy relevant to many of our efforts is one of a dog chasing seagulls on the beach. She chases one, then sees another and chases that, then another, then another, and so on. She is a very busy dog, exhausted at the end of this, but she catches no seagulls. Many of our DHBs are very busy with quality improvement projects, based on good ideas, or a successful example from another DHB, or based on precedents from an overseas health system. Staff become frustrated when, despite their efforts, things don't seem to be improving. This results in another 'double whammy' of failure. First, the expected improvements aren't forthcoming. Second, those clinicians who committed to these activities walk away in frustration, more reluctant to commit to similar activities in the future.

Two questions should be asked in relation to such activities. First, how do they fit into the scheme of things? Second, what exactly is the scheme of things? In other words, what is the structure for change? What will change look like once achieved? Is there a group of people leading this, including clinicians with appropriate representation and authority? Is it well supported by management and does it have people to provide 'process improvement grunt' (understanding of process improvement and opportunity to get things done)? What methodology is used so that, of all the good things that might be done, the best things are done in the right order? Without a shared vision, an appropriate structure and good methodologies to populate a comprehensive yet prioritised plan, the seagulls will forever be safe.

How have we changed?

After the first year of the target, all DHBs had been visited at least once by the Target Champion, and the challenges they were facing and the innovations making progress were collated.[11] The 10 most significant barriers to achieving the target, at that time, are listed in Table 1.

More details of these can be found in the paper, but they emphasise the need for an appropriate structure and plan, as they are generally not problems confined to a single department or speciality and, indeed, many are the concern of multiple departments. Consequently, overcoming these challenges is unlikely unless all concerned parties gather round a single table with others who can provide appropriate support and authority.

Table 2, from the same publication,[11] outlines some of the specific actions being undertaken by DHBs at that time.

Again, more detail can be found in the publication, however, it is not these actions, but the context in which they are occurring, that is the key to success. For example, the creation of special beds (ED observation beds and in-patient assessment units) is listed at the top of the table. While these physical spaces have great utility, of utmost importance is how they are used. Further discussion of the appropriate use of such beds can be found in a guidance statement[12] but, suffice it to say, if they are not used well they will not be a success. To define how they are used and to govern their ongoing use requires a structure with components

Table 2: Some specific examples of DHB initiatives to improve performance

Special beds	Creation of ED observation units and inpatient assessment units so that patients with a particular need, for example further observation or treatment by ED staff to achieve discharge or 'work up' by inpatient teams, have that need fulfilled in a space well suited to that purpose.
Hospital Operations Planning	Dedicated and sophisticated daily hospital operations planning to enhance the use of the human and physical resource, and to improve patient flow between the ED and inpatient wards.
Discharge planning	Good discharge planning, beginning early with multidisciplinary input and as a particular focus of daily activities to reduce unnecessary patient waits and free hospital capacity.
Access to imaging	Guidelines and pathways for accessing imaging and a responsive service for the provision of both images and expert interpretation.
Responsive acute secondary services	Separation of acute and elective medical roster conflicts so that the availability of inpatient specialties is adequate to enable the hospital to provide a responsive acute service.
Pathways for acute patients	Pathways or agreements so that patients with common and relatively straightforward presentations, for example fractured neck of femur, can be transferred to the ward without having to wait in the ED for au inpatient registrar assessment.
Acute demand mitigation	Analysis of the drivers of increased demand for acute services and interventions to mitigate this demand.
Enhanced ED layout	Layout of EDs to enhance function, including 'streaming' of patients and good 'command and control'.
Enhanced ED senior staffing	A greater senior staff presence to enhance decision-making and overview of department activities.
Engagement of staff	Engagement of all staff by 'marketing' changes with an appropriate whole of system and patient focused emphasis.

Figure 1: National Performance broken down by DHB.

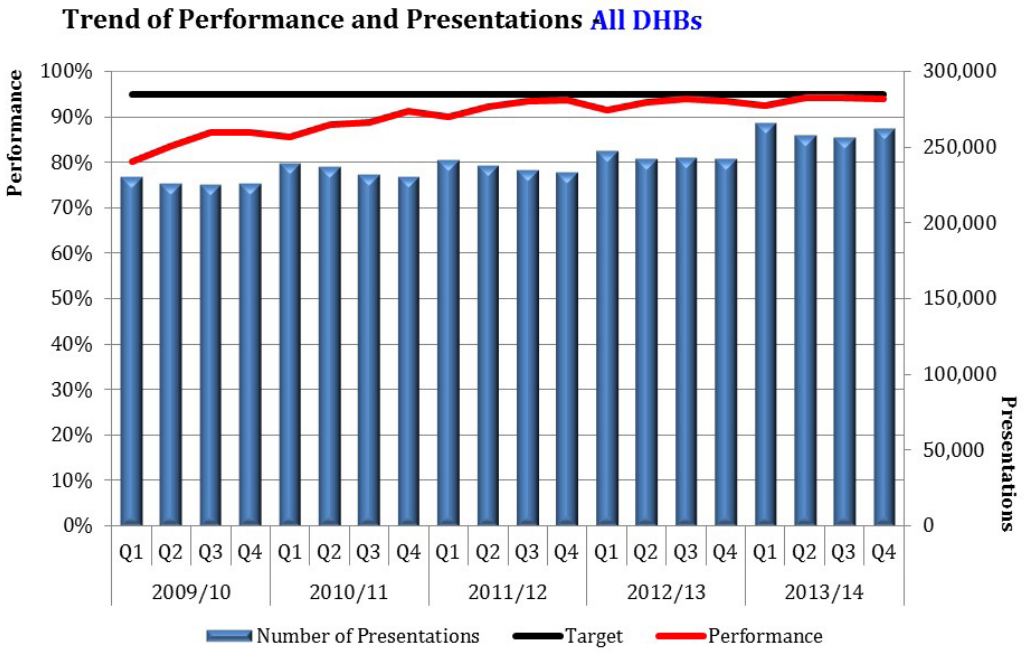
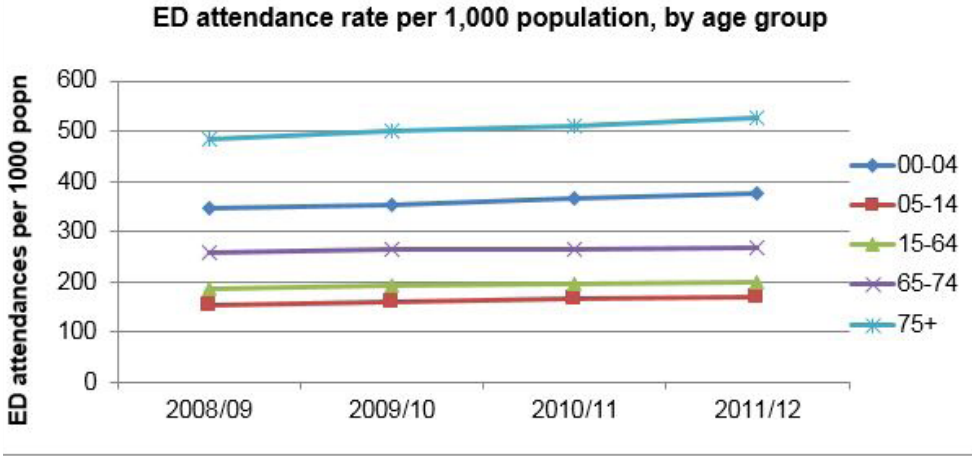


Figure 2: ED attendance rates per 1,000 of population, by age group



of appropriate representation, authority, collaboration and a shared vision.

How have we performed?

Prior to the target few DHBs regularly scrutinised patient length of stay in their EDs. Performance after the first quarter of 2009/10 (July, August and September 2009) showed a national performance of 80% of patients discharged, admitted or transferred within 6 hours of arrival at an ED, with a range from 100% down to 61%. With the exception of Counties Manukau and Canterbury DHBs, which had commenced work on improving acute patient care prior to target instigation, the busier hospital EDs were the poorest performers.

Since then national performance, at the end of five years (quarter four, 2013/2014), had risen to 94%. More importantly, the lowest performing DHB was at 89%, 11 DHBs were over 95% and a further 8 were over 90% (ranging from 94 to 90%). Figure 1 shows the improved national performance from quarter one 2009/10, to quarter 4 2013/2014, and the year-on-year improvements each quarter one.

Of course, performance against the target is less important than improvement in the quality of care. Clinicians report decreased ED overcrowding and generally more pleasant working environments. Nationally available data is not sufficiently discerning to appreciate small changes in various outcome measures amongst the large variations, fluctuations and pre-existing trends, but data available to the Target Champion suggests the performance against the target has not been associated with increased admissions to hospital, increased re-presentations to EDs or increased in-hospital mortality. A criticism of the NHS target was that it was not subject to appropriate research of its utility.2 In New Zealand, a sophisticated, independent 'before and after' study is soon to report on other parameters which might have been influenced by target activities.[13]

What next?

ED presentations and acute admissions to hospital are increasing at a rate greater than population growth, with the greatest rise (in most DHBs) occurring in the elderly (Figure 2). The elderly have a higher ED utilisation rate and a higher rate of admission to hospital from the ED. Effort will be required simply to maintain performance. Considerable effort will be required to continually improve it. If performance is poor because demand exceeds capacity then, in general, two options exist—reduce demand or increase capacity.

Reducing demand through admission avoidance and discharge facilitation initiatives is important to lower the trajectory of growth. However, it is optimistic to think that demand can be made to decrease. Efforts to manage increasing acute demand must continue.

Increasing capacity can be achieved by purchasing more (staff, space, equipment), or by freeing up existing capacity through efficiency gains. Much of the improvement against the target has been through efficiency gains from improvements in process. There is still much scope for improvement in processes, as we still have an office-hours orientated health system, junior doctor-lead acute hospital services, late

definitive decision making, poor use of pathways and other standardised processes, services which work together poorly, and poor command and control of hospital demand and capacity. It is in these areas we must make the most change in the next five years. However, there isn't unlimited scope for freeing up existing capacity. In reality, of the three options—reducing demand, freeing up capacity through efficiency gains and purchasing more capacity—we will need some combination of all three. We are obliged to exhaust the first two as best we can, but inevitably we will need to invest in the third.

Finally, blindly seeking to achieve the target, despite the best intentions, is insufficient. We need a better understanding of what quality is, how we measure it, and how we know if we are achieving it. To this end an important step is the implementation of 'A quality framework and suite of quality measures for the ED phase of acute patient care in New Zealand.' A description of this framework and these measures has been published[14] and DHBs are required to implement it from July 2014—the five year anniversary of the target.

Summary

Five years of the shorter stays in the emergency department health target has seen a maturing 'whole-of-system' collaboration leading to better patient care. However, there is still much to do and demand continues to increase. Assisted by the 'A quality framework and suite of quality measures for the ED phase of acute patient care in New Zealand,' a good structure and methodology driving improvement, and a patient centred focus, this work must continue.

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Regulating our emergency care paramedics

Bronwyn Tunnage, Andrew Swain, David Waters

ABSTRACT

Ambulance paramedics administering emergency care to patients are delivering a health service as defined in the Health Practitioners Competence Assurance Act, 2003. Paramedics practice a wide range of skills without direct supervision and these can potentially put the public at risk if the paramedic is not competent. Paramedic practice is also rapidly expanding beyond the traditional ambulance role. However, this emerging profession falls outside the Act and paramedics remain unregistered. In this paper we state the case for extending regulation to these frontline healthcare professionals.

The principal aim of regulating the health workforce is to protect the public. The Health Practitioners Competence Assurance (HPCA) Act, 2003, recognises and addresses the vulnerability of the person who is accessing healthcare and the power imbalance between the patient and the provider. Regulation is a means to ensure that health practitioners are both clinically competent and conduct themselves in accordance with the set of legal rules established by the Act. The HPCA Act restricts the use of professional titles to registered practitioners, limits specialist skills to registered healthcare practitioners and ensures that healthcare professionals are competent to practice in accordance with qualifications and standards, maintain regular certification of their competency, and act safely within their specified scope.[1]

The HPCA Act regulates the practice of 22 health professions within New Zealand (Table 1) through delegation of three primary functions to the relevant responsible authority: qualifications (including scope of practice); competency; and complaints. Responsible authorities are concerned with the education of health professionals, ensuring that the delivery of entry-level education and continuing professional development meet the national standards for the profession through the accreditation of programmes. These authorities establish a register and require individual practitioners to maintain certification of their competency to practice. Performance criteria have to be monitored as registration is renewed annually. Finally, it is also the responsibility of these authorities to identify practitioners that pose a risk

Table 1: Professions regulated under the Health Practitioners Competence Assurance Act 2003.[1]

Chiropractic		Medical Radiation	Optometry
Clinical Dental Technology		Medical Sciences	Osteopathy
Anaesthetic Technology		Medicine	Pharmacy
Dental Technology		Midwifery	Physiotherapy
Dental Therapy	Dental Hygiene	Nursing	Podiatry
Dentistry		Occupational Therapy	Psychology
Dietetics		Optical Dispensing	Psychotherapy

of harm and to suspend or revoke registration for behaviour that does not meet clinical or ethical standards of conduct.[1] However, not all health professions are regulated under the Act; paramedics are a case in point.

Since the 1970s, ambulance services have undergone a paradigm shift from primarily providing emergency transport to delivering advanced medical care to the patient in his or her community.[2] Ambulance paramedics care for more than 450,000 medical and trauma patients in New Zealand every year.[3,4] They also work in the New Zealand Defence Force (NZDF), in industrial settings and as flight paramedics. In response to increasing demands on the New Zealand healthcare system, the paramedic role continues to expand. The Ministry of Health has clearly signalled that health care must be delivered closer to the patient's home.[5] The ambulance sector's response to this directive has been the establishment of extended care paramedics who treat patients at home, minimising unnecessary hospital presentations.[6] Paramedics are already working with general practitioners and in hospital emergency departments.

Healthcare practitioners are regulated under the Act if their activities expose the public to a risk of harm. Paramedics deal with life and death. They triage, assess and manage patients, making clinical decisions on their behalf often without knowing their medical or social history. Patients may be incoherent, combative, unconscious or not competent to make an informed decision. The environments that paramedics work in are uncontrolled, and may be isolated, complex and dangerous. Skills, including invasive procedures and the administration of controlled drugs, which were once the preserve of doctors, now fall within autonomous paramedic practice and are performed without direct supervision. There is clearly a risk of harm to the patient if clinical competence and an ethical approach are not achieved and maintained by individual paramedics, and this is the strongest justification for paramedics to be regulated by the HPCA Act.[7]

As an unregulated profession, paramedics are still responsible for their practice. Paramedics are required to uphold the same common law standards as any individual, but this has clear limitations. Patients, or their advocates, may also lay a complaint with the Health and Disability Commissioner based on their rights as consumers of healthcare services. However, the sanctions available to the Health and Disability Commissioner are limited and do not include the withdrawal of registration to practice which applies to regulated health practitioners. Behaviour that, while not illegal, takes advantage of the functional relationship between the practitioner and patient, is only addressed within the jurisdiction of the HPCA Act. In a regulated profession, the Professional Conduct Committee may suspend or withdraw registration when care does not meet the standard reasonably expected from a registered health practitioner of equivalent training or experience, or if the practitioner is not considered a fit and proper person to hold registration in the profession. In the absence of professional registration, this type of misconduct is typically treated as an employment issue, enabling the employee to resign, relocate and seek new opportunities to practice without formal restraint. Without mandatory reporting to a disciplinary committee, unprofessional behaviour has the opportunity to continue unchecked. Furthermore, a performance concern identified in another country may not be detected without information sharing between the responsible authority and similar bodies overseas.

In 2014, the Accident Compensation Corporation (ACC) approached ambulance services with a request that the medical directors identify, and formally report to ACC, instances where treatment injury occurred during the provision of care by paramedics. Although the intention for ACC is to assist the patient by addressing the impact of iatrogenesis, this arrangement would also enable ambulance services to identify adverse events through audit, which is an integral component of clinical monitoring for registered health practitioners. ACC's proposal was accepted. If registration is established, paramedics would be able to treat and refer patients to ACC.

The absence of registration of paramedics creates a number of specific administrative difficulties. At present, anyone can claim to be a paramedic or establish an

Table 2: Health and Care Professions Council UK: Standards of Proficiency for Registered Paramedics 2014.[9]

be able to practise safely and effectively within their scope of practice
be able to practise within the legal and ethical boundaries of their profession
be able to maintain fitness to practise
be able to practise as autonomous professionals, exercising their own professional judgement
be aware of the impact of culture, equality and diversity on practice
be able to practise in a non-discriminatory manner
understand the importance of and be able to maintain confidentiality
be able to communicate effectively
be able to work appropriately with others
be able to maintain records appropriately
be able to reflect on and review practice
be able to assure the quality of their practice
understand the key concepts of the knowledge base relevant to their profession
be able to draw on appropriate knowledge and skills to inform practice
understand the need to establish and maintain a safe practice environment

ambulance service without appropriate qualifications or standards, and there is no mechanism for referral to the Health Practitioners' Disciplinary Tribunal. The title protection included by regulation would prevent unregistered practitioners from representing themselves as paramedics. For the NZDF, medics sent on relief and aid missions are unacceptable to many nations without additional 'credentialing', whereas registered healthcare practitioners may become immediately operational. During the Christchurch earthquake disaster, it was necessary for the NZDF medics to have a specific order issued to allow them to treat civilians.[8]

The regulation of paramedics is not novel; paramedics are registered in the UK, South Africa and some provinces of Canada. In Australia, several states have legislated to protect the title of 'paramedic', and the Victorian Government has recently drafted a Paramedics Registration Bill. Under regulation in the UK, comprehensive standards of proficiency for paramedics have been established.[9] The list of proficiency criteria expected from registered UK paramedics is contained in Table 2. While many of these criteria are assumed by ambulance services in New Zealand, registration would allow them to be formalised and monitored through the accreditation of paramedic education providers.

In 2011, Ambulance New Zealand, as the representative body of ambulance and aeromedical services, applied on behalf of the paramedic workforce for the services delivered by paramedics in New Zealand to be designated as a health service under the HPCA 2003, and for paramedics to be regulated under that Act. The application has been received by the Ministry of Health. However, all new applications for coverage under the HPCA Act were suspended until the reorganisation of the secretariat structure for regulatory groups, and the review of the HPCA Act were completed at the end of 2014. It is anticipated that the application will be considered during 2015. In February 2015, Peter Dunne (Associate Health Minister responsible for Ambulance) expressed his support for registration of paramedics, identifying it as a priority area for this term of government.

In summary, paramedics deliver a health service as defined in the HPCA Act and have significant potential to cause patient harm if the paramedic is not fully competent. Regulation would provide consistent standards of entry to the profession and set standards for conduct and competence of paramedics. Paramedic educators would become accountable for the quality of education delivered, which would support improved health outcomes of patients.

The primary purpose of regulating healthcare practitioners is the protection of the public. There is no other governing mechanism in New Zealand that would give similar protection to the public as the HPCA Act. Regulation of paramedics by the Act is both possible and practical to implement, as the practitioners are identifiable, there is an accepted body of knowledge and qualifications, and paramedics take part in continuous professional development. For the public, the benefits of regulation outweigh the potential financial costs. We call upon all health practitioners to support the regulation of paramedics.

Competing interests:
Bronwyn Tunnage reports she is a registered nurse, former advanced paramedic and a senior lecturer at Auckland University of Technology, currently undertaking a PhD with the support of a Health Research Council of New Zealand Clinical Research Training Fellowship. She is on the Board of Paramedics Australia Ltd, a professional organisation representing the interests of paramedics. She receives no compensation as a Board member, but my travel expenses as a Board member are reimbursed.

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Post lumbar puncture leg weakness mimicking cauda equina syndrome

Prashanth Hari Dass

Case report

A 60-year-old man was scheduled for his third cycle of intrathecal Methotrexate as prophylaxis central nervous system treatment for Stage 1Ae diffuse large B cell lymphoma of the left nasal cavity. His previous lumbar puncture (LP)s were technically difficult. Due to his prior traumatic experience, it was decided that more analgesia be administered locally to alleviate his pain and anxiety.

The patient was well built and slim, mobilised independently prior to LP. He had neither medical problems nor medications prior to his diagnosis and had no allergies. He had normal platelet count and coagulation screen.

Under aseptic technique, standard landmarks were identified. The patient was positioned in the left lateral position. L3 and L4 disc space interfaces were identified. Skin and subcutaneous tissue was infiltrated with eight millilitre (ml) of one percent Lignocaine using a 21 gauge needle. Routine aspiration was performed during administration of local anaesthetic with no venous flashback.

LP was performed using a 22 gauge tuhoy needle with a single pass using the same tract. The patient tolerated the procedure well. Five ml of initial bloody cerebrospinal (CSF) fluid eventually became colourless. CSF fluid was sent for analysis (Table 1) after which 12.5mg in 5ml of intrathecal Methotrexate was administered by a certified doctor as per protocol. There was no resistance on intrathecal chemotherapy administration.

The patient described sensation of gradual onset paraesthesia followed by bilateral persistent leg weakness upon removal of the LP needle. He denied any back pain, nausea, or headache. His vital signs were stable. Lower limb neurology showed reduced tone bilaterally & absent reflexes. Babinski reflex was down going. Power on hip flexion, & knee extension was 4-/5. Power on foot dorsiflexion, plantar flexion & knee flexion was 3/5.

Table 1: CSF analysis consistent with a traumatic tap.

CSF fluid Constituents	Result
Macroscopic appearance	Clear and colourless
White Blood Cell Count	Tube one: $<1x10^6$/L Tube two: 1 x 10^6/L Tube three: <1 x 10^6/L
Red Blood Cell Count	Tube one: 80 x 10^6/L Tube two: 70 x 10^6/L Tube three: 56 x 10^6/L
Chemistry: CSF Glucose CSF Protein	 2.8 (2.8 – 4.4 mmol/L) 0.18 (0.15–0.45) g/L
Bacterial Culture	No growth

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Perianal sensation and tone were absent. Sensation to light touch and pin prick was diminished below L3 with a sensory level at L3. Feet were cool to touch with intact pulses. Upper limb neurology was normal. Abdomen was soft and non tender with no peritonism. No bleeding was noted from the LP puncture site.

Our patient was kept under close observation. His leg weakness began to improve two hours post LP. However, he was still unsafe to weight bear and had to be admitted to the ward for further observation. His neurological weakness & bladder function fully recovered six hours post LP and he was subsequently discharged home. No post LP imaging was performed as his neurology was improving with complete resolution. He declined subsequent intrathecal chemotherapy administrations. He has now had complete response following four cycles of R-CHOP chemotherapy, and has completed radiation therapy to the nasal cavity for consolidation therapy. He remains on routine surveillance.

Discussion

In more than 5% of cases, back ache and shooting pain down the legs occur during LP. This usually resolves upon completion of the procedure. Bleeding may occur more commonly due to either intrinsic factors, for example thrombocytopenia & deranged coagulation profile or extrinsic factors for example anticoagulants & antiplatelet agents. This may be immediate or delayed. Post lumbar puncture headache is described to occur between 13–32% with a median duration of five days.[1] Cauda Equina Syndrome (CES) is an exceedingly rare complication post LP, ie, between 0.01 and 0.7%.[2] Differential diagnosis of CES in this case include lignocaine neurotoxicity, spinal dural AV fistula (SDAVF) & epidural hematoma.

Classical CES is rare and occurs in 1 in 33,000 cases. For unknown reasons, women (63%) are more commonly affected than men (37%). It is classically accompanied by sciatica, saddle anaesthesia, sexual dysfunction and leg weakness. The gold standard imaging is MRI. The main causes of the syndrome include disc herniation in more than two thirds of cases, followed by tumour, spinal fractures, canal stenosis, infections, post-surgical manipulation, post-spinal anaesthesia, ankylosing spondylitis and fire arm wounds. Urgent surgical decompression is usually done 48 hours before onset of symptoms and usually improves neurological sequealae and improves prognosis.[3]

The initial impression in this case was that of leg weakness secondary to spinal lignocaine causing neurotoxicity as that caused by an epidural.[4] This is supported by the rapid onset of symptoms and the patient's reversible neurology. Our patient's sensory level was below L3, and hip flexion was also noted to be weak. This is likely due to spinal lignocaine infiltrating motor nerve roots of L2 & L3 as well. A Cochrane review of local anaesthetics showed that the risk of developing transient neurologic symptoms (TNS) is about seven times higher for lignocaine compared to bupivacaine, prilocaine, procaine, ropivacaine and levobupivacaine. Despite this risk of TNS, lignocaine's benefit outweighs its risk in comparison to other local anaesthetics as it works much more rapidly, has a shorter half-life and has a much more intense nerve blockade.[5] Our patient denied any back pain or gluteal pain which made this an atypical presentation of CES. Unintentional intrathecal injection of large doses of local anaesthetic may also cause hypotension, respiratory compromise, and in rare cases, seizures and cardiac arrest, which were absent in this case.

CES after an epidural block may also be secondary to spinal cord ischemia from spasm of the anterior spinal artery or the Adamkiewicz artery. Kim et al have also described a case of transient CES, but related to a sacral schwannoma with cauda equina compression after a lumbar epidural block.[6] Neurotoxicity secondary to repeated intrathecal chemotherapy administrations have been described in a few case reports. These more often cause gradual onset of neurological weakness ranging from weeks to months. In these instances, neurological weakness is much more prolonged in duration. In some instances, the neurology recovers with rehabilitation and some patients may have permanent neurological disability. In some cases, paraplegia has also been described.[7]

Transient leg weakness post LP has also been described post myelography, epidural steroid injection & spinal dural arteriovenous fistula (SDAVF) which were less likely given the patient's history, prior normal CT imaging of his back and relatively rapid resolution of symptoms.[8-12] Nevertheless, CT is not a sensitive test for SDAVF and hence we are unable to completely exclude the presence of fistula in this patient. SDAVF is the most common vascular malformation of the spine and typically present in older men.[13] Leg weakness exacerbated by exercise is a common manifestation of thoracic SDAVF and occurs in 43% of patients. Fistula level only corresponds to sensory level in 40% of cases and often cannot guide the level of imaging, hence warranting imaging of the entire spine when SDAVF is suspected.[14]

Other differentials include epidural hematoma. A prospective study by Kang et al evaluating major complications of epidural anaesthesia in more than 5,000 patients only revealed one case of epidural hematoma (0.02%) and post-operative neurological deficits in 57 patients (1.12%). Spinal epidural hematoma may present with signs that include local back pain, paraparesis, sensory loss with a discernible level, and bowel or bladder incontinence.[15] Urgent MRI of the spine is warranted if there is clinical suspicion of spinal epidural hematoma. The American College of Physicians best practice advice recommend urgent MRI imaging of the back in patients with acute low back pain who have risk factors for spinal infection (new onset of low back pain with fever and history of intravenous drug use or recent infection), risk factors for or signs of the CES (new urinary retention, faecal incontinence, or saddle anesthesia), or severe or progressive neurologic deficits.[16] The absence of lower back pain, risk factors for bleeding and improving neurological signs gave us the reassurance to observe the patient clinically with regular neurological observations. These explanations also gave the patient reassurance.

In summary, although rare, leg weakness mimicking CES post LP needs to be recognised as a potential complication of LP. Superficial as opposed to deeper infiltration of local anaesthesia is recommended. A smaller volume of local anaesthesia infiltration, without compromising on patient's level of comfort is also suggested. Clinical acumen is critical in identifying patients that require urgent imaging post LP, particularly in those with hemodynamic compromise and persistent or progressive neurological weakness, as they may require surgical decompression or intensive care monitoring.[17-18]

Competing interests: Nil

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Heerfordt's syndrome

Alessandro Andreani, Giulio Rossi, Michele Giovannini, Gaia Cappiello

A 35-year-old man, an ex-smoker and a varnisher, presented a few days history of left thoracic pain, low-grade fever, asthenia, swelling of both parotid glands and dry eyes. Once cardiac diseases were excluded, we performed a physical examination which only revealed enlargement of both parotid glands (this was also confirmed from ultrasonography of the parotid glands see Figure 1) and bloodshot eyes (with uveitis, as stated later by the ophthalmologist). The chest radiograph (Figure 2) showed the presence of bilateral hilar lymphadenopathy. We performed a computed tomography of the thorax, which confirmed the presence of lymphadenopathy in paratracheal, subcarinal and hilar station associated with bilateral interstitial thickening of lung parenchyma (Figure 3).

We performed bronchoscopy with transbronchial needle aspiration (TBNA) (using a histologic 19 G needle) in subcarinal station (station number 7 according to IASLC lymph node map) and in right interlobar station (station R11). Pathological tissue demonstrated the presence of non-caseating granulomas without necrosis (Figure 4). He was given a diagnosis of Heerfordt's syndrome, a rare form of sarcoidosis (present only in 6% of the cases of sarcoidosis) characterised by the presence of enlargement of the parotid gland associated with major symptoms as uveitis, facial paralysis (absent in our case) or fever.[1,2] He was started on 50 mg of prednisone daily, and at follow-up 15 days later, he was completely asymptomatic (and the swelling and bloodshot eyes resolved).

Figure 1: Ultrasounds examination showing an enlarged parotid gland with multiple hypoechoic and partially septated structural lesions within the parenchyma.

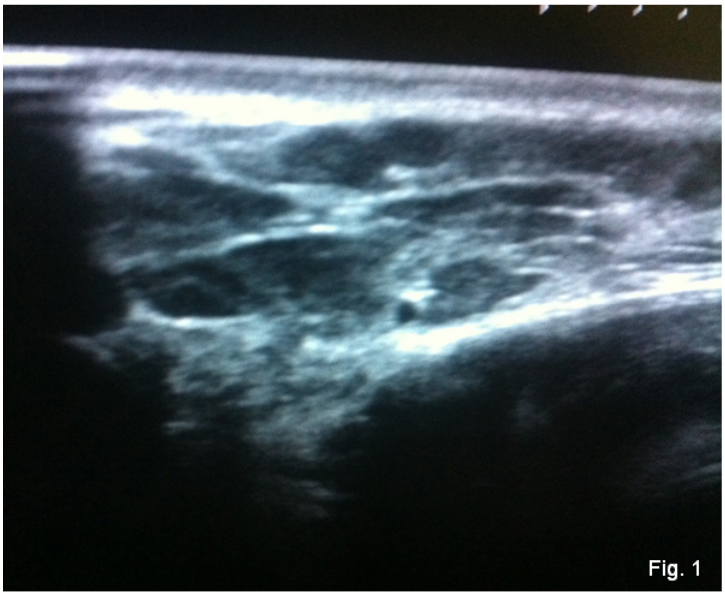


Figure 2: Chest X-ray showing the presence of bilateral hilar and mediastinal lymphadenopathy.

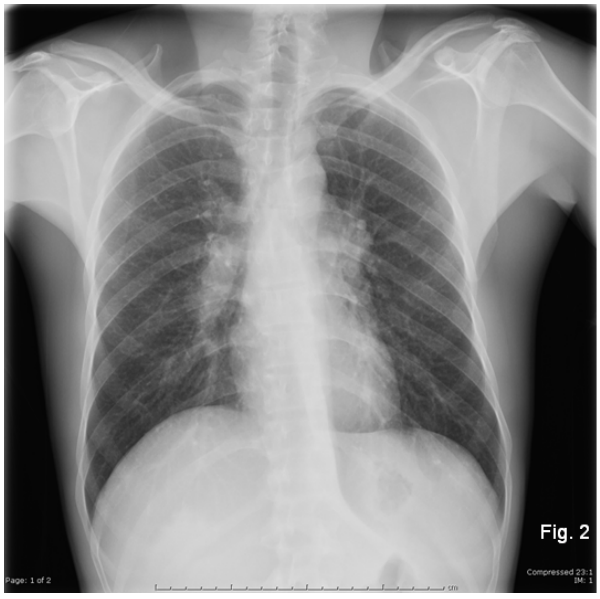


Figure 3: Axial image of a contrast CT scan showing the presence of bilateral paratracheal, subcarinal and hylar lymphadenopathy.

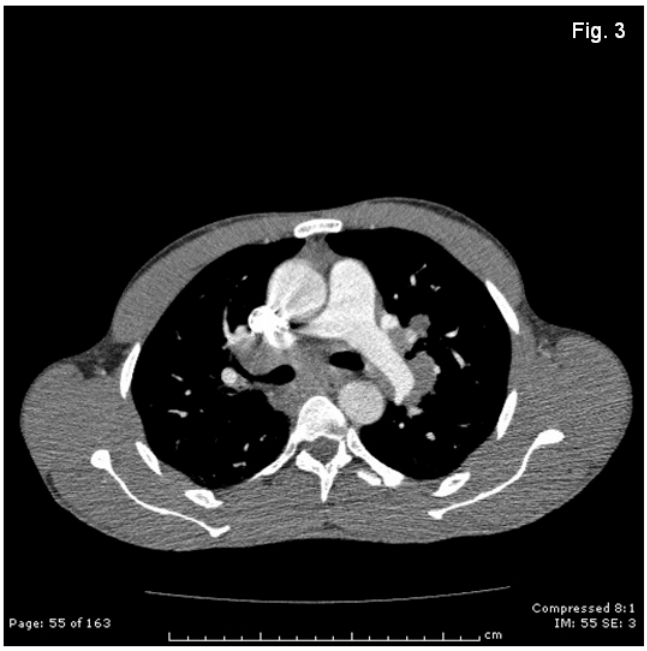
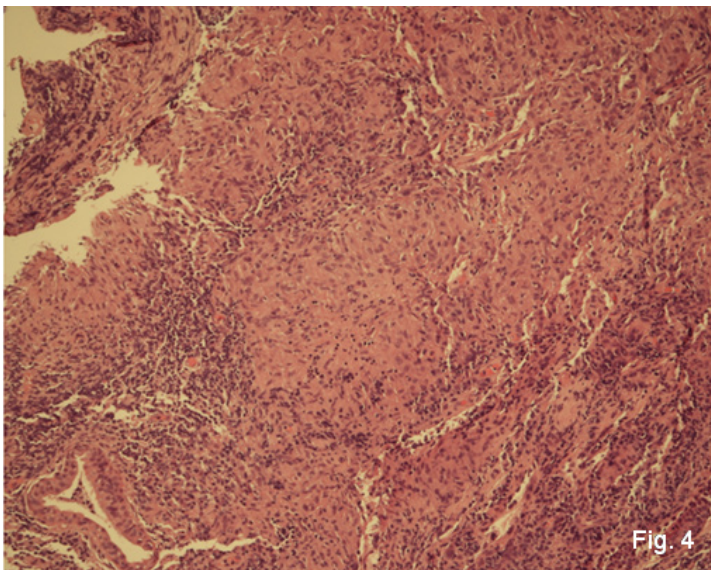


Figure 4: Cytohystological analysis (hamatoxylin-eosin stain) of transbronchial needle aspiration of the mediastinal lymphadenopathy showing the presence of noncaseous granuloma with epithelioid cells and multinucleated giant cells surrounded by lymphocytes: this pattern is compatible with sarcoidosis.



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Susceptibility to e-cigarette use among never-users: findings from a survey of New Zealand adult smokers and ex-smokers

Judy Li, Rhiannon Newcombe, Darren Walton

Susceptibility to tobacco smoking has been identified as a stage that precedes tobacco experimentation,[1,2] and cohort studies have provided strong evidence that susceptibility predicts subsequent tobacco use.[1,3] Susceptibility to e-cigarette use could also be an important measure. Understanding susceptibility allows for the projection of trends in e-cigarette use, enables the understanding of the acceptability of e-cigarettes among different population groups, and has important policy implications on the availability and marketing of e-cigarettes.

So far, only one published study has directly applied the concept of susceptibility from tobacco research to e-cigarettes use.[4] Here, respondents who were not currently using e-cigarettes were classified as being susceptible or non-susceptible, based on their e-cigarette ever-use status, and their responses to the question "How likely are you to try e-cigarettes in the future?". All e-cigarette ever-users (but not current users) were classified as being susceptible; never-users who indicated they were "very likely" or "somewhat likely" to try were also classified as being susceptible. Never-users who were "somewhat unlikely" or "very unlikely" to try were classified as being non-susceptible. The proportion of respondents who were susceptible differed by tobacco smoking status, with 3% of never-smokers being susceptible, compared with 25% of recent quitters and 50% of current smokers. The authors noted that they have used a more conservative definition for susceptibility. Studies on susceptibility to tobacco smoking would typically classify those who are "somewhat unlikely" to try a cigarette as being susceptible to smoking ("very likely" + "somewhat likely" + "somewhat unlikely" = susceptible), whereas the study on e-cigarettes by Zhu et al[4] did not ("very likely" + "somewhat likely" = susceptible).

Zhu et al contributes to the literature on e-cigarettes by being the first to assess susceptibility. However, classifying all e-cigarette ever-users as susceptible could inflate the proportion of susceptible users. Previous studies have shown that a high proportion of ever-users tried e-cigarettes out of curiosity,[5,6] and other studies found that some ever-users had stopped using e-cigarettes because of the negative experience they had with e-cigarettes (eg, did not like the taste; did not satisfy craving; the product malfunctioned).[7,8] It is therefore reasonable to assume that some of the ever-users will not use e-cigarettes again in the future.

To extend the understanding of susceptibility to e-cigarette use, we have conducted

a small study that investigates how it correlates to a range of modifiable and non-modifiable factors. Different from the study by Zhu et al, only e-cigarette never-users were included in the analysis.

Our data were collected from a 12-month follow-up survey, where respondents were first interviewed for the New Zealand Smoking Monitor (NZSM) between 15 August and 28 December 2013. The sampling and fieldwork procedure of the NZSM has been mentioned elsewhere.[9] Out of 442 potential respondents, 265 completed the follow-up survey (60%).

To assess the susceptibility to e-cigarette use, all never-users (n=172) were asked "If you are offered an electronic cigarette by a friend, how likely do you think you are to try it?". For comparison, this study also adopted a conservative definition of susceptibility.[4] Respondents were classified as being non-susceptible if they answered "very unlikely" or "unlikely", while remaining respondents were classified as being susceptible ("neither likely nor unlikely"/ "unlikely"/ "very unlikely" / "don't know"). Independent variables were: gender; ethnicity; age; household equivalised income; highest qualification; smoking status; past two-week exposure to e-cigarette advertising; past two-week exposure to e-cigarette use; and attitudes towards e-cigarettes.

About one-half of the respondents were susceptible to e-cigarette use, with a higher prevalence among current smokers (63%) than ex-smokers (20%) (see Table 1). Despite the use of different survey instruments, the differences by smoking status are consistent with the findings of Zhu and colleagues.[4] The association between susceptibility to e-cigarette use and tobacco use is so strong that in the current study, after controlling for other factors, the odds of current smokers being susceptible (compared with ex-smokers) increased from seven to 17. Other than smoking status, the adjusted model shows that these variables also predict susceptibility: age; household equivalised income; qualification; and attitudes towards banning e-cigarette use in indoor areas of cafes.

A recent population-based survey found that in 2014, 50% of the current smokers in New Zealand have tried e-cigarettes.[6] With the current study showing a high rate of susceptible never-users, substantial increases in the prevalence of e-cigarette ever-use in the future are expected. This trend has been observed in other countries,[10] and highlights the importance of understanding factors that determine regular use of e-cigarettes after first trying one.

This study builds on the traditional research on susceptibility to tobacco use, but is limited by the small sample size and of representativeness. The extension of this tradition to e-cigarette use is still exploratory and in development. Future longitudinal studies that assess the predictive power of susceptibility on future e-cigarette use will validate susceptibility as an indicative measure for future e-cigarette use.

Table 1: Proportion of respondents who were susceptible to try an e-cigarette when they are offered by a friend

	%	OR	AOR
Overall		-	-
Susceptible	47.2		
"Very likely" (25.0%)		-	-
"Likely" (16.9%)		-	-
"Neither likely nor unlikely" (1.2%)		-	-
"Don't know" (4.1%)		-	-
Non-susceptible	52.9	-	-
"Unlikely" (19.8%)		-	-
"Very unlikely" (33.1%)			
Gender			
Male	48.7	1	1
Female	45.8	.90 (.49–1.64)	.55 (.21–1.43)
Ethnicity			
Non-Māori	43.3	1	1
Māori	64.5	**2.38 (1.06–5.35)**	.67 (.18–2.49)
Age group			
18–24 years	75.0	2.67 (.25–28.28)	5.73 (.21–157.85)
25–34 years	52.9	1	1
35–54 years	49.4	.87 (.39–1.93)	**.23 (.07–.82)**
55+ years	36.7	.52 (.21–1.26)	**.11 (.02–.52)**
Household equivalised income			
Low <NZ$34,601	58.0	**2.42 (1.10–5.30)**	**5.25 (1.41–19.57)**
Med NZ$34,601-66,500	49.0	1.68 (.77–3.66)	1.24 (.40–3.85)
High NZ$66,501+	36.4	1	1
Unspecified	43.8	1.36 (.44–4.21)	1.85 (.25–13.87)
Highest qualification			
No formal qualification	33.3	1	1
Secondary school	55.4	2.48 (.97–6.34)	4.80 (.96–23.96)
Trade cert/ diploma	41.7	1.43 (.51–4.04)	**7.14 (1.28–39.75)**
Degree	45.0	1.64 (.59–4.51)	2.63 (.48–14.52)
Smoking status			
Current smokers	63.0	**6.67 (3.24–13.75)**	**17.23 (5.58–53.27)**
Ex-smokers	20.0	1	1
Past two-week exposure to e-cigarette advertising			
Not exposed	47.1	1	1
Exposed	43.8	.87 (.31–2.46)	1.47 (.27–8.14)
Past two-week exposure to e-cigarette use			
Not exposed	46.7	1	1
Exposed	48.0	1.05 (.54–2.03)	2.57 (.87–7.60)
E-cigarettes should be banned from use in indoor areas of cafes, restaurants or pubs			
Did not agree	56.3	1	1
Agree	35.9	.44 (.23–.83)	**.21 (.07–.61)**
E-cigarettes are for people who want to stop smoking			
Did not agree	35.7	1	1
Agree	57.5	**2.43 (1.28–4.60)**	1.62 (.56–4.64)
E-cigarettes are for people who want to cut down			
Did not agree	31.3	1	1
Agree	50.9	**2.37 (1.04–5.39)**	1.58 (.47–5.28)
E-cigarettes are for people who want to smoke in restricted public places			
Did not agree	52.8	1	1
Agree	40.3	.60 (.32–1.15)	.45 (.17–1.15)

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Did we have the wrong debate about Elixinol™ and medicinal cannabis?

Marta Rychert, Chris Wilkins

The recent approval of a cannabis-derived product Elixinol™ for the treatment of a coma patient suffering from *status epilepticus* has renewed the public debate on medicinal cannabis reform in New Zealand.[1] The Associate Minister of Health, Peter Dunne, approved the one-off use of Elixinol™ "on compassionate grounds", despite the lack of clinical evidence about the efficacy of the product for the treatment of this particular condition.[2] The public and media debate which followed ignored the fact that Elixinol™ is not a medicine or a pharmaceutical-grade cannabis product.

Elixinol™ is actually marketed and sold as a dietary supplement, with claimed benefits limited to the antioxidant properties of cannabidiol (CBD).[3] It is 18% CBD oil extract produced from pressing stalks and seeds of industrial hemp,[3] ie, a variety of *cannabis sativa* plant with low tetrahydrocannabinol (THC) content (generally below 0.3%).[4] Although there is a growing evidence base supporting the therapeutic benefits of CBD,[5] the US manufacturer of Elixinol™ does not make any therapeutic claims. The product is non-psychoactive as it does not contain any THC, the psychoactive constituent of *cannabis sativa*. Despite being a non-psychoactive and non-medicinal product, in New Zealand Elixinol™ falls either under the Misuse of Drugs Act, 1975 (MODA) which prohibits the use, possession and supply of cannabis preparations, or under the medicines regime if granted ministerial approval for therapeutic use on case-by-case basis (as in the recent case).

Cultivation of industrial hemp is licensed in New Zealand[6] and there are a number of hemp-derived products available on the market.[7] For example, hemp soap is regulated as a cosmetic product, hemp seed oil (a non-psychoactive oil pressed from industrial hemp seeds) is regulated as a food product, hemp protein powder and whole hemp seeds are allowed for sale in animal fodder.[7] These examples show that the default classification of *cannabis sativa* under the MODA does not preclude regulation of non-psychoactive hemp products under alternative legal regimes, as long as the products comply with the requirements of these regimes, including product safety standards. Non-psychoactive CBD oil extracts, such as Elixinol™, could be regulated in a similar way, resulting in wider access to these products. According to the MedSafe categorisation of products guidelines,[8] the CBD oil extracts appear to fit under the legal regime for dietary supplements.

The issue of products with broadly the same ingredients being regulated under different regulatory regimes with implications for legal status has assumed greater importance since the enactment of the Psychoactive Substances Act, 2013 (PSA). For example, kava (*Piper methysticum*), a plant traditionally used in Pacific cultures, can be legally sold when it falls under the Food Act (traditional representation as a drink) and the Dietary Supplement Regulations (pills marketed for their nutritional value),[9] but is currently prohibited as an ingredient in 'legal highs', ie, when it is represented as a recreational drug under the PSA.[10] In such a complex regulatory environment, there needs to be greater transparency about how products are classified and more clarity about the legal status of different products.

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A response to 'Childhood obesity in New Zealand' by Steven Kelly, Boyd Swinburn

Richard Flint

I read with interest your recent editorial by Kelly and Swinburn[1] and their enthusiasm for NZMA's "landmark document that sets the scope of and solutions to New Zealand's obesity epidemic". [2] Landmark? Really? I would hope that the scope of our strategy extends beyond maligning the food industry and funding community dietary programs. What leads the authors to claim that a tax on sugary drinks is "based on good evidence"? The metanalysis[3] used by the NZMA to support this approach could only find three studies that showed a reduction in BMI (a paltry 0.003 to 0.07 kg/m2). Although taxing drinks reduced consumption, some studies actually found an increase in the BMI. What is the "growing evidence" that the NZMA refer to when advocating dietary programs? Their allusion to a review of the UK's community weight management programs failed to mention an appalling drop-out rate of 55% in the first year and mean weight loss of just 3 kg (Counterweight program).[4]

It is disappointing that Kelly and Swinburn have failed to give credit to weight loss surgery in their "all-of-society approach". Recently, the group at Middlemore Hospital described great success with sleeve gastrectomy in an adult population. Five years after surgery their cohort of 96 patients had maintained a mean BMI loss of 10.9 kg/m2 (mean weight loss of 30.8 kg).[5] There is growing evidence that the results of adult weight loss surgery can be replicated in obese children. A recent review of 23 studies of weight-loss surgery for obese children described a mean reduction of BMI of 13.5 kg/m2.[6] Complication rates are similar to adult series with a mortality of just 0.3%: a frequency comparable to appendicectomy.[7] Previous concerns over failure to reach growth and sexual maturation, and poor post-op compliance appear to be unfounded. Although the data is not without bias, there is surely enough to suggest that this modality should be considered and not dismissed with a single sentence at the end of an exhaustive document, as in NZMA's "landmark document".

It may benefit the reader for the authors to explain why they have recently criticised the government for not embracing weight-loss surgery, yet now champion a document that ignores it. And what reasons do they have for not exploring a surgical option for childhood obesity when other centres are publishing encouraging results.

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Smartphone apps for weight loss and smoking cessation: Quality ranking of 120 apps

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The tobacco epidemic and burden from overweight/obesity are major causes of health loss in New Zealand.[1] Changes to the obesogenic environment and the use of various price signals are probably the most critical interventions required (eg, tobacco tax increases[2,3]). But there is potentially a place for the promotion of individual-level interventions, including the use of innovative internet and smartphone technologies.

In New Zealand, smartphone access has been increasing, and a survey in 2013 found 59% smartphone ownership or access by New Zealand adults.[4] It was even higher, at 71%, for those aged 18 to 54 years, and also for Māori or Pacific peoples compared to New Zealand European (70% vs 55% respectively).

There is some New Zealand randomised control trial (RCT) evidence for the effectiveness of mobile phone text messaging for smoking cessation,[5] with this being equally effective for Māori as non-Māori.[6] Work has also been done in New Zealand on smartphone-mediated cardiovascular management[7] (eg, as per a New Zealand trial on 'Text4Heart'[8]). Internationally, there is evidence detailed in a systematic review that computer-based and other electronic aids can assist with smoking cessation, and are "highly likely to be cost-effective".[9] Another systematic review of five RCTs has reported that mobile phone interventions are effective for smoking cessation.[10] But the evidence from RCTs of 'smartphone apps' for smoking cessation is fairly limited (eg, we only identified two trials[11,12]).

For smartphone apps for weight loss, one review reported on 10 RCTs which used text messaging or app interventions to support weight loss in women, with significant improvements being observed in eight studies.[13] Another review of 17 studies[14] that utilised smartphone applications, text messaging and web resources, reported overall weight loss of 0.43 kg (95% CI 0.25–0.61, p-value≤0.01). But not included in this review were some other smartphone app specific studies which did not report statistically significant weight loss[15-18] (albeit some of these being small pilot studies).

Given this background of some promising evidence, we aimed to assess the quality of existing apps for weight loss and smoking cessation available for downloading to smartphones by New Zealanders.

Method

We screened potential weight loss and smoking cessation apps to identify a final list of 120 Android and Apple apps (four groups of 30 apps each) based on their focus on the topic, price (all under $4), being in English language and download popularity as estimated by a relevant website (xyo.net). Each app was examined by two assessors and was rated against a published "Mobile App Rating Scale" (MARS),[19] (45% of the total score); in terms of weight loss/smoking cessation as appropriate (45% of the total score); and cultural appropriateness criteria (10% of the total score). We designed these other criteria (in addition to the MARS) based on relevant New Zealand literature: eg, weight loss/smoking cessation criteria were based on New Zealand weight management guidelines[20] and New Zealand smoking cessation

Table 1: Scores and final ranking for smartphone apps in each of the four groupings (weight loss, smoking cessation, Android and Apple) for the top five apps and mean results for the 30 per category

App purpose and name (for top five and summarised for all 30 apps in each of the 4 categories)	App developer	MARS score	Weight loss / smoking cessation criterion score	Cultural-appropriateness criterion score	Overall score* (ranked)
Weight loss, Android					
Noom Coach: Weight Loss Plan	Noom Inc	83%	68%	17%	70%
Lifesum – The Health Movement	Lifesum	79%	68%	17%	68%
Calorie Counter – MyFitnessPal	MyFitnessPal, Inc	86%	50%	17%	63%
Calorie Counter & Diet Tracker	SparkPeople	73%	59%	17%	61%
Lose weight without dieting	Harmonic Soft	77%	55%	17%	61%
Mean for all 30 apps studied	–	62%	32%	18%	44%
Range for all 30 apps studied	–	37%–86%	0%–68%	0%–33%	20%–70%
Weight loss, Apple					
Calorie Counter and Food Diary by MyNetDiary	MyNetDiary Inc	82%	64%	17%	67%
Calorie Counter, Dining Out, Food, and Exercise Tracker	Everyday Health, Inc	72%	68%	17%	65%
Calorie Counter & Diet Tracker by MyFitnessPal	MyFitnessPal.com	78%	59%	17%	64%
5K Runner: 0 to 5K run training, Couch to 5K running, free	Clear Sky Apps Ltd	80%	55%	17%	62%
Jillian Michaels Slim-Down: Weight Loss, Diet, Fitness, Workout & Exercise Solution	Everyday Health, Inc	76%	55%	17%	60%
Mean for all 30 apps studied	–	60%	29%	17%	42%
Range for all 30 apps studied	–	27%–82%	5%–68%	17%–17%	16%–67%
Smoking cessation, Android					
My Quit Smoking Coach	Andreas Jopp	83%	48%	33%	62%
You Can Quit Smoking	Insplisity	69%	52%	50%	59%
STOP Cigarettes – Quit smoking	Academiacea	61%	44%	17%	49%
Quit Pro: stop smoking now	Muslim Pro Ltd	76%	26%	17%	48%
SmokeLess!	Kroaqs	61%	30%	17%	43%
Mean for all 30 apps studied	–	52%	18%	17%	33%
Range for all 30 apps studied	–	33%–83%	0%–52%	0%–50%	17%–62%
Smoking cessation, Apple					
Quit Now: My QuitBuddy	Australian National Preventive Health Agency	94%	70%	33%	77%
LIVESTRONG MyQuit Coach – Dare to quit smoking	Demand Media, Inc	79%	61%	50%	68%
Stop-tobacco	Université de Genève	75%	65%	17%	65%
MyQuitSmokingCoach: Europe's No 1 Quit Smoking APP	Oliver Fuxen	68%	48%	17%	54%
Smoke Free – Quit smoking now and stop for good	David Crane	61%	52%	17%	53%
Mean for all 30 apps studied	–	51%	20%	17%	33%
Range for all 30 apps studied	–	30%–94%	0%–70%	0%–50%	15%–77%

* Overall score based on the weightings of: 45% for the MARS criterion, 45% for the weight loss/smoking cessation criterion, and 10% for cultural appropriateness criterion.

guidelines.[21,22] We also collected 48 hours of experiential data on 10 of the weight loss apps. The full details of the methods are detailed in an online report.[23]

Results

Overall, these 120 apps did not perform particularly well against the various criteria (eg, mean scores by group for the MARS: 51%, 52%, 60%, 62%; for weight loss: 29%, 32%; for smoking cessation: 18%, 20%; and for cultural appropriateness overall: 17%. See Table 1). The poor scores for the cultural appropriateness criterion reflected the lack of specific designs for the New Zealand market. Nevertheless, there were still some high-scoring individual apps, with the top five in each category shown in Table 1. The top weight loss app was "Noom Coach: Weight Loss Plan" (score: 70%), and the highest-scoring smoking cessation app was "Quit Now: My QuitBuddy" (77%).

The latter was produced by an Australian Government agency.

In 48 hours of experiential use, we found that some of the top 10 weight loss apps (5 Android, 5 Apple), had additional desirable features of note: low battery usage, provision of feedback, provision of motivation/encouragement, memory functions retaining previously logged meals, and offline functionality. But most did not have a food barcode scanning capacity that was relevant to the New Zealand market. Additional details on the top five apps in each category are given in an online seven minute video (http://vimeo.com/133304804). Other more detailed results and discussion of study limitations are in an online report.[23]

Discussion

This study found that these 120 apps were generally of limited quality—but the top scoring apps did have some reasonable high quality aspects. As such, these particular high scoring apps could be subject to further research, including head-to-head comparisons with text-messaging interventions (eg, the Txt2Quit service provided by the NZ Quitline). There may also be a case for New Zealand health authorities (eg, the Ministry of Health, the Health Promotion Agency, and DHBs) to systematically evaluate such apps and list the top ones on their official websites (eg, the National Health Service in the UK has a website that includes "approved" apps: http://www.nhs.uk/Conditions/online-mental-health-services/Pages/introduction.aspx).

Health professionals could consider suggesting the highest quality apps to interested patients. But given the uncertainties with the evidence-base for app effectiveness, they could do this in conjunction with recommending more well-established evidence-based measures (eg, Quitline support and pharmacotherapy for smoking cessation) and referral to a dietician for dietary counselling for weight management.

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Paediatric empyema in New Zealand

Simon Briggs, Eamon Duffy, Rupert Handy, Mitzi Nisbet, Stephen Ritchie, Mark Thomas

We read with interest the article by Cameron Burton and colleagues, Paediatric empyema in New Zealand: a tale of two cities[1] published in the May 29 edition of this journal.

Given that the usual causative organisms of paediatric empyema are *Streptococcus pneumoniae*, *Streptococcus pyogenes* and *Staphylococcus aureus*, we were surprised by the unnecessarily broad spectrum empiric antibiotic regimen of intravenous cefotaxime and flucloxacillin used at Christchurch Hospital. This contrasted with the more narrow-spectrum intravenous amoxicillin-clavulanic acid or cefuroxime antibiotic regimen used at Starship Children's Hospital. Despite being a more narrow-spectrum regimen, amoxicillin-clavulanic acid provided better coverage than cefotaxime and flucloxacillin for the organisms isolated from the patients with empyema. None of the isolated organisms that were susceptible to the combination of cefotaxime and flucloxacillin were resistant to amoxicillin-clavulanic acid.

The authors did not comment about the implications of their findings on the empiric antibiotic regimens used at Christchurch Hospital and at Starship Children's Hospital. We suggest that amoxicillin-clavulanic acid should be the empiric antibiotic regimen in both hospitals. With the growing appreciation of the significant benefits that can be obtained from enhanced antimicrobial stewardship,[2] this is an obvious next step. Changing from cefotaxime and flucloxacillin to amoxicillin-clavulanic acid would provide improved coverage of the usual causative organisms, avoid the unnecessarily broad antimicrobial activity of cefotaxime against aerobic Gram-negative bacilli thereby reducing antibiotic selective pressure, require fewer intravenous antibiotic doses per day, save nursing time, and lower the cost of both antibiotics and consumables. If amoxicillin-clavulanic acid is in the future used as the empiric antibiotic regimen in both hospitals, then this could be deescalated to a narrower spectrum antibiotic depending on the susceptibility profiles of the organism(s) isolated.

It could be argued that penicillin and flucloxacillin would be the most appropriate empiric antibiotic regimen as this would result in the narrowest spectrum treatment that would cover the same proportion of causative organisms as cefotaxime and flucloxacillin and almost the same proportion as amoxicillin-clavulanic acid. The use of penicillin and flucloxacillin would however result in a significant increase in the number of antibiotic administrations per day when compared with amoxicillin-clavulanic acid.

The way forward is clear, let's make this "the age of wisdom".

Competing interests: Nil

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Response to Briggs, et al

Emma Best, Tony Walls

Thank you for your letter regarding our article.

Until now there has been very little evidence on what to base the choice of empiric antibiotics for paediatric empyema in New Zealand. The Starship guidelines are based on a consensus of expert opinion, international guidelines and evidence, while the Christchurch Hospital Paediatric Guideline was based on a similar guideline from Australia. Our aim was to document which pathogens most frequently caused paediatric empyema and use this information to evaluate the current guidelines. Wherever possible antimicrobial guidelines should be based on local data.

We agree that our findings support the use of co-amoxyclavulinate as the first line empiric antibiotic choice for children in New Zealand with empyema. The Christchurch guidelines are now in the process of being changed to reflect this. Clinicians still need to be aware that in up to 15% of cases empyema may be due to an organism not sensitive to amoxicillin-clavulanate. In children who do not have a good clinical response to first line antibiotics, further consultation with surgical and paediatric infectious disease specialists is recommended.

Competing interests: Nil

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Chewing the saturated fat: how many more negative studies do we need?

Simon Thornley, George Henderson, Grant Schofield

We respond to the recent editorial and letters written by Swinburn,[1] Jackson and Ni Mhurchu[2] which address the effect of saturated fatty acids (SFA) in the diet on human health. Jackson and Ni Mhurchu[2] question the evidence that several meta-analyses of dietary trials that have failed to demonstrate a clear effect of modifying SFA intake. Instead, they argue that the trials suffer from low statistical power, are contaminated, have diluted treatment effects, and that the negative statistical evidence presented in summary meta-analyses is less important than other biomarker and ecological studies.

To restate our argument, we believe that if reducing saturated fat were truly to reduce cardiovascular disease (CVD) incidence, without adverse effects on other causes of death, it would also improve overall mortality. The evidence that overall mortality is not reduced cannot be easily dismissed. Unlike disease specific outcomes, such as CVD, there are no competing risks associated with overall mortality, and measurement is less error prone and more objective than for specific disease outcomes. Overall mortality is also clinically relevant: a reduction means that following this dietary advice leads to people living for longer, not swapping one cause of death for another. This is implied by a meta-analysis which reports a reduction for a disease-specific outcome, but not for overall mortality, if statistical power is sufficient.

Jackson and Ni Mhurchu argue that overall mortality reduction is not observed because there are few deaths in the meta-analyses. We have taken a closer look at this claim by examining the latest Cochrane meta-analysis of trials which addresses the effect of SFA intake (versus usual care). It shows no association between SFA intake and overall mortality.[3] In this meta-analysis,[3] there were many participants (55,858) and many deaths (3,276) and essentially no difference in mortality in the two groups (1,377/22,819; 6.3% in reduced SFA and 1,899/33,039; 5.8% in the usual diet group). This study is large enough and would have had sufficient power to detect a reduction, at least one that is clinically meaningful, if there were a SFA effect.

Swinburn's editorial[1] argues that the disappointing trials with hard endpoints may be dismissed in favour of the evidence that links saturated fat intake with markers of risk:

> *"The rock-solid, central planks of the saturated fat intake to heart disease relationship are that diets high in saturated fat increase LDL [low density lipoprotein]-cholesterol and that high LDL-cholesterol is a major risk factor for coronary heart disease".*

However, this evidence is sinking sand, as The American Academy of Nutrition and Dietetics has recently concluded, stating:

> *"The evidence is clear that changes in LDL and HDL [high density lipoprotein] induced by diet cannot be assumed to correspond to the expected changes in actual cardiovascular disease risk, and thus this body of evidence that uses lipoproteins as surrogate endpoints for cardiovascular disease must be excluded from considerations of the impact of diet on cardiovascular health."*[4]

No evidence of benefit to survival, or cardiovascular disease, has been reported from several other meta-analyses on the subject.[5-7] In short, the enormous resource

spent on reducing saturated fat has led to disappointing results. While the negative evidence continues to accumulate, and continues to be dismissed, we renew our advice to the public to chew the saturated fat, and focus on restricting components of the diet that are consistently associated with poor health: sugar,[8] and starch.[9,10]

Competing interests: Nil

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A snapshot of antimicrobial use in New Zealand hospitals—a comparison to Australian and English data

Eamon Duffy, Sharon Gardiner, Tanya du Plessis, Kristen Bondesio, Brijul Morar

Antimicrobial stewardship is recognised internationally as a key strategy to help combat the risk to health from increasing antimicrobial resistance. The primary aim of stewardship programmes is to improve the *quality* of antimicrobial use (ie, right antimicrobial at the right dose via the right route for the right duration) as well as monitor the *quantity* of antimicrobial consumption in both hospital and community settings. The Australian government funds both quality and quantity based approaches to monitoring antimicrobial use in hospitals. The National Antimicrobial Prescribing Survey (NAPS)[1], run by the Australian Commission on Safety and Quality in Healthcare, is a good example of point prevalence, whereas the National Antimicrobial Utilisation Surveillance Program (NAUSP)[2] is a centrally-run quantity survey. At present there is no central government support for routine monitoring of antimicrobial use in New Zealand.

Cooke et al (2014)[3] recently published a longitudinal analysis of 5 years (2009—2013) of antimicrobial use from 158 National Health Service (NHS) Trusts in the UK. They also included a cross-sectional analysis of one year (April 2012—March 2013) focusing on four key antimicrobial agents/classes (fluoroquinolones, cephalosporins, carbapenems and piperacillin/tazobactam). The tenth annual report of the NAUSP in Australia has also been published recently and includes data from a similar time frame (July 2012–June 2013).[4] We present comparative figures from five New Zealand District Health Boards (DHBs)—Auckland, Canterbury, Capital and Coast, Counties-Manukau and Waitemata—with dedicated full-time equivalent antimicrobial pharmacists (Table 1). The data are presented as Defined Daily Doses (DDDs) per 1,000 occupied bed days, an international World Health Organization (WHO) standard for measurement of medication usage.[5] The time frame studied is as for the English study (April 2012–March 2013), and inclusion and exclusion criteria essentially match these original papers.[3,4] That is, only antibacterial agents belonging to the British National Formulary class 5.1 that were issued or dispensed to wards (imprest) or inpatients were included. Paediatric, outpatient, psychiatric and day surgery issues were excluded.

Total antibacterial consumption showed only slight variation between the five DHBs, with Counties-Manukau using the least, and Capital and Coast the most at 704 and 798 DDDs/1,000 occupied bed days, respectively (Table 1). The three Auckland regional DHBs showed similar usage figures (704–735 DDD/1,000 occupied bed days). All DHBs used markedly lower amounts of total antibacterials than both the Australian[4] and English[3] national averages (~940 and 1,300, respectively).

The type of antimicrobial agent used varied between the DHBs. Cephalosporin use across New Zealand varied 2-fold, and was much higher than in England where use of this antimicrobial class has been restricted following introduction of government targets to reduce the incidence of *C. difficile* disease.[6] Consequently, piperacillin-tazobactam (and likely other beta-lactam classes) is used more frequently

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in England than in New Zealand. The use of both quinolones and carbapenems was generally less in New Zealand than the other two countries, although quinolone consumption in Canterbury DHB was comparable to that seen in England. The variation observed between DHBs will reflect a mix of factors, including differences in local antimicrobial prescribing policies and guidelines, and case mix. It should also be recognised that the picture presented here is incomplete, with the antimicrobials chosen for comparison with the English study.

A recent survey of retail and hospital pharmacy sales data from 71 countries suggested that New Zealand, like Australia, had "very high antibiotic use" (~70 and 87 units per person in 2010, respectively) compared with other high-income countries, like the Netherlands and France (~8 and 23 units per person, respectively).[7] A local study that focused on community antimicrobial consumption also suggested high use in New Zealand compared with many European countries.[8] The hospital data presented here is encouraging with the mean total antibacterial use in five of our 20 DHBs (~735 DDD/1,000 occupied bed days) considerably less than observed in Australian and English hospitals. However, it remains higher than reported in countries such as France, Switzerland and Sweden at 633, 540 and 329 DDDs/1,000 occupied bed days, respectively[9-11] indicating that there is considerable room for improvement.

In order to monitor our usage of antimicrobials across the country, a systematic process for collection and reporting of data should be implemented at a central government level. Currently, extraction and clean-up antimicrobial usage data for calculation of DDDs is difficult depending on the available data systems (pharmacy, prescribing and bed management), personnel and IT support. The national introduction of ePrescribing may enable faster data extraction, depending on the data warehousing and reporting capabilities that DHBs invest in. Comparison and benchmarking across all 20 DHBs and against other countries should be encouraged to make further gains in our AMS efforts.

Table 1: Antibacterial use (DDDs/1000 occupied bed days) in New Zealand, Australia and England (2012–2013)

2012–2013 Antibacterial use (DDD/1,000 occupied bed days)	New Zealand					Australia[4]	England[3]
	ADHB[a]	CDHB[b]	CCDHB[c]	CMDHB[d]	WDHB[e]	NAUSP mean	NHS mean
Total antibacterials	735	707	798	704	727	942	1,297
Quinolones	20	48	28	35	32	43	~50
Cephalosporins	125	120	197	99	178	183	~50
Carbapenems	21	14	20	15	10	21	~30
Piperacillin-tazobactam	1.6	8	19	1.1	2.5	42.7	~43

Comprised Auckland City Hospital[a], Christchurch, Christchurch Women's, Burwood and The Princess Margaret Hospitals[b], Wellington and Kenepuru Hospital[c], Middlemore Hospital[d], and North Shore and Waitakere Hospitals[e].

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3D programme Sunday August 2 on Screening Mammography

Ian Campbell

I was very disappointed to see the sensationalist, biased presentation on screening mammography from 3D on Sunday. The presenters promoted two of the worlds' most famous and vocal screening opponents—Peter Gotzche and Michael Baum—but did not provide any form of balance from leading proponents of screening mammography.

As a specialist breast surgeon working with one of our screening programmes (BSM), I already hear of women cancelling their mammography appointments as a result of this programme. This just highlights the need for some more responsible journalism from individuals in influential positions. Both sides of these debates need presenting—not a one-sided picture.

The NHS commissioned an independent review of screening a few years ago (by Professor Sir Michael Marmot[1]) because of the ongoing criticism from the antagonists above. This review concluded that based on the original randomised trials, screening reduced risk of death from breast cancer by about 20%. On the major TV program issue, overdiagnosis, the review group made it plain how difficult it is to accurately calculate this problem. They considered that some overdiagnosis did occur, and estimated the frequency at between 11 and 19% of cancers diagnosed in a group of screened women. In other words, for women age 50–52 facing 20 years of screening, a 1% chance. I quote from their abstract:

> *"Since the estimates provided are from studies with many limitations and whose relevance to present-day screening programmes can be questioned, they have substantial uncertainty and should be regarded only as an approximate guide. If these figures are used directly, for every 10,000 UK women aged 50 years invited to screening for the next 20 years, 43 deaths from breast cancer would be prevented and 129 cases of breast cancer, invasive and non-invasive, would be overdiagnosed."*

In the literature, estimates of overdiagnosis range from 0 up to 50% of all screen detected breast cancers (including DCIS in this definition).

One of the problems with the Marmot review, and the other data quoted, on benefits and harms of MG screening is that it is based on randomised trials which are now 25–40 years old. They represented the learning curve for screening mammography. Since then, we have much better equipment; we routinely do 2-view mammography; we have quality assured programmes with properly trained and accredited radiologists who independently double read or even triple read every screening MG in New Zealand women; and we have sorted our appropriate screen intervals etc. All these refinements improve the sensitivity of screening for cancer detection (especially so for the very small breast cancers which are the ones where we are most likely to save lives), and the specificity of the test—our ability to appropriately exclude women with normal breasts from further recall and anxiety.

A recent review of modern service screening in Europe[2] has estimated the mortality reduction from screening for women who actually attend at 38–48%! Their estimate of overdiagnosis, was 6.5% of all cancers diagnosed, and four cases overdiagnosed for every 7 to 9 lives saved.

Saving lives is not the only benefit of screening. The introduction of the screening

programme has been behind major improvements in the facilities and quality controls for diagnosis of breast cancer and for raising general awareness of breast cancer in our population. As a surgeon, I see every week how much more frequently we are able to perform breast conservation surgery and get good results in women with screen detected cancers compared with those presenting with a symptom. As for DCIS cases detected by screening, only a minority are low grade, and only a minority of these are treated with mastectomy. In addition, many women avoid chemotherapy and some avoid radiotherapy because of early diagnosis. These benefits also need to be weighed into the balance versus uncertain levels of overdiagnosis.

One of the reasons we do not know the benefits or otherwise of finding and treating DCIS, is that no-one has been prepared to do an 'Unfortunate experiment' and leave DCIS in the breast untreated in a formal study previously. How ironic to have Sandra Coney criticise the screening programme on this basis. A recent study[3] suggests significant breast cancer survival benefits for removing intermediate and high grade DCIS with surgery. None was seen for surgical treatment of low grade DCIS. This may mean that we do not need to treat low grade DCIS in this way, or it may mean we need more than 10 years follow-up to know whether surgical treatment results in benefit. For women with invasive breast cancer we usually need 10–15 year follow up to determine survival outcomes, so it is not surprising this should take longer with DCIS. At any rate, two randomised trials, are getting underway—one in the UK, and one based in the US—that are planning observation of low grade DCIS. Hopefully they will generate answers, but that will depend on whether women are prepared to enter these studies.

Māori and Pacific women in New Zealand are at much higher risk of death from breast cancer. Over half of this increased risk is due to later stage at diagnosis.[4] We need to turn this around, and better screening coverage is one way to do this.

Let's make sure we do present the 'true story' of the screening to New Zealand women.

Competing interests: Nil

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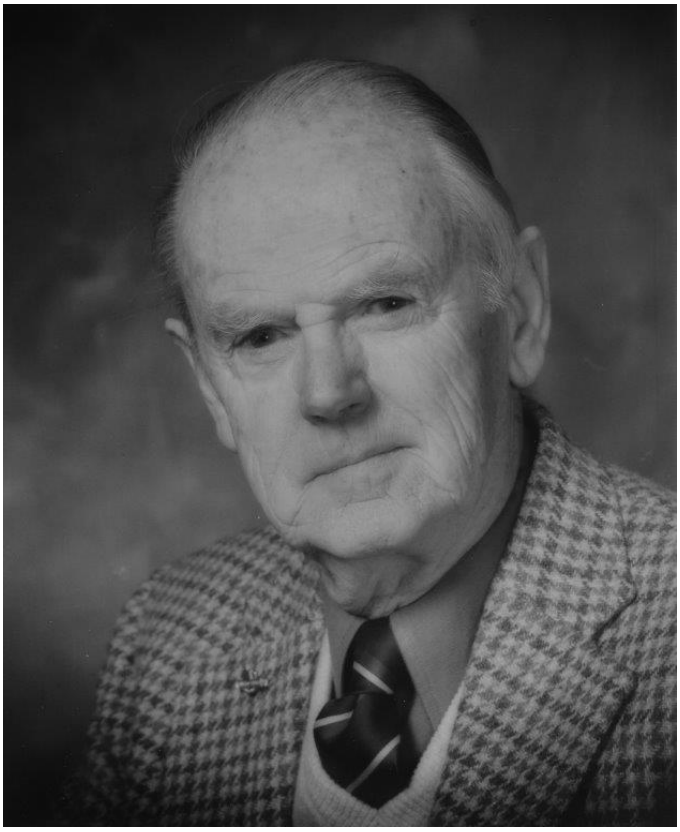
David Renfrew White

(28 December 1914—3 August 2015)

MB ChB, D.D.R.,F.R.A.C.R



David White was born and bred in Dunedin. He was the son of a lawyer, and grandson of the first New Zealand Professor of Education. His uncle was well-known Dunedin orthopaedic surgeon, James Renfrew White

Following a family conference, he was directed into a career in medicine despite his strong preference for a practical 'hands-on' occupation, which had a bearing on his later direction.

He graduated with a class of 65 in 1938, and while a house surgeon at Wellington Hospital met Zita Treahy to whom he was happily married for 52 years. At this time he was rejected for military service for what he termed a "dicky ticker".

During the next 3 years at Tauranga Hospital, David's practical ability led him to establish their first radiology department with some "clapped-out stuff" from Christchurch.

Subsequent reappraisal of his "dicky ticker" led to army entry and service from 1943 to 1946 in Egypt and Italy, where he served in a front-line hospital X-ray service, treating German and British casualties, with the use of local Italians as orderlies.

In 1946, he was appointed to a full-time position as a radiologist at Waikato Hospital, assistant to visiting radiologist Harold Harris. He spent two 6-month periods in Melbourne, away from his wife and family, studying for the University of Melbourne Diploma of Radiology.

David spent 33 years at Waikato Hospital, where he oversaw the development of a wide range of new imaging techniques, including ultrasound, CT and MRI scanning, and managed a huge increase in the size and complexity of staff and facilities.

He established a successful departmental School of Radiography in 1951, and in 1957 purchased the practice of Harold Harris and

established Hamilton Radiology. He led this with subsequent partners, Keith Robertson, Robin Gee, Hugh Douglas, Malcolm Baigent, Pek Low, Sabaratnam Muthukumaraswamy, and Alison Sommerville until his retirement in 1987.

In 1989 he was made a Life Member of the Royal Australian and New Zealand College of Radiologists.

He played an active role in education at Waikato Hospital, being involved in the establishment of a Postgraduate Committee in 1944, and serving as the first President of the Waikato Postgraduate Medical Society from 1966 to 1970.

In his private life, David was a skilled model maker of aircraft, boats, and railways, and extended his home to accommodate this hobby. He built both his Hamilton home and his holiday home on Lake Tarawera. He was a skilled painter, and a superb musician (piano and drums).

David was a competent professional and a colourful character who had an unorthodox turn of phrase, which earned him the affectionate nickname "Dr David bloody White"

He managed in his own home after his beloved wife's death 23 years ago, until the last few years when he needed nursing care.

He is survived by his two daughters, Catherine (Raglan) and Dierdre (Wellington).

At his funeral on 28 August, a moving eulogy centred on his great love and life at his holiday home at Lake Tarawera was delivered by neighbour Brigadier General Ian Thorpe CBE.

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Follow-up of glycemic control and cardiovascular outcomes in type 2 diabetes

In the US, the Veterans Affairs Diabetes Trial previously showed that intensive glucose-lowering, as compared with standard therapy, did not significantly reduce the rate of major cardiovascular events among 1,797 military veterans (median follow-up, 5.6 years). The trialists now report on an extended follow-up.

The primary outcome sought was the time to the first major cardiovascular event and the secondary outcomes were cardiovascular mortality and all-cause mortality. The conclusions reached were that after nearly 10 years of follow-up, patients with type 2 diabetes who had been randomly assigned to intensive glucose control for 5.6 years had 8.6 fewer major cardiovascular events per 1,000 persons-years than those assigned to standard therapy, but no improvement was seen in the rate of overall survival.

NEMJ 2015; 372:2197-206

Methotrexate use and risk of lung disease in psoriasis, psoriatic arthritis and inflammatory bowel disease

Numerous case reports and observational studies have suggested a link between methotrexate and pulmonary disease. This important issue is reviewed in this paper.

The researchers have reviewed seven randomised studies which have compared the use of methotrexate with either placebo or another active drug in the management of these diseases.

504 respiratory adverse events were documented in 1,630 participants. Methotrexate was not associated with an increased risk of adverse respiratory events, respiratory infections or non-infectious respiratory events. Good news, as methotrexate is commonly regarded to be the first choice treatment in these non-malignant inflammatory diseases.

BMJ 2015; 350:h1269

Efficacy and safety of very early mobilisation within 24h of stroke onset

Early mobilisation after stroke is thought to contribute to the effects of stroke-unit care. However, until now there has been no strong evidence to confirm this hypothesis. This report concerns a randomised trial comparing early mobilisation with usual care.

Over 2,000 stroke patients from 56 acute stroke units in five countries were involved. The primary outcome sought was a favourable outcome at 3 months. Such an outcome would improve functional outcomes, reduce immobility-related complications and accelerate walking recovery with no increase in neurological complications.

Unfortunately, fewer patients in the group mobilised within 24 hours had a more favourable outcome than those in the usual care group. The odds ratio was 0.73 in favour of the usual care group.

Lancet 2015; 386:46-55

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Feminism following orchidectomy

William Young, M.D., F.R.C.S.E.

It is well known that in Italy castration was frequently performed on boys, so that they could retain in manhood their voices of pure, clear, high timbre (in the eighteenth century it was estimated that yearly 4,000 boys were castrated for musical purposes, and were known as castrati). But whether eunuchs often develop female physical characteristics it would be interesting to know.

The following case is that of a man, aged 32, who offered himself as a recruit and was shown at the June meeting of the Wellington Division of our Association by Dr Robert Stout. He gave the history of having had both testicles removed for chronic abscesses, at Middlesex Hospital, when he was twelve years old. His voice was masculine, but he was beardless and had a smooth, soft skin. His body and limbs were well rounded and well padded with fat. The shoulders were small and well rounded off. Well-developed breasts and a distinct waist were marked characteristics. The hips were broad and the abdomen rounded and prominent below the umbilicus.

The accompanying photograph gives a fair idea of this “effeminate” man.

NZMJ AUGUST 1915

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Abstracts for the 228th Otago Medical School Research Society Summer Student Speaker Meeting sponsored by the Otago Medical Research Foundation

Wednesday 13 May, 2015

Fruit consumption is not positively associated with serum urate or risk of prevalent gout

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Gout, the second most common form of arthritis in New Zealand, is caused by reaction of the innate immune system to monosodium urate crystals that form in synovial fluid when serum urate (SU) levels are elevated. There are many dietary risk factors for high SU and gout; dietary changes are an important part of managing gout. This project aimed to determine if fruit consumption affects SU and gout risk, as previous evidence is limited and conflicting.

Linear regression was used to investigate association of fruit with SU, and logistic regression to investigate association of fruit consumption with prevalent gout. Data from the Atherosclerosis Risk in Communities study, Cardiovascular Health Study, and stage three of the Framingham Heart Study Generation 3, which collected information on individuals of European ancestry from the US, were used for the SU analysis. Data collected from NZ subjects of East Polynesian (NZ Māori and Cook Island Māori), West Polynesian, mixed East and West Polynesian, or European ancestry were used for the gout analysis.

There was significant inverse association of fruit consumption with SU with standard adjustment (BMI, whole-genome principal component analysis vectors 1 and 2, calorie intake, and menopausal status) (mean, 95% CI, ß=-0.328, -0.461 to -0.194 µmol.L-1/weekly serving of fruit, P<1x10-4, n=12,674), but not when also adjusted for other dietary factors (ß=-0.121, -0.282 to 0.040 μmol.L^{-1}/weekly serving of fruit, P=0.14, n=12,572). Similarly, inverse associations of apples, bananas, citrus fruit, or peaches with SU were not significant when adjusted for other dietary factors. There was no evidence for association of fruit consumption with gout in Polynesians (n=1,549) or Europeans (n=834).

These results do not support reduction of fruit intake in management of gout. These results do not rule out the possibility that fruit consumption is a marker for another urate-lowering behaviour.

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The use of styrene maleic acid nanomicelles encapsulating the cannabinoid synthetic analogue WIN55, 212-2 for the treatment of breast and prostate cancer

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Synthetic cannabinoid WIN55,212-2 (WIN) has shown promise as an anti-cancer agent with minimal toxicity. However, cannabinoids cross the blood brain barrier (BBB) to cause psychoactive side-effects. Their poor solubility in blood also makes clinical application difficult.

In the present study, styrene-maleic acid (SMA)-WIN nanomicelles were synthesised to test whether the encapsulation of WIN would solubilise the drug, increase drug efficacy and reduce side-effects. SMA-WIN55,212-2 micelles were characterised and their *in vitro* cytotoxicity compared to free WIN in triple-negative breast (MDA-MB-231), hormone-receptor positive breast (MCF-7) and castrate-resistant prostate cancer (PC3) cell lines, each treated with concentrations ranging from 0–10μM for 72 hours.

WIN was encapsulated in amphipathic copolymer SMA to form a water-soluble spherical nanostructure. The average diameter was 132.7 nm, a size exceeding the threshold to cross the BBB, kidney and endothelial junctions of normal blood vessels, but still able to move through defective tumour vasculature. As lymphatic drainage of tumour tissue is often also impaired, the drug can selectively accumulate in the tumour tissue – exploiting what is known as the enhanced permeability and retention (EPR) effect, allowing increased drug delivery and reduced adverse effects.

Equal potency against all cell lines was found for both micellar and free WIN. The concentration of drug required to produce 50% of maximum

cell death (IC_{50}) was found to be 3.8 ± 0.1, 4.8 ± 0.0 and 6.1 ± 0.5 μM for free WIN, compared to 4.1 ± 0.2 μM, 5.9 ± 0.2 μM and 6.3± 0.4 μM for MDA-MB-231, MCF-7 and PC3 cell lines respectively, treated with equal drug concentrations of SMA-WIN. A 2-tailed T-test comparing variations between data points at each concentration of free versus micellar WIN found *P*-values >0.05 across all cell lines, rendering them not statistically significant.

These results show that SMA-WIN nanomicelles can be synthesised which possess evident cytotoxicity against breast and prostate cancer cells, and characteristics which may improve *in vivo* bio-distribution and drug efficacy and decrease adverse effects. SMA-WIN may show promise as a novel anti-cancer treatment.

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The repair protein MGMT and scavenger receptor CD163 are independent prognostic factors for metastatic brain tumours

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For those with metastatic brain tumours the survival time is highly variable ranging from 2–30 months. Molecular markers may aid to better predict prognosis leading to personalised treatment. The repair protein 0-6- methylguanine-DNA methyltransferase (MGMT), paired box transcription factor 8 (PAX8), and scavenger receptor CD163 are implicated in the prognosis of primary tumours. This pilot study aimed to find if these molecular markers were present in brain metastases and whether these markers should be studied in a larger cohort to better estimate patient prognosis.

A total of 23 brain metastases procured from surgery between 2008 and 2014 were chosen. Tumour sections from paraffin embedded tissue were stained for each marker using immunohistochemistry. A double-stain was performed for MGMT and CD163 in which MGMT positive cells were detected using DAB and CD163 detected using Warp Red chromogens. A single stain was performed for PAX8 using DAB. Positive cells were identified by light microscopy. Molecular marker results were correlated with patient survival.

MGMT status was a positive prognostic factor for brain metastases. MGMT positive metastases had a mean survival time of 13.4 months (95% CI 9.6- 17.2, n=15) whereas MGMT negative tumours had a mean survival of 8.5 months (95% CI 4.2-12.8, n=8), *P*=0.03 (logrank test). CD163 status was also a positive prognostic factor with a mean survival of 39.0 months (95% CI 19.2 - 58.8, n=10) compared to 8.5 months (95% CI 4.0 -12.9, n=13), *P*=0.02 for CD163 positive and negative metastases respectively. Sixty-seven percent of brain tumour metastases were PAX8 positive; however, no association with patient survival was found.

The CD163 and MGMT markers were associated with patient survival and may provide an improved estimation of prognosis for individual patients. Patients with MGMT negative tumours may benefit from temozolomide as they are sensitive to this type of chemotherapy.

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Inability of Matrix-Assisted Laser Desorption/Ionization Time-of-Flight Mass Spectrometry to differentiate between different *Staphylococcus aureus* strains

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Rapid and accurate discrimination between methicillin-resistant *Staphylococcus aureus* (MRSA) and methicillin-susceptible *S. aureus* (MSSA) is essential for effective treatment and prevention of transmission. This project investigated the ability of matrix-assisted laser desorption/ionisation time-of-flight mass spectrometry (MALDI-ToF MS) to discriminate between MRSA and MSSA and between the seven major MRSA strains found in New Zealand.

The mass spectra for 35 pre-characterised MRSA isolates, representing a collection of the seven major MRSA strains in New Zealand, and 42 clinical specimens were acquired using a mass spectrometer. The spectra were then processed and analysed to create an unsupervised hierarchical dendrogram.

The dendrograms showed that MALDI-TOF MS is not sensitive enough to discriminate *S. aureus* beyond species level identification. No distinctive clusters could be associated with MRSA, MSSA or the seven MRSA strains. The formic acid extraction preparation method resulted in mass spectra of higher quality than the direct preparation method, however it had minimal effect on the dendrograms with no obvious clustering of MRSA and MSSA.

Rapid detection of methicillin resistance using MALDI-ToF MS would be extremely useful, however this project has shown that MALDI-ToF MS lacks the resolution to discriminate beyond the species level for *S. aureus*. Therefore we cannot recommend the use of MALDI-ToF MS for identification of MRSA isolates, nor for discriminating the seven major MRSA strains found in New Zealand.

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Circulating miR-34a as biomarker for diabetes mellitus

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Diabetic heart disease (DHD) is associated with increased cardiomyocyte apoptosis and senescence, although the underlying mechanisms are unknown. MicroRNAs (miRs) have been shown to have pathological effects in the development of heart disease and diabetes. miRs are short, non-coding, singe-stranded RNA molecules that regulate gene expression. Among several miRs, miR-34a is predominantly expressed in the diseased heart and importantly, demonstrated to have implications in cardiomyocyte apoptosis and senescence. The aim of this research is to determine the role of miR-34a in the onset of DHD.

Plasma samples were collected from Type II diabetic and age-matched non-diabetic volunteers without any history of heart disease at varying stages of diabetes, <5 years, 5–10 years, and >10 years. Total RNA was extracted from plasma, reverse transcribed to cDNA with miR34a specific probe and amplified by real time PCR analysis to determine the level of miR-34a. As miRs are bound to high-density lipoprotein (HDL) in circulation, we also measured the level of HDL to normalise the level of circulating miR-34a.

RT-PCR analysis showed significant increase in the level of miR-34a in all the diabetic groups (<5 years 1.8 ± 0.4, $P \leq 0.05$; 5–10 years 2.8 ± 0.5, $P \leq 0.01$; >10 years 2.6 ± 0.7, $P \leq 0.05$, unpaired t-test vs non-diabetic). ELISA showed marked decrease in the level of HDL in people with diabetes ($P \leq 0.001$ vs non-diabetic, n=25). Importantly, normalisation of miR-34a expression to the HDL level eliminated the significance in <5 years (<5 years 1.1 ± 0.2, $P > 0.05$; 5–10 years 1.7 ± 0.3, $P \leq 0.01$; >10 years 1.8 ± 0.5, $P > 0.05$ vs. non-diabetic).

Results suggested expression of circulating mir-34a may increase before the development of clinical manifestations, indicating that measurement of circulating mir-34a could be a potential diagnostic biomarker for heart disease in people with diabetes. Importantly, the results warrant the need to consider the level of HDL while determining the expression of circulating miRs.

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Incidence and characteristics of insulin pump-associated adverse events in New Zealand children and adults with type 1 diabetes mellitus

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Insulin pumps for continuous subcutaneous insulin infusion (CSII) are commonly used in the treatment of type 1 diabetes mellitus (T1DM) as part of an intensive insulin regimen in both adult and paediatric populations. There have been many outcome-focussed studies on CSII and its advantages, and a number of recent studies considering the adverse events (AEs) associated with CSII. No studies have considered the incidence and characteristics of pump-associated AEs outside of the Australian context, or the effects of pump manufacturer, ethnicity or socioeconomic status on experience of AEs.

We approached adults, and families of children and adolescents on CSII for T1DM in diabetes clinics in three major centres in New Zealand. Participants completed a self-report retrospective questionnaire examining pump-related issues they had experienced in the preceding twelve months. Data on pump AEs as well as information related to readiness to deal with an AE and overall confidence were collected.

This survey had a response rate of 54% with 126 of 232 eligible people participating in the study. Eighty five percent of subjects reported one or more CSII-associated AEs in the previous 12-month period. Of these, 9.8% had an event serious enough to require a hospital presentation or admission; the majority of admissions were secondary to the failure of the giving set. Set/site problems were the AE most commonly reported (68.2% of all AEs), followed by skin complications (51.4%) and pump malfunction (40.2%). Fifteen percent of respondents experienced a pump malfunction that resulted in pump replacement in the previous 12 months. On average, time to pump replacement was 2 days.

AEs appear common and should be anticipated by patients and health professionals alike. While insulin pumps are able to alert patients to some problems, frequent self-monitoring is important in order to prevent complications associated with pump AEs. Patient education and training is therefore likely to be important to the successful and safe use of CSII.

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Development of a technique to specifically ablate hypothalamic RF-amide related peptide 3 (RFRP-3) neurons, and characterisation of the resulting anxiolytic phenotype

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Changes in the stress axis during chronic anxiety and other affective disorders remain unclear. RFRP-3 is

produced by hypothalamic neurons and has recently been shown to induce stress responses. To demonstrate a role for endogenous RFRP-3 in stress and affective disorders, we developed a mouse model that specifically ablates RFRP-3 expressing neurons by crossing a new mouse line in which the *Rfrp* gene also produces Cre recombinase with a line that enables Cre-dependent expression of the diphtheria toxin receptor (DTR). Diphtheria toxin (0.5, 1.0 or 1.5 mg/kg) was injected subcutaneously into 7-week-old *Rfrp*-DTR mice. Pronounced ablation of RFRP-3 neurons occurred at all doses compared to Cre-negative controls 3 weeks post-treatment (1.5 ± 0.33 vs 9.25 ± 1.7 neurons/brain section respectively; $P<0.05$; unpaired t-test). Because the highest dose caused adverse health effects, we selected the 0.5 mg/kg dose for the next experiment. In this pilot study (3 Cre- expressing and 3 Cre-negative control mice) we assessed anxiety behaviour (elevated plus maze [EPM] and light/dark box tests), obsessive-compulsive behaviour (marble burying test) and glucocorticoid hormone responsiveness (acute restraint test) 3 weeks post-diphtheria toxin treatment.

In the EPM, RFRP-3 deficient mice spent more time in the aversive open arms compared to controls (8.02 ± 2.47 vs 1.46 ± 0.75 seconds respectively; $P<0.05$). Non-significant trends towards improved performance were recorded in the light/dark box (46.81 ± 15.6 vs 10.47 ± 3.48 seconds in lighted area respectively; $P=0.41$) and marble burying tests (2.5 ± 0.5 vs 4.5 ± 2.5 marbles buried respectively; $P=0.19$).

We have established an effective and safe technique for RFRP-3 neuronal ablation using diphtheria toxin. Preliminary behavioural data indicate that endogenous RFRP-3 promotes anxiety responses. The technique will be used in a larger study to further characterise roles of RFRP-3 in affective disorders.

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Clinical Glycaemic Performance of the STAR Protocol

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Aims: Critically ill patients often experience stress-induced hyperglycaemia, resulting in increased morbidity and mortality.[1] Stochastic Targeted (STAR) Glycaemic Control (GC) is a tablet-based protocol which provides patient specific recommendations of insulin and nutrition to reduce hyperglycaemia, ensure a maximum risk of light hypoglycaemia of 5% and maximise nutrition.

Methods: STAR has been implemented in the Christchurch Hospital Intensive Care Unit (ICU), New Zealand (203 Patients) and the Gyula Hospital, Hungary (39 Patients) over the past few years. The clinical results were analysed and compared to SPRINT, a paper-based protocol previously implemented in the Christchurch Hospital ICU, New Zealand (340 Patients).[2]

Results: STAR performed well in Christchurch and Hungary, achieving over 80% time in band (4.4–8.0 mmol/L) with very low incidence of hypoglycaemia (<0.03% time). SPRINT had slightly greater time in band (86%), but did not feed adequately (67% Goal Feed) compared to STAR (97.5% Goal Feed). The length of time on protocol was also reduced for STAR Christchurch (4.1 Days) compared to SPRINT (5.1 Days).

Conclusions: STAR successfully maintained a high performance at multiple locations with different ICU cultures. In Christchurch ICU, STAR managed to feed higher than its predecessor SPRINT and also reduce the length of time on protocol by 24%.

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Evaluating *BRCA1* and *BRCA2* sequence variants that modulate isoform expression

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Routine diagnostic *BRCA1* and *BRCA2* gene screening is typically performed for individuals from high-risk breast-ovarian families. A significant number of *BRCA1/BRCA2* sequence variants in or near splice sites and splicing regulatory regions, such as ESEs (exonic splicing enhancers), result in a disruption of the mRNA splicing process. Splicing assays undertaken to assess the clinical relevance of rare sequence variants in these genes are often limited in their ability to quantify isoforms expression changes that may be associated with cancer risk.

Our study aims to generate a comprehensive expression profile of *BRCA1/BRCA2* isoforms and measure allele-specific expression changes of risk-assessed rare and common *BRCA1/BRCA2* variants. We have profiled mRNA isoforms in 27 lymphoblastic cell lines (LCLs) carrying common and/or rare variants predicted to alter splicing using targeted RNA-seq technology.

RNA-seq data showed that the expression profile of a rare variant of unknown clinical significance (*BRCA1* c.2521C>T) caused an up-regulation of the Δ9,10 isoform, together with the down-regulation of the 10-11 junction, despite previous studies suggesting it did not cause aberrant splicing. These results provide evidence for using mRNA isoform expression changes for the future interpretation of splicing analyses results in a diagnostic setting.

Vitamin-mineral treatment for assisting with smoking cessation:

a pilot double-blind randomised placebo-controlled trial

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Introduction: Smoking cessation interventions must assist smokers to make quit attempts and remain abstinent long-term thereafter. Micronutrients (vitamins and minerals) have shown positive effects on quitting and abstinence when treating drug addiction.

Aims: A double-blind randomised placebo-controlled pilot trial compared nutrition supplementation by micronutrients against placebo in a smoking cessation intervention with 24 adult, nicotine-dependent smokers.

Methods: Following a baseline phase when smoking history, daily consumption and nicotine dependence were measured, participants were randomly assigned (12/group) to placebo or micronutrient groups. A four-week pre-quit phase permitted participants to titrate up to 12 capsules/day. In the smoking cessation phase (12 weeks), participants registered with a smoking-cessation help line and consumed micronutrient or placebo capsules daily.

Results: Drop-out before making a quit attempt was significantly lower in the micronutrient group (0% vs 36.4%; OR = 13.8) and those taking micronutrients were significantly more likely to make a quit attempt (91.7% vs 41.7%; OR = 15.4) and be successful at quitting (83% vs 33.3%; OR = 10).

Conclusion: Using micronutrient supplements as a smoking cessation treatment is supported by the study and further investigation is recommended.

Differentiating lipid, water and calcium-rich regions within atherosclerotic plaques using multi-energy CT

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Aims: The superior spatial resolution and multi-energy data acquisition of the photon counting MARS scanner will provide a leap forward in non-invasively identifying atherosclerotic plaques. Previous MARS work distinguished spotty calcifications and lipid-rich regions, two hallmarks of plaques vulnerable to rupture, using low energy x–rays (10-50keV)[1] and a gallium arsenide sensor within clinical range (30-120keV).[2] Clinical range data are presented from the newest Medipix3RX camera with a cadmium telluride sensor and functional Charge Summing Mode (CSM), which reduces spectral distortion.

Methods: Excised, carotid plaques were scanned with a calibration phantom of water, lipid and calcium chloride. To simulate a neck scan, 10mm of aluminium eliminated photons below ~30keV. Four CSM energy thresholds maximised contrast between lipid-, water-, and calcium-rich regions. Material data, reported as concentration (gCaCl2/ml) and/or volume fraction (lipid vs water), were derived from raw photon counts using MARS software.

Results: Phantom results show clear separation of water, oil and calcium. Plaque scans show detailed mapping of calcium deposits and reveal significant lipid-rich regions in the expected areas of the plaque core.

Conclusions: Multi-energy CT with the photon counting Medipix3RX chip and CdTe sensor shows promise for detecting intrinsic biomarkers of atherosclerotic plaques vulnerable to rupture.

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Impact-induced muscle damage contributes to oxidative stress in professional rugby union

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Aims: Rugby union is known to increase oxidative stress and inflammation.[1] Pterins have been used clinically as markers of oxidative stress, inflammation and neurotransmitter synthesis.[2] This study investigates the release of myoglobin from muscle tissue due to rugby force related impacts and how it is related to the subsequent oxidation of 7,8-dihydroneopterin to specific pterins.

Methods: Effect of iron and myoglobin on 7,8-dihydroneopterin oxidation were examined *in vitro* via SCX-HPLC analysis of neopterin, xanthopterin and 7,8-dihydroxanthopterin. Urine samples were collected from 25 professional rugby players pre and post four games and analysed for myoglobin by ELISA, and 7,8-dihydroneopterin oxidation products by HPLC.

Results: Iron and myoglobin oxidised 7,8-dihydroneopterin to neopterin, xanthopterin and 7,8-dihydroxanthopterin at concentrations at or above

10μM and 50μg/mL respectively. All four games showed significant increases in myoglobin, neopterin, total neopterin, biopterin and total biopterin which correlated between each variable ($p<0.05$). There was also a moderate correlation ($p<0.001$, $r=0.38$) between myoglobin and neopterin.

Conclusions: *In vivo* delocalisation of myoglobin due to muscle damage may contribute to oxidative stress and inflammation after rugby. Increased concentrations of biopterin and total biopterin may indicate production of nitric oxide and monoamine neurotransmitters in response to the physical stress.

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Routinely asking about sexual orientation using non-binary measures: implications for physicians and researchers

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Introduction: Knowledge of patient sexual orientation is crucial for provision of patient centred care. Despite this, sexuality is not routinely gathered by many healthcare providers. When sexual orientation is considered, it is usually measured as a stable dichotomous variable.[2,3] Thus, patients may only be asked about their sexual orientation once, and only provided with binary options.[2,3]

Methods: Sexual orientation of undergraduate medical students was measured three times throughout the academic year as part of a larger project. Sexual orientation was measured using a 5-point Likert scale where 1 was "only attracted to the opposite sex" and 5 "only attracted to the same sex". Students were also given the option "none of these options apply to me".

Results: Friedman's test showed that use of a non-binary measure revealed sexual identity to be fluid over time $X2(2)=23.41$, $p<0.001$. Pairwise comparisons indicated same-sex attraction increased from a mean report of 1.87 at the first measure to 2.12 at the last ($p=0.035$).

Conclusions: Actual changes in sexual attraction may have occurred, or sexual attraction may be stable and increased disclosure may be a result of reduced social response bias. Patients may be more likely to disclose same-sex attraction when doctor-patient rapport is well established. Sexual orientation should asked about routinely with due consideration of non-dichotomous options.

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Progression to Dementia in Parkinson's disease over four-years: Risk with alternative MCI criteria

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Aims: To assess which of several currently-accepted criteria for mild cognitive impairment in Parkinson disease (PD-MCI) best predicts progression to dementia (PDD) within four years.

Methods: Four-year risk of PDD was determined for 121 PD patients using the International MDS Task Force1 Level II recommendations and alternative cut-off variants (2SD, 1.5SD, or 1SD below normative data).

Results: Twenty-five patients converted to PDD (21%). A 1.5SD cut-off was optimal to maximise relative risk and minimise subsequent reversion to 'non-MCI' status, but only when two impairments were identified within a single cognitive domain (31% of the sample). This criterion produced a PDD relative risk of 7.2 (95% CI=3.4-16.6), whereas the criterion of only one impairment at 1.5SD within two domains was not predictive (relative risk 1.7, CI=0.5-7.4). Many of the latter group progressed to having two impairments within a single domain rather than to PDD at follow-up.

Conclusions: Using a Task Force1 Level II criterion in which two impairments at 1.5SD exist within one of the five recommended cognitive domains generates PD-MCI samples with a high risk of PDD over four-years. Additional study is now needed to find the optimal battery of tests to refine this proposal.

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Neutrophils in cutaneous squamous cell carcinoma: potential prognostic markers?

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Aim: While the majority of CSCC patients have an excellent prognosis, more clinically useful prognostic models for patients with high-risk CSCC are still required. We assessed circulating and tumour-localised neutrophil and lymphocyte populations for associations with high-risk tumour characteristics and metastasis free survival (MFS) in patients with CSCC.

Methods: A clinical audit of patients who were operated for primary CSCC through Christchurch Hospital between 2009 and 2011. Prospectively collected patient matched blood and primary CSCC tumour samples were analysed by flow cytometry for circulating G-MDSC, and by immunohistochemistry for tumour localised neutrophils and lymphocytes.

Results: In immunocompetent individuals, circulating frequencies of G-MDSC were higher in patients with higher stage versus lower stage tumours. Furthermore, high circulating neutrophil counts (≥4.5x10^{9}cells/L) were associated with tumour thickness ≥5mm, Clark level V and T-stage 2b/3. In univariate analysis an elevated circulating neutrophil count was associated with poor MFS. Moreover, tumours ≥5mm thick had greater numbers of peritumoral and tumour-localised neutrophils than tumours <5mm thick. Tumour thickness ≥5mm remained the only independent predictor of poor MFS, after adjusting for age and immunosuppression.

Conclusions: These easily measureable neutrophil parameters provide potentially useful prognostic markers, and merit further investigation.

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Charge

On 12 March 2015, the Health Practitioners Disciplinary Tribunal considered a charge laid by a Professional Conduct Committee against Dr U (the Doctor).

The charge alleged that over a period of five years the Doctor had falsely completed her application to the Medical Council for an annual practising certificate. She said she was complying with the continuing professional development requirements necessary for her general practice vocational registration. She claimed she was fulfilling the requirements of the College of General Practitioners Maintenance of Professional Standards Programme when she was not.

Finding and Penalty

The Tribunal found the charge established and that the actions of the Doctor were likely to bring discredit to the medical profession.

The Tribunal considered in the circumstances of this case there should be no penalty ordered against the Doctor. She was ordered to pay costs of $9000.00.

The full decision relating to the case can be found on the Tribunal web site at www.hpdt.org.nz
Reference No: Med14/298D

URL:
www.nzma.org.nz/journal/read-the-journal/all-issues/2010-2019/2015/vol-128-no-1421-4-september-2015/6658