Updated New Zealand health system cost estimates: further improvements in the age of ‘big data’

- New Zealand's growing thirst for a sugar-sweetened beverage tax
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Trust, transparency: and why we need them both


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Predictors of vitamin D status in pregnant women in New Zealand

Alec J Ekeroma, Carlos A Camargo Jr, Robert Scragg, Clare Wall, Alistair Stewart, Ed Mitchell, Julian Crane, Cameron C Grant

New Zealand has a sun avoidance health policy and minimal dietary vitamin D fortification. Vitamin D deficiency was present in 109/259 (42%) of pregnant women in a south Auckland cohort. Of those enrolled in winter (June-August)/spring (September-November), vitamin D deficiency was present in 43% of European, 67% of Māori, 80% of Pacific and 59% of women of other ethnic groups. Supplementation for all pregnant women during winter/spring could be an appropriate intervention for prevention of vitamin D deficiency during pregnancy in New Zealand.

The community pharmacy-based anticoagulation management service achieves a consistently high standard of anticoagulant care

Paul Harper, Ian McMichael, Dale Griffiths, Joe Harper, Caire Hill

People taking the blood thinning drug, warfarin, require regular blood tests to maintain safe control. In the past this service was provided by doctors using laboratory based blood tests. In 2012 a service was introduced to enable trained pharmacists to provide warfarin management through community pharmacies. Our audit confirms that pharmacists provide a safe, efficient and convenient service for patients and that the standard of anticoagulant control is above international recommendations and has remained high in spite of a five-fold increase in the number of patients using the service.

Analysis of the Auckland 2014 measles outbreak indicates that adolescents and young adults could benefit from catch-up vaccination

Gary Reynolds, Cassandra Dias, Simon Thornley, Ronald King, Anne Morrison, Angela Matson, Richard Hoskins

A single child with measles at a high school would almost certainly cause a serious outbreak, because immunity in that age group is well below the national average. The rate of immunity in New Zealand is close to 95%, which suggests a high level of herd immunity, but the level of immunity among secondary school age children is between 65 per cent and 80 per cent. One of the reasons is that a controversial study linking the measles mumps and rubella vaccine to autism – later proven to be false - persuaded many parents not to vaccinate their children at that time. That means they remain vulnerable today, especially while gathered together at school. They would benefit greatly from national, targeted vaccination catch-up.
Updated New Zealand health system cost estimates from health events by sex, age and proximity to death: further improvements in the age of ‘big data’

Tony Blakely, June Atkinson, Giorgi Kvizhinadze, Nhung Nghiem, Heather McLeod, Anna Davies, Nick Wilson

This study benefited from the relatively high quality and comprehensiveness of health cost data. It showed how widely this expenditure varied across the life course – with relatively more being spent in the last year of life (though this varied widely by age of death). This analysis has benefited from quality improvements in cost data and methods refinements but yet further improvements in coming years are likely. This is particularly so with access to additional data sources and with the move towards better integration of “big data” in the New Zealand health sector.

Prevalence of human papillomaviruses in the mouths of New Zealand women

Rebecca Lucas-Roxburgh, Jackie Benschop, Magdalena Dunowska, Matthew Robert Perrott

Human papillomavirus (HPV) infection in the mouth is associated with an increased risk of developing HPV-positive head and neck cancer. This study of 234 young women found HPV in the mouths of 7 women. Of those positive for HPV, two were positive for an HPV type able to cause cancer. The other five women were positive for a non-cancer causing HPV. No associations were found between putative risk factors (smoking, alcohol consumption, and the number of sexual partners) and the presence of oral HPV infection.
EDITORIAL

Trust, transparency: and why we need them both

Stephen Child, Sanji Gunasekara

Perhaps the culture of accountability that we are relentlessly building for ourselves actually damages trust rather than supporting it. Plants don’t flourish when we pull them up too often to check how their roots are growing: political, institutional and professional life too may not go well if we constantly uproot them to demonstrate that everything is transparent and trustworthy.” – Onora O’Neill

Calls have been made recently for the publication of outcome data from individual surgeons. While the intent of this is laudable—wanting to be transparent about care and to assist patient decision making—the implementation may not only present difficulties but is a direct affront to the trustworthiness component of our doctor-patient relationship.

The New Zealand Medical Association recognises the value of reliable, accurate data in informing clinicians, and in influencing planning and investment in health systems. As a professional body, we want to ensure the development of robust systems that will generate meaningful data. We agree with the underlying principles of the Medical Council’s view that—if gathered accurately, used correctly and explained well—qualitative data down to individual clinician level could benefit clinicians, administrators and regulators.

In other words, the concept of ‘transparency’ is laudable but that of ‘accountability’ may have unintended consequences.

We remain unconvinced of the perceived benefits of releasing these data to the public and in particular, any moves to report ‘raw’ or partially-adjusted performance/outcome data. While the role of data in clinical improvement and Quality Assurance (QA) is incontrovertible, the public release of such data is not.

‘Blaming and shaming’ individual surgeons will not improve patient care nor increase the trustworthiness of the profession. On the contrary, the more we try to increase the ‘accountability’ of the profession, the more we reduce the motivation of altruism, which is designed to put patients’ interests above our own interests.

On a wider scale, many ‘accountability’ measures—such as rewarding with financial incentives or developing clinical pathways and then punishing or rewarding to reduce variation—are developed because confusion has evolved between measures that are supposed to reflect accountability, and doctors being trusted to deliver the best possible care to our patients in the most efficient manner. Of course, key to this argument is that we, as doctors, must remain ‘trustworthy’ and to honour our commitment to professionalism.

Our concerns with the public reporting of outcome/performance data are based on a number of issues with a sampled few outlined below;

• **variation in the type and quality of outcome data collected**: Reporting poor quality outcome data without identifying the necessary limitations will lead to meaningless debate and generate spurious conclusions about apparent variations. The consequences of false identification of poor performance can negatively affect clinicians and patients.

• **multiple confounding factors**: Failure to adequately take these confounding factors into account could lead to misleading information that does not reflect the actual competence of any
individual named as lead clinician. If reported in its raw format to the public, unadjusted outcome data could also undermine confidence in the public health system. These factors include:

- patient factors (e.g., age, comorbidities, ethnicity, socioeconomic deprivation, health literacy, diagnostic validity, complexity/severity of condition)
- system factors (e.g., diagnostic/interventional facilities, healthcare team factors, supervision, resources vs competing demands, management and governance)
- clinician factors (e.g., volume of procedures, training, experience, and case-mix).

**failure to recognise the impact of systems, processes and infrastructure:** Post-operative outcomes (including mortality) relate to many factors other than the operative skill/competence of the surgeon, including the quality of postoperative and nursing care, etc.

**failure to take into account the contribution of the multidisciplinary team:** Reporting outcomes for individual surgeons ignores the effect of the multidisciplinary team and the context in which surgery is done. A lack of evidence of poor performance is not evidence of acceptable performance.

**promoting the practice of risk-averse medicine:** Fears of a negative outcome can lead to a range of negative impacts—from unnecessary investigations (and associated costs) to reduced learning opportunities for trainees, to a disincentive to provide treatment for the most seriously ill patients. In the UK, for example, publication of surgeon-specific data (SSD) has coincided with a drop in both the proportion and variety of cases performed by trainees, suggesting that the publication of SSD provided a disincentive for consultants to provide surgical training. The best surgeons may take on the highest risk cases, which may have worse outcomes. Public reporting may lead to the selection of lower risk patients.

**limitations of observational data:** Much of the evidence referred to here is non-experimental observational data and, despite risk adjustment, confounding is inherent—which is precisely the problem with the use of surgeon-specific data; the low-grade evidence may be useful for generating hypotheses but is inadequate for robustly testing these. A risk assessment-based system might allow comparison of actual outcome against predicted outcome over time, but still understates the complexity, and may in itself compound the issue.

**undermining the environment that is most conducive for quality improvement:** The best environment for quality improvement is one where clinicians feel safe to disclose adverse events and near misses, openly and frankly. Publicly reporting incomplete, confounded outcome/performance data could undermine the very environment that is most conducive for quality improvement.

**overlooking the performance outcomes of executive managers:** Executive managers must be held as accountable as clinicians for health outcomes that matter. Indeed at Mid Staffordshire, failings in hospital management and overall systems were found to be major contributors to the adverse health outcomes. The medical profession might, eventually, become more comfortable with publicly reporting on individual clinicians’ outcomes when there is similar reporting of:

- individual managers’ outcomes—over time and regardless of location
- health funders, for the populations they serve—measuring opportunity costs and health benefits forgone by the mix of decisions made to fund some things and not others.

**failure to recognise professionalism and the doctor-patient trust relationship:** Discussion on this issue should explicitly recognise the professionalism that underpins the autonomy granted to the medical profession via the original societal
Analogies between doctors and pure service providers are unhelpful and fail to acknowledge the unique nature of the doctor-patient trust relationship. Providing raw performance data to the public, without context, is contrary to the professionalism that is at the core of being a doctor.

**cost considerations:** Any costs of generating and managing performance/outcome data are likely to come out of Vote Health. Could the limited health dollar and resources be put to better use to improve the health of New Zealanders and to reduce health disparities?

**advantages of reporting at an aggregate level:** There are compelling arguments to focus on performance at relatively aggregated levels rather than at the level of individual practitioners.

Overall, it is much more appropriate to look at a unit, service or DHB-level analysis, which includes the total team effect and not just one participant in the care.

Thought also needs to be given to what a patient can realistically do with clinician-specific outcome/performance data, particularly as most New Zealanders rely on the public hospital system. The notion that such information can facilitate a patient’s informed choice of clinician is neither tenable nor ethical (if the only choice available entails a choice between public and private health care).

What patients and the public want to know is that the doctors caring for them are competent; public release of inadequate data inadequately explained will not achieve that and has potential to “disturb the roots while checking the tree”.

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**Competing interests:** Nil

**Author information:**
Stephen Child, Director Clinical Education Training Unit, Auckland DHB; Chair, New Zealand Medical Association. Sanji Gunasekara, Policy Manager, New Zealand Medical Association.

**Corresponding author:**
Dr Stephen Child, Auckland City Hospital, Private Bag 92024, Auckland 1023.
stephenc@adhb.govt.nz

**URL:**

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5. Delamothe T. Government’s initial response to Mid Staffordshire report. BMJ. 2013 Apr 9;346:f2209;
Administrative health data in New Zealand: we have come so far; where are the next opportunities?

Wing Cheuk Chan

In this issue of the *Journal*, Blakely et al provide an update on their New Zealand health system cost estimates based on health events that were captured in the New Zealand administrative data by age, sex and proximity to death. Consistent with previous published studies, their work demonstrates that the captured health system costs were skewed to the last year of life. Furthermore, Blakely et al included an updated discussion on the strengths and limitations of the use of the New Zealand administrative data.

We should celebrate the fact that New Zealand has a national unique patient identifier: the National Health Index (NHI) for all health care users in New Zealand, something that many developed countries cannot claim to have. There are ongoing processes in place to ensure duplicated NHIs are cleaned or merged as appropriate. The unique NHI has enabled many linkage studies to be carried out at the population level in New Zealand. The ongoing improvement of NHI coverage and data quality over time across a number of administrative health datasets has opened up a number of new opportunities, not just for ‘professional researchers’, but also for working clinicians who would like to undertake clinical audits or reviews, particularly in regard to longer term health outcomes, or identification of potential management gaps for improvement. Having a good visibility of longer term outcomes for our local populations can be challenging for clinicians because New Zealand has a very mobile population, and often there is no formal access to health care data outside one’s jurisdiction to capture the complete sets of subsequent health service events.

Examples of research or clinical audit opportunities in the future that could be explored via data linkage of New Zealand administrative data may include (and not be limited to):

1. Describing possible treatment gaps in a patient subgroup where there may be clinical safety concerns or opportunity for quality improvement: eg, are there people with a mechanical heart valve who are not on any form of anticoagulation for more than a year?

2. Undertaking a retrospective cohort study to describe outcomes of patient subgroups who had a procedure in hospital where benefits and risks were less certain: eg, what is the 2-year case fatality rate for people over 80 years of age and who had a right hemicolecotomy for colorectal cancer by cancer stage?

3. Facilitating an audit of a part of a treatment pathway: eg, what proportions of patients with breast cancer died prior to completing chemotherapy by age and stage?

4. Describing hospital events and costs associated with an entire interventional pathway: eg, transcatheter aortic valve implantations are often carried out in a tertiary facility, but costs for the associated procedures, such percutaneous coronary intervention or pacemaker implants, might sit in other hospitals where the tertiary facility may have limited visibility.

5. Describing practice patterns or service provision at a population level: eg, how many people with...
prostate cancer were managed by immediate radical treatment at diagnosis, active surveillance or watchful waiting in the wider Auckland region in New Zealand?

Blakely et al have acknowledged Craig Wright and the New Zealand Ministry of Health (MoH) for the development of the Health Tracker. The MoH’s Health Tracker has operationalised the concept of the “health service utilisation” population into a reality. Since the number of people in the health service utilisation population is very similar to the estimated resident population, this suggests the population coverage of the people who recently used health services is excellent. The Health and Disability Intelligence team from the MoH is expecting to lead ongoing updates of the Health Tracker in due course.

While there are many exciting opportunities to use administrative data more widely, potential interested users should be fully aware of the limitations related to the use of the administrative datasets, in particular in relation to cost estimates. As noted by Blakely et al, virtually all of the administrative health datasets list prices or cost weights related to the events, rather than the actual costs of events. District Health Boards (DHBs) are funded predominately on a capitation basis by the population-based funded formula, and only some of the pricing recorded in the datasets are used for reimbursement purposes between DHBs when a patient attends a facility outside the patient’s own domicile DHB. Some services are funded based on inputs rather than based on outputs, such as mental health services; it is important this is kept in mind when undertaking analyses involving health system costs.

The New Zealand MoH is currently undertaking a review of the population-based funding formula. The analytical insights gained as part of the review will provide further understanding on how the administrative data could provide robust cost estimates in a pragmatic way.

The other limitation of administrative data is that it is often difficult to make definitive claims of attribution between cause and effect because there are likely to be confounding factors that are not captured by the administrative data. One option to mitigate this limitation is to combine some of the clinical data available from other sources and link them against the administrative data or use administrative data to facilitate part of the clinical audit. For example, alerting a clinician that there were other hospital events occurring outside the index hospital of interest may be helpful. In situations where quantitative adjustments for confounding factors are not feasible, then making such limitations explicit in the appropriate context is helpful to enable the reader make a more informed interpretation of the findings: e.g., over the counter medications available in supermarkets or pharmacies are not captured in the Pharmaceutical Collection jointly owned by the MoH and PHARMAC.

While there are number of safeguards in place to ensure the administrative data is accurate, some errors do occasionally occur. If the actual errors are confirmed, they should be reported to the responsible department so that the administrative data can be corrected, or a system improvement can be put in place, so similar errors in the future may not recur. However, we also have to be cautious of the fact that many claims of data inaccuracies, particularly from inexperienced data users, could be related to poor understanding on how the original data is captured, the purpose of the data collection, and how they should be used, rather than actual errors related to the administrative data themselves.

It can be very helpful to liaise with the analytical, data quality and coding teams at the MoH to clarify coding practices, data enquiries and discuss how data should be used. The MoH teams can be contacted via: data-enquiries@moh.govt.nz and coding_helpdesk@moh.govt.nz. Depending on the nature of the enquiry, a study protocol is often required, including the research questions to be answered and the proposed methods. If potentially identifiable data is requested, ethics approval may be required from Health and Disability Ethics Committees. Data security and safe guards to ensure privacy and confidentiality must be in place.

Finally, Blakely et al highlight the recent development of Integrated Data Infrastructure (IDI) by Statistics New Zealand.
The IDI combines information in an anonymous way from a number of sectors, including health sector, along with data from the Ministry of Education and the Ministry of Social Development. While IDI is at an early phase, it is potentially a very exciting platform to undertake research to gain better understanding of the broader determinants of health, and more importantly, to develop potential pragmatic solutions that improve population health and equity.

References:

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Author information:
Wing Cheuk Chan, Public health physician, Population Health, Counties Manukau District Health Board.

Corresponding author:
Wing Cheuk Chan, Counties Manukau District Health Board
wingcheuk.chan@cmdhb.org.nz

URL:
Updated New Zealand health system cost estimates from health events by sex, age and proximity to death: further improvements in the age of ‘big data’

Tony Blakely, June Atkinson, Giorgi Kvizhinadze, Nhung Nghiem, Heather McLeod, Anna Davies, Nick Wilson

ABSTRACT

AIMS: We aimed to: (i) update previous health system cost estimates (Blakely et al NZMJ 2014;127(1393)) using updated costing data and more refined methods; and (ii) provide context around current developments in the improved networking of health information systems in New Zealand.

METHODS: As per our previous work, national health event data were linked for hospitalisations, inpatient procedures, outpatient events, pharmaceuticals, laboratory tests, and primary care consultations for the whole country. For each health event a cost was assigned. Health expenditure by sex and age, and proximity to death (last 6 or 12 months of life), was then calculated.

RESULTS: The updated and more accurate method allocated lower amounts of total public health expenditure than the previous work: $6.1, $6.0 and $6.7 billion dollars (inflation-adjusted to 2011 NZ$) in 2007/08, 2008/09 and 2009/10 financial years, respectively. But the latter is still only 52% of total health system costs ($6.7/$12.98 billion). Health system costs for people not within six months of death were similar to the previous work, except for being reduced in the most elderly age groups (range: $495 per person-year in 10–14 year old females; to $5,239 per person-year in 85–89 year old males). Costs in the last six months of life remained highly variable by age group (by a factor of 14 and being maximal at $23,400 or more among 1–4 year olds). The proportion of cumulative health expenditure in the last year of life declined with increasing age of death: eg, 47%, 25%, 13% and 6% for individuals aged 40, 70, 80 and 90 respectively.

CONCLUSIONS: Health system costs vary markedly across the life course, and are skewed to the last year of life. This analysis has benefited from quality improvements in cost data and method refinements, but further improvements in coming years are likely. This is particularly so with access to additional data sources, and with the move towards better integration of “big data” in the New Zealand health sector.

We have previously published, in this journal, estimates of health system costs by sex, age and proximity to death, using rich New Zealand data (‘Health Tracker’). Since then, there have been substantial improvements with the data sources, and ‘learnings’ about the reliability of various facets of the data. Also, improvements to the allocation of person-time and timing of cost occurrence have been developed. For example, standard treatment of health costings assigns individuals to the date of discharge, a practice which is not problematic for short-stay events, but is problematic for long-stay events (eg, multi-year admissions to hospital-level care leading to death) if all that cost is then attributed to the last year (or last six months) of life. Additionally, we have identified an error in our previous calculations of person-time which impacted on first year of life and last year (and six months) of life costings.
Given all these changes, our primary aim in this paper was to present updated results for all the objectives and analyses in the previously published article, namely: to estimate health system costs by demographics; for people within and not within six or 12 months of death; to estimate what proportion of health system costs over a person’s life occur in the last year of life; and to determine how much impact using costs stratified by proximity to death has on future national health expenditure projections (in the face of population growth, aging and increasing longevity).

Our second aim was to provide additional context to the current developments in access to health data in New Zealand. Third, we aimed to outline the next steps to further improve the quality of New Zealand health system costing data for research.

By way of background, we note that 83% of all health system expenditure in New Zealand is estimated to be publicly funded, with many of the health events (eg, hospitalisations and outpatients) not involving any fee-for-service. The remainder of the costs are private and include out-of-pocket payments and co-payments in primary care and for health insurance. There is growing research interest in understanding health system costing at the national level in New Zealand (eg, for all costs and for cancer costs), but also at the district health board (DHB) level (eg, Chan et al).

Methods

We repeat below the basic methods detailed in our previous paper analysing cross-sectional health system cost data (albeit with some minor changes) and follow this with a list of more substantively updated and refined methods.

Linked administrative health care datasets with costs attributed

The New Zealand health system has had a unique identifier of high quality since about 1990 (the National Health Index [NHI] identifier). The following datasets were linked using a unique identification number based on the NHI identifier to create a record for each New Zealander of all publicly funded health care events (eg, hospital admission, and laboratory test) occurring from July 2007 to June 2012. However, only the actual 2007/08 to 2009/10 financial years were used to estimate the costs, a restriction for two reasons. First, it is necessary to discard the most recent year of data for costs, as it is not possible to ‘know’ whether someone is within a year of death. Second, it became apparent that for earlier and later years, data were not complete on all health events and costs.

Each health event was then assigned a cost weight or unit price: casemix-funded hospitalisations (using Ministry of Health cost weights per event); primarily medical/surgical events); community laboratory tests; non-admitted patient events (eg, outpatients and emergency departments); community pharmaceuticals dispensed (including patient contribution); expected general practice costs (ie, using the capitation funding formula) and some actual general practice consultations (when not an enrolled patient in a capitated practice (ie, the general medical subsidy)). Goods and sales taxes were excluded as this is a transfer payment. All costs were inflation-adjusted to 2011 New Zealand dollars.

Data not (as of early 2015) included in our Health Tracker analysis included: lead maternity carer-provided care; rest-home and hospice care; mental health care; dental health care outside of hospitals; patient transport (eg, National Travel Assistance); care directly funded by Accident Compensation Corporation (ACC); and community physiotherapy. For the purposes of our objectives, missing rest-home and hospice care means costs proximal to death will be underestimated (although these data should become accessible for research in coming years; see Discussion).

Data management and person-time allocation

We used tabular analyses on the 2007/08 to 2009/10 data, calculating summed and average costs per person-year in each strata of interest: sex by five-year age group by financial year (2007/08, 2008/09, 2009/10) and whether within six or 12 months of death or not. We censored people at death. Immigration data were not linked in with these files, preventing correct censoring for emigration, but data were restricted to individuals who were both listed as a New Zealand resident on the NHI, and
had a record in at least one of the data sources used (including being enrolled with a primary health organisation) in the particular financial year. Finally, we calculated person-time weighted average costs over 2007/08 to 2009/10.

**Estimating future health expenditure**

We assembled Statistics New Zealand (SNZ) population count projections from 2011 to 2041 for the median growth scenario, for males and females by five year age-group (using the table builder at: http://www.stats.govt.nz/). The total population is projected to increase by 25% over these 30 years, but by over 150% for ages 75 and older. We then estimated future sex by age-specific mortality rates, by applying a 2% per annum mortality rate reduction to the single year of age mortality rate from the 2010–12 SNZ life-tables. (A 2% per annum mortality rate reduction equates to gains of 2.5 years in life expectancy per decade seen in recent decades in New Zealand, a pattern that seems likely to continue6).

We also undertook sensitivity analyses using SNZ projected mortality counts and rates with death data obtained from the projection from 2011 (base year) to 2061.7 (These SNZ projections equate to 1.3% (85–89 year old males) to 3.4% (55–59 year old males and females) annual percentage changes in mortality rates, for 35+ year olds.) We then applied health system costs for health events per person-year, both ‘simplistically’ using health system costs observed in 2009–11 not stratified by proximity to death, and then using costs separately for people within six or 12 months of death. We did not add in any trend data for changes in either health service usage by age-group or changes in health costs over time given the very large uncertainties involved. For example, for the latter there is uncertainty around the future ability of PHARMAC to keep constraining costs of pharmaceuticals, vaccines and devices; and also the variable potential performance of the New Zealand economy (which provides the resources to fund health services), given its dependence on commodity prices for exports and on international tourism levels.

**Updated data and methods since the previous analyses**

Since the previous analyses,1 we made a number of data and methods enhancements. These are detailed in full in the Appendix, but include: the use of financial years instead of calendar years; a revised core population of New Zealand residents; more accurate allocation of costs by timing; revised restrictions when considering casemix funding; changes to the cost weight used for the calculation of hospitalisation costs; along with a number of other fairly minor improvements.

**Results**

The health system costs associated with individual health events included in Health Tracker in 2011 NZ$, summed to $6.1, $6.0 and $6.7 billion in 2007/08, 2008/09 and 2009/10 financial years, respectively. But the latter still remained only 52% of total health system costs (6.7/12.98 billion). Pooling these years, the per person-year costs by sex, age and proximity to death are shown in Table 1 and Figure 1. Costs per person-year disregarding proximity to death varied approximately 10-fold from $535 for 10–14 year olds (sexes combined) to $5,600 for 85–89 year olds (Table 1).

The median values for the 21 age groups, regardless of proximity to death, were $1,518 per year for males and $1,457 per year for females. Removing person-time for people within six or 12 months of death did not alter these costs much at young ages (due to death being rare), but did quite considerably reduce the costs among the very old. For example, the cost per person-year among 90–94 year olds (sexes combined), regardless of proximity to death, was $5,600, but was reduced to $4,629 if not in the last six months of life.

Considering the assigned costs among people within six months of death, these costs varied only three-fold between age groups (in the under 95-year-old population). That is, there was less percentage or relative variation by age in costs during the last six months of life. A similar pattern was apparent also for costs in the last 12 months of life (Table 1).

Differences in costs over the life course between males and females showed a
### Table 1: Estimated health system costs attributable to specific health events for New Zealand citizens from Health Tracker (per person-year and per death event during 2007/08 to 2009/10, in 2011 NZ$ inflation-adjusted values).*

<table>
<thead>
<tr>
<th>Age group in years</th>
<th>Per person-year</th>
<th>Per death</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Regardless of proximity to death</td>
<td>Not in the last 6 months of life</td>
</tr>
<tr>
<td></td>
<td>Female</td>
<td>Male</td>
</tr>
<tr>
<td>&lt;1</td>
<td>4,189</td>
<td>4,890</td>
</tr>
<tr>
<td>1–4</td>
<td>1,009</td>
<td>1,166</td>
</tr>
<tr>
<td>5–9</td>
<td>517</td>
<td>589</td>
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<tr>
<td>10–14</td>
<td>498</td>
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</tr>
<tr>
<td>15–19</td>
<td>777</td>
<td>609</td>
</tr>
<tr>
<td>20–24</td>
<td>1,006</td>
<td>632</td>
</tr>
<tr>
<td>25–29</td>
<td>1,096</td>
<td>650</td>
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<tr>
<td>30–34</td>
<td>1,253</td>
<td>715</td>
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<tr>
<td>35–39</td>
<td>1,193</td>
<td>784</td>
</tr>
<tr>
<td>40–44</td>
<td>1,079</td>
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<td>45–49</td>
<td>1,221</td>
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<td>50–54</td>
<td>1,457</td>
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<td>60–64</td>
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<td>65–69</td>
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<td>3,450</td>
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<td>75–79</td>
<td>4,234</td>
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<td>80–84</td>
<td>4,834</td>
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<td>85–89</td>
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<td>90–94</td>
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<tr>
<td>95+</td>
<td>4,533</td>
<td>6,238</td>
</tr>
</tbody>
</table>

Notes: Bolded values show the higher costs when comparing females relative to males and vice versa.

*But due to current data limitations this is still for only 52% of total health system costs ($6.7/$12.98 billion), see Discussion.

Figure 1: Estimated health system costs attributable to specific health events for New Zealand citizens during 2007/08 to 2009/10, disregarding proximity to death, and separately for within and not within six months of death.*

![Health System Costs Graph](image)

*But due to current data limitations this is still for only 52% of total health system costs ($6.7/$12.98 billion), see Discussion.

mixed picture (Table 1). Costs were higher for males up to age 15 years, then costs were higher for females up to age 50 years (no doubt partly due to obstetric- and women’s health-related costs). There were quite large sex differences in costs in the last six months of life (often higher in females). This probably reflects higher incidence rates of sudden death in males without preceding chronic illnesses (eg, occupational injuries and suicide). To indicate the distribution of costs at different points in the life course, Figure 2 presents the cumulative health system costs (in 2011 NZ$) for deaths at different ages. This analysis is artificial as it assumes a steady state (as per 2011) for life span, treatment effectiveness and costs throughout the life course with no discounting. (This ‘artificiality’ is, however, similar to the way period life expectancy is calculated, whereby mortality rates
observed at one point in time are assumed to apply to a synthetic population over their lifetime.) Even so, these results give some indication of how the proportion of assigned health expenditure in the last year of life declines as the age at death increases, eg, 76% for death at age 10 years, 42% at age 50 years, 25% at age 70 years, 13% at age 80 years, and 6% at age 90 years.

Table 2 shows the estimated future health system costs with and without accounting for proximity to death (both 6- and 12-month scenarios), and for the ‘simplistic’ scenario of ongoing 2% per annum reduction in mortality rates into the future for all sex by age groups and the more sophisticated SNZ estimates of mortality counts and rates.

Regardless of the scenario, not accounting for proximity to death overestimates these future health system costs. That is, not allowing for deaths in the future being ‘pushed out more’ to older ages resulted in overestimated costs. This overestimate was by 1.3% to 4.5% by 2041, depending on scenario.

Discussion

What is new about these updated results?

This current work has produced updated values for all of the analyses in our previous study published in this journal. The general patterns are similar to that previously published, with two exceptions. Firstly, the costs being studied within the last six months of life now decline from around age 60 years for both sexes (rather than continuing to increase with age as suggested previously; Figure 1). Secondly, the costs regardless of impending death now plateau in the 80+ age-group (rather than continuing to increase; Figure 1). These new results arise from the methods improvements around attributing costs proximal to the time of death (see Methods).

These results are also more consistent with our knowledge of how the health system in New Zealand typically operates...
Table 2: Estimated future health system costs* (in 2011 NZ$ million) for the total New Zealand population with and without accounting for proximity to death, for varying scenarios of future mortality rates and six versus 12-month proximity to death.

<table>
<thead>
<tr>
<th></th>
<th>2011</th>
<th>2021</th>
<th>2031</th>
<th>2041</th>
</tr>
</thead>
<tbody>
<tr>
<td>a. Assuming 2% per annum reduction in mortality rates uniformly for all sex by age groups</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>i. By 6-month proximity to death</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Accounting for proximity to death</td>
<td>6,569</td>
<td>7,690</td>
<td>8,907</td>
<td>9,878</td>
</tr>
<tr>
<td>Not accounting for proximity to death</td>
<td>6,569</td>
<td>7,725</td>
<td>8,988</td>
<td>10,009</td>
</tr>
<tr>
<td>% overestimate due to not accounting</td>
<td>0.0%</td>
<td>0.5%</td>
<td>0.9%</td>
<td>1.3%</td>
</tr>
<tr>
<td>ii. By 12-month proximity to death</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Accounting for proximity to death</td>
<td>6,767</td>
<td>7,866</td>
<td>9,056</td>
<td>9,986</td>
</tr>
<tr>
<td>Not accounting for proximity to death</td>
<td>6,767</td>
<td>7,982</td>
<td>9,327</td>
<td>10,432</td>
</tr>
<tr>
<td>% overestimate due to not accounting</td>
<td>0.0%</td>
<td>1.5%</td>
<td>3.0%</td>
<td>4.5%</td>
</tr>
<tr>
<td>b. Assuming SNZ projected future mortality rates uniformly by sex by age groups</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>i. By 6-month proximity to death</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Accounting for proximity to death</td>
<td>6,568</td>
<td>7,683</td>
<td>8,896</td>
<td>9,862</td>
</tr>
<tr>
<td>Not accounting for proximity to death</td>
<td>6,568</td>
<td>7,721</td>
<td>8,981</td>
<td>9,992</td>
</tr>
<tr>
<td>% overestimate due to not accounting</td>
<td>0.0%</td>
<td>0.5%</td>
<td>1.0%</td>
<td>1.3%</td>
</tr>
<tr>
<td>ii. By 12-month proximity to death</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Accounting for proximity to death</td>
<td>6,764</td>
<td>7,854</td>
<td>9,043</td>
<td>9,987</td>
</tr>
<tr>
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<td>6,764</td>
<td>7,978</td>
<td>9,321</td>
<td>10,418</td>
</tr>
<tr>
<td>% overestimate due to not accounting</td>
<td>0.0%</td>
<td>1.6%</td>
<td>3.1%</td>
<td>4.3%</td>
</tr>
</tbody>
</table>

* But due to current data limitations this is still for only 52% of total health system costs ($6.7/$12.98 billion) in 2011, see Discussion.

Figure 3: Estimated future health system costs (in 2011 NZ$) for the total New Zealand population. Labels are percentage overestimates when not accounting for proximity to death.
ie, less intensive provision of health services for the very old for whom such interventions as major surgery might be less appropriate and in some cases for whom palliative care might be the service being provided.

**Updated consideration of study limitations**

Researchers and policymakers can have confidence about the general patterns suggested by these results, but they should remain particularly cautious about the accuracy of all the specific values reported in this study. Furthermore, some of our analyses (as shown in Figure 2), involve assumptions eg, a steady state in costs throughout the life course (which is in contrast to the historical pattern of increases in health costs in high-income countries). Below we provide an updated list of the other major limitations with these cost estimates identified to date:

1. Using the linked administrative datasets in Health Tracker, $6.7 billion (2011 inflation adjusted NZ$) of almost exclusively Government health expenditure was attributed to individual patient events in 2009. But this is still only just over half (52%) of the combined Vote:Health appropriation in 2009–10. One reason is that we have restricted hospitalisation costs to only those that are casemix-funded (as detailed earlier). Also, important components of Vote:Health expenditure are not yet available to us, including data on maternity care, immunisation, cervical screening, specific programmes (eg, diabetes care improvement package, performance-related payments), and more importantly for this study, Disability Support Services and other funding covering rest home and palliative care. The latter will have resulted in us underestimating some of the near-end-of-life costs. Nevertheless, due to capital and ‘back office’ expenditure on administration, not all of Government funding can readily be attributed to individual patient events (eg, over 10% of public funding goes to prevention and public health services, and health administration²).

That said, this Health Tracker dataset is an extremely rich dataset for analyses, and will continue to improve in the future. As examples, it is already contributing data for other work by the National Health Committee on a high-level scan of health spending in order to select domains of health service use for further work on prioritisation,⁸ and for Treasury projections of future health expenditure.²

2. Primary care costs are very simply assigned on a per capita basis (considering age, sex and ethnicity) to the New Zealand population using the country’s health system’s capitation formula. Therefore, our analyses will tend to underestimate costs near death if primary care utilisation increases near death. But, given that primary care expenditure is not a large component of end-of-life care in New Zealand, this probably would not cause much of an underestimation in the costs in the last six months of life.

3. Current Health Tracker data also include very little privately funded health expenditure. But, given that 83% of all health system expenditure is estimated to be publically funded in New Zealand,² this limitation is not too severe.

4. This study did not estimate costs by ethnicity, since it seems likely that any such cost differences will be due to conflated differences in need, access and utilisation of health services, and as such requires separate and careful analysis and interpretation. But, given the importance of health inequalities in New Zealand society, this should be a priority area for future work.

5. Many of the datasets used in this analysis use ‘prices’ that are potentially charged by agencies to funding bodies and which do not necessarily represent the actual cost of the health event. For example, many community lab contracts are bulk-funded and so the prices are only indicative and potentially have not been updated for a number of years. This pricing issue
may mean that true costs are actually higher where costs go up, but where prices charged stay the same and become out-of-date. But if lower costs are achieved (eg, from operational efficiencies obtained) then prices charged might be sometimes higher than the true costs.

6. Our modelling around future health costs does not fully address any future compression or expansion of morbidity that is not captured directly by proximity to death. Further details of this are in the Appendix.

What is the context for further developments?

While we have made use of Health Tracker in this study, we have also been considering big picture issues for the New Zealand health system. One of us (TB) has been engaged in national-level ‘big data’ and health systems discussions. We are also aware that DHB level interest in ‘big data’ is growing (eg, Counties Manukau DHB has been using Ministry of Health data to inform health service and policy development for a number of years, see: http://www.countiesmanukau.health.nz/about-us/performance-and-planning/health-status-documents/).

But now there is a likely imminent step-change in data access occurring in New Zealand, with moves to place routine health data (eg, mortality, hospitalisation, laboratories, etc) linkable via the NHI into the SNZ Integrated Data Infrastructure (IDI). In the last decade, research groups such as PREDICT/VIEW at the University of Auckland (https://www.fmhs.auckland.ac.nz/en/soph/about/our-departments/epidemiology-and-biostatistics/research/view-study/research.html; accessed 11 February 2015) and BODE at the University of Otago (www.otago.ac.nz/bode3; accessed 11 February 2015) have received copies of multiple routine administer health datasets for their dedicated research purposes—what is sometimes called ‘bespoke’ linkage. But in the age of ‘big data’, research productivity can be enhanced (and duplication and errors minimised) by allowing researchers easier and fuller access to fully integrated data. Successful international examples of this move from ‘bespoke’ to ‘fully integrated and wider access', include the “ScottisH Informatics Programme (SHIP)” (http://www.scot-ship.ac.uk/) and the Ontario Institute for Clinical Evaluation Sciences (http://www.ices.on.ca/). The New Zealand Ministry of Health has already migrated health data to the SNZ IDI, and is working through the feasibility of placing most national health data collections in the IDI to facilitate research (personal communication, Jackie Fawcett, Ministry of Health, December, 2014). To support this initiative, a Virtual Health Information Network (VHIN) has been established with joint membership of university academics and public sector researchers. One of the goals of the VHIN is to encourage sharing of knowledge about health data (eg, metadata) and analytical approaches (eg, rationale of the methods, definitions, cross-checking with clinicians, data management and analysis code) between researchers in a collaborative model that enhances the productivity and accuracy of New Zealand health research using routine data. Formal structures for such a VHIN are evolving (eg, health researchers using the IDI may be strongly encouraged, or even required, to make available to other researchers their programing code).

What all these developments mean is improvements in the type of analysis presented in this article are imminent—and will allow for both improved research by New Zealand researchers and more nuanced decision-making by policy makers and planners.

Regarding cost data specifically, we foresee two parallel streams to improve the quality of data for modelling in the next five years. First, the ‘bottom-up’ costing in this paper can be complemented by allocating remaining Vote:Health (and Vote:ACC) across individuals under plausible scenarios. For example, taking the total maternity care budget, and allocating it across woman pro-rata to age-specific birth rates. Second, and a ‘longer-term’ option which should replace the previous blended ‘bottom-up’ and ‘top-down’ approach, is to continue to work on the individual-level data and costing rules, and ‘liberate’ them for researcher use (cost models are already...
in use within the Ministry, for example)—perhaps through the SNZ IDI and VHIN.

Conclusions

Health system costs are large in New Zealand, vary across the life-course, and are skewed to the last year of life (eg, around 25% of costs being in the last year of life of a 70-year-old). This analysis has benefited from quality improvements in cost data and methods refinements relative to the previously published work on health costs in New Zealand. Nevertheless, the patterns in the costs are largely unchanged from previously—except the decline in some costs with age among older New Zealanders. Furthermore, we show (as before) that projections of future health system expenditure are slightly overestimated when not accounting for proximity to death in costs.

Further health data improvements in coming years are likely with access to additional data sources (eg, from Disability Support Services) and as New Zealand continues to move towards better integration of ‘big data’ in the health sector. It is often said that “New Zealand has some of the best health data in the world”. The goal now should be to better harness these data for informing policy and undertaking world-class research, matching and even exceeding the potential realised in other jurisdictions such as Scotland and Ontario.

Appendix: additional methods details

Updated data and methods since the previous analyses

Since the previous analyses, the following data and methods enhancements were performed:

1. **Years covered:** The financial years 2007/08, 2008/09 and 2009/10 are now used instead of calendar years 2007, 2008, 2009.

2. **Core population:** A revised core population of New Zealand residents was used. Previously the population inclusion criteria was broader and included those not listed as New Zealand resident if they had health system records with points of contact three or more months apart in any one year (including enrolment with a primary health organisation).

3. **Cost allocation:** More accurate allocation of costs by timing was performed. That is according to usual ‘administrative’ practice, costs were previously assigned to the end date of an event regardless of duration of event. That led to skewed costs in the last six months of life. In the current analyses, we re-allocated costs evenly over the duration of each event in time.

4. **Use of casemix-funding:** Another modification was made after more exhaustive examination of the input datasets. Hospitalisation costs were restricted to casemix-funding only as cost weights applied to non-casemix-funded events are unlikely to accurately reflect the true (opportunity) cost to the New Zealand health sector. Furthermore, without this restriction there was a risk of double counting the costs of some events where they appear in two datasets (eg, emergency department events in the National Non Admitted Patients Collection and those in the NMDS). We therefore decided to only allocate costs to those events that we have high confidence in: casemix-funded hospitalisations; community laboratory tests; non-admitted patient events (eg, outpatient and emergency department events); community pharmaceuticals dispensed (including patient contribution); general practice consultations (both that calculated based on the capitation funding formula routinely used in New Zealand, and fee-for-service when not an enrolled patient in a capitated practice). Restricting to these files resulted in around 50% of all Vote:Health funding being allocated to event-based expenditure. The ‘missing’ 50% includes the files not yet linked (maternity, rest-home, community mental, dental and physiotherapy care; see above) and inpatient events excluded from casemix-funding (which include but are not limited to
inpatient mental health events; events directly funded by ACC; events where the admitted person was a boarder; cancelled treatments; some transplant events; some spinal injuries; some same day chemotherapy for cancer events; some same day lithotripsies, colposcopies, cystoscopies, colonoscopies, gastroscopies, and bronchoscopies; and some same day blood transfusions).

5. **Calculation of hospitalisation costs:** In addition to the exclusion of non-casemix-funded hospitalisations, the cost weight used for the calculation of hospitalisation costs changed from using one cost weight for all years, to using the cost weight used for funding in the specific financial year (ie, a different cost weight for each year, along with the appropriate year’s unit price). The reasons for this were pragmatic, but also because it reflects how events were actually costed that year.

6. **Other improvements:** A number of other fairly minor improvements were made (eg, with the calculations of PHO data), the details of which are available from the authors on request.

The SAS code used in our analyses is available by contacting the authors (if not available on our website: http://www.otago.ac.nz/bode3).

**Compression or expansion of morbidity: implications for modelling of future costs**

Our modelling around future health costs does not fully address any future compression or expansion of morbidity that is not captured directly by proximity to death. For example, the diabetes epidemic may increase morbidity (and demand for health services) if our society is less successful at reducing incidence than we are at keeping people alive with diabetes, thereby seeing an expansion in morbidity (diabetes disease severity held constant, and likewise other causes of morbidity held constant). Conversely, if New Zealand society successfully controls obesity trends, this may reduce morbidity prevalence (through diabetes, but also cardiovascular disease, musculoskeletal and other impacts). Determining past trends in compression or expansion in morbidity is challenging, let alone estimating future trends. That said, we suggest that one method to include in future expenditure projections is to use disability-adjusted life expectancy (DALE; as estimated in the recent New Zealand Burden of Disease study), assume the same ratio of DALE to life expectancy (DALE:LE) in the future, and then back estimate by what percentage the prevalent years of life lived with disability (pYLDs) would need to change in the future to keep the DALE:LE ratio constant (or whatever other ratio is considered plausible). The percentage change in pYLDs across all sex by age groups necessary to generate the desired DALE:LE ratio in the future can then be used as a proxy for morbidity change, and therefore rescaling of the costs not within the last six or 12 months of life shown in Table 1.
Competing interests: Nil

Funding:
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Acknowledgment:
Access to Health Tracker data was provided by the Ministry of Health. In particular, we acknowledge the efforts and foresight of Craig Wright in initially assembling the data and managers within the Ministry who had the foresight to ensure this data source was created and made available. We thank Bronwyn Croxson and Dr Wing Cheuk Chan for helpful comments on early versions of this work and the two anonymous journal reviewers for very helpful comments.

Author information:
Tony Blakely, Research Professor, Department of Public Health, University of Otago, Wellington; June Atkinson, Data Analyst, Department of Public Health, University of Otago, Wellington; Giorgi Kvizhinadze, Postdoctoral Fellow, Department of Public Health, University of Otago, Wellington; Nhung Nghiem, Research Fellow, Department of Public Health, University of Otago, Wellington; Heather McLeod, Professor, School of Management Studies, University of Cape Town, South Africa; Anna Davies, Research Fellow, Department of Public Health, University of Otago, Wellington; Nick Wilson, Associate Professor, Department of Public Health, University of Otago, Wellington.

Corresponding author:
Professor Tony Blakely, Department of Public Health, University of Otago, Wellington, PO Box 7343, Wellington, New Zealand.
tony.blakely@otago.ac.nz

URL:

REFERENCES:
Predictors of vitamin D status in pregnant women in New Zealand

Alec J Ekeroma, Carlos A Camargo Jr, Robert Scragg, Clare Wall, Alistair Stewart, Ed Mitchell, Julian Crane, Cameron C Grant

ABSTRACT

INTRODUCTION: Newborn vitamin D status is largely determined by maternal vitamin D status during pregnancy. New Zealand has a sun avoidance health policy and minimal dietary vitamin D fortification. Vitamin D deficiency (serum 25-hydroxyvitamin D (25(OH)D) concentration <50nmol/L) is present in 57% of a sample of newborns from Christchurch and Wellington. To inform vitamin D supplementation policy, our aim was to describe the frequency of, and factors associated with, vitamin D deficiency during pregnancy.

METHODS: We enrolled an ethnically diverse sample of pregnant women from a community maternity clinic in South Auckland, New Zealand, with serum 25(OH)D concentration measured at 27 weeks gestation. We examined the associations of enrolment season, maternal demographics, health, sunlight exposure and vitamin D intake with vitamin D deficiency.

RESULTS: Vitamin D deficiency was present in 109/259 (42%). Enrolment season (P<0.001) and ethnicity (P=0.003) were independently associated with the odds of vitamin D deficiency, but not sunlight exposure or dietary vitamin D intake. Of those enrolled in winter (June–August)/spring (September–November), vitamin D deficiency was present in 43% of European, 67% of Māori, 80% of Pacific and 59% of women of other ethnic groups.

CONCLUSIONS: These findings suggest that New Zealand's targeted strategy for vitamin D supplementation may miss up to 42% of women with vitamin D deficiency in our population. Supplementation for all pregnant women during winter/spring could be an appropriate intervention for prevention of vitamin D deficiency during pregnancy in New Zealand.

The importance of vitamin D in maintaining calcium homeostasis is well defined, and those with severe deficiency suffer bone disease, such as rickets. The role of vitamin D in pregnancy and its effects on maternal, foetal and neonatal health is still unclear, although earlier systematic reviews concluded there was insufficient evidence to suggest lower vitamin D status during pregnancy was associated with adverse pregnancy outcomes. However, two recent meta-analyses showed low vitamin D status is associated with an increased risk of poor pregnancy outcomes. A meta-analysis of 31 observational studies that used a range of serum 25-hydroxyvitamin D (25(OH)D) cut-off values from 20 to 80 nmol/L showed a lower 25(OH)D concentration during pregnancy was associated with an increased risk of gestational diabetes (OR 1.49, 1.18–1.89), pre-eclampsia (OR 1.79, 1.25–2.58), and small for gestational age (OR 1.85, 1.52–2.26). A meta-analysis of 24 studies showed a serum 25(OH)D concentration <50 nmol/L was associated with an increased risk of gestational diabetes (OR 1.38, 1.12–1.70), pre-eclampsia (OR 2.09, 1.50–2.90), preterm birth (OR 1.58, 1.08–2.31) and small for gestational age (OR 1.52, 1.08–2.15). Although not establishing causation, the consistency of the associations of low vitamin D status with poorer pregnancy outcomes that these recent meta-analyses showed, are of potential policy relevance in countries where vitamin D deficiency is prevalent.

Vitamin D deficiency is common in New Zealand. Two New Zealand studies of pregnant women have shown a high prevalence of vitamin D deficiency. The 2008/2009 New Zealand Nutrition Survey reported that one-third of 2,204 women of...
child-bearing age had vitamin D deficiency,\textsuperscript{7} as defined by the New Zealand Ministry of Health (MoH) as a serum 25(OH)D concentration <50 nmol/L.\textsuperscript{8} In a sample of 929 healthy newborns born in Christchurch and Wellington between 1997 and 2001, 350 (57\%) had serum 25(OH)D < 50 nmol/L.\textsuperscript{9}

Studies performed in New Zealand have shown associations of low sunlight exposure, higher latitude, winter and spring seasons and non-European ethnicity to be associated with an increased risk of vitamin D deficiency.\textsuperscript{6,10,11} These associations are consistent with those identified in other studies, which also showed, in addition, a lack of vitamin D supplementation, greater body mass index (BMI),\textsuperscript{12} smoking, multiparity, skin colour\textsuperscript{13} and a range of variables describing socioeconomic disadvantage.\textsuperscript{14}

The MoH guidelines recommend vitamin D supplementation be considered for high-risk women, whom they defined as those that are dark skinned, avoid sunlight, or are resident at more southern latitudes during the winter months.\textsuperscript{8} Specifically, routine measurement of serum 25(OH)D concentration during pregnancy is discouraged in current New Zealand clinical practice, therefore the decision making regarding vitamin D supplementation is based on the presence or absence of risk factors. A screening tool, based on predictors of vitamin D deficiency, would potentially assist clinicians in deciding who to supplement. Ideally, a clinical screening test should: address a significant public health condition for which treatment is available; have a high sensitivity and specificity; be safe, inexpensive and widely available; and lead to an improvement in health outcomes.\textsuperscript{15}

Our aim is to identify and quantify the risk factors of vitamin D deficiency in an ethnically diverse sample of pregnant women in New Zealand. We sought to develop a simple predictive tool for vitamin D status based on the identified risk factors.

**Methods**

**Study design and setting**

This study was completed within a randomised trial of vitamin D supplementation during pregnancy and infancy, the findings of which have been reported.\textsuperscript{16}

Ethical approval was obtained from the regional MoH ethics committee (Northern X committee, Application number NTX09/11/101) and written informed consent obtained from all participating women. Women were recruited from a community-based primary care maternity clinic in Auckland (latitude 36°S) New Zealand, from April 2010 to July 2011.

**Study participants**

Women were eligible for enrolment if their estimated gestation was 26 to 30 weeks and they had a singleton pregnancy. We excluded pregnant women taking vitamin D supplementation that exceeded 200 IU/day, those with a history of renal stones or hypercalcaemia, or with any serious complication of pregnancy at the time of enrolment.

**Data collection**

Face-to-face interviews were completed with women at enrolment with the data collected allowing description of maternal demographics and health, pregnancy health, dietary sources of vitamin D and sunlight exposure. We defined enrolment seasons as summer (December–February), autumn (March–May), winter (June–August) and spring (September–November). Ethnicity was defined as the mother’s self-prioritised ethnicity.

Dietary vitamin D intake was estimated using an interviewer-administered semi-quantitative food frequency questionnaire (FFQ). The FFQ captured the major sources of vitamin D in the New Zealand food supply derived from the New Zealand Food Composition Database.\textsuperscript{17} The FFQ contained 12 food items using standard food serving sizes. Frequency of recent consumption of each item was described across an 8-point frequency range (never, < monthly, 1–3 times per month, weekly, 2–4 times/week, 5–6 times/week, daily, ≥ 2 times per day). Frequencies were converted into daily intake, for example a response of 2–4 times per week was converted to 0.4 servings/day (ie, 3 times per week).

The vitamin D content of each food was obtained from the New Zealand Food Composition Database.\textsuperscript{17} Any foods not in this database were obtained from the AUSNUT2007 food database.\textsuperscript{18} When estimating participant vitamin D intake
standard serving sizes were used, for example each serving of yoghurt was 150g and each serving of milk 250ml. These are recommended standard serving sizes for the New Zealand population. Brands of specific foods known to be fortified with vitamin D were also captured (margarine, yoghurt, milk). Frequency of consumption of each food item in the FFQ was converted to intake of vitamin D in µg/day.

Exposure to ultraviolet B radiation was estimated indirectly by determining the number of self-reported hours spent outdoors in the sun during the preceding four weeks. In New Zealand adults, reported sunlight exposure correlates with serum 25(OH)D concentration.19

Venous blood samples were obtained from the pregnant women at enrolment and serum 25(OH)D concentration was measured using isotope-dilution liquid chromatography-tandem mass spectrometry in a Vitamin D External Quality Assurance Scheme-certified laboratory.20,21

Statistical analysis
Statistical analysis was performed using SAS version 9.3 (SAS Institute Inc, Cary, NC, USA). The sample was described using proportions and means with standard deviations or, for non-normally distributed data, medians with interquartile ranges. External prioritization was used for respondents with more than one prioritized ethnicity, with the priority order being: Māori, Pacific, Asian and European/Other.22

For the purpose of this study, vitamin D deficiency was defined as serum 25(OH)D concentration <50 nmol/L and severe vitamin D deficiency as 25(OH)D <25 nmol/L. For outcome analyses we categorised serum 25(OH)D concentrations into four groups: <25; 25 to <50; 50 to <75; and ≥75 nmol/L. Using the chi-square and Wilcoxon rank-sum test, we determined unadjusted associations of variables with vitamin D status as defined by these four groups and with vitamin D deficiency.

Multivariable logistic regression was used to determine the independence of associations of variables with vitamin D deficiency. Variables were entered into the model, if the p-value in univariate analyses was <0.15 and were removed from the model sequentially until the model only contained variables significantly associated with vitamin deficiency. A simple predictive tool for vitamin D deficiency was developed which included the variables identified with this multivariate model.

Associations were described using odds ratios (OR) and 95% confidence intervals (CI). A two-tailed P value of <0.05 was considered statistically significant.

Results
Enrolment of the 259 pregnant women was evenly distributed by season (summer 59 (23%), autumn 71 (26%), winter 67 (27%), spring 62 (24%)). The sample was ethnically diverse (European 40 (15%), Māori 62 (24%), Pacific 113 (44%), and all other ethnic groups 44 (17%)). Median (interquartile range) age was 28 (22–31) years and median body mass index (BMI) 32 (27–38) kg/m². Fifty-six percent of the women had a tertiary education. The mean (SD) serum 25(OH)D concentration was 63 (35) nmol/L. Vitamin D deficiency was present in 109 (42%) women, while severe vitamin D deficiency (serum 25(OH)D<25 nmol/L) was present in 28 (11%).

In unadjusted analyses, vitamin D status varied with season, ethnicity, BMI, and time spent outdoors (Table 1). More specifically, there was an increased odds of vitamin D deficiency for women enrolled in winter (OR=16.7) or spring (OR=9.9); for women of Pacific (OR=5.5) or of other (OR=10.0) ethnic groups; and a decreased odds for women who used sunscreen (OR=0.5) (Table 2). Sunscreen use varied by ethnicity (European 65%, Māori 41%, Pacific 32%, Other 47%, P=0.003).

When these unadjusted analyses were restricted to the non-European women (n=219) the increased risk associated with enrolment during winter (OR=18.6, 95%CI 3.5–342.5) or spring (OR=9.7, 95%CI 1.7–183.1) compared with summer persisted. While sunscreen use was no longer associated with a reduced odds of vitamin D deficiency (OR=0.7, 95%CI 0.3–1.7) avoidance of sun exposure during summer was (OR=0.37, 95%CI 0.1–0.9).

In the multivariable analysis, the variables independently associated with the odds of vitamin D deficiency were season of enrolment and maternal ethnicity (Table 3).
Table 1: Participant characteristics, by maternal serum 25-hydroxyvitamin D concentration during pregnancy.

<table>
<thead>
<tr>
<th>Variable (n=259 unless otherwise stated)</th>
<th>Serum 25-hydroxyvitamin D concentration in nmol/L, n (column %) or median (IQR*)</th>
<th>P value†</th>
</tr>
</thead>
<tbody>
<tr>
<td>Enrolment season</td>
<td></td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Summer</td>
<td>1 (4) 6 (7) 15 (24) 37 (42)</td>
<td></td>
</tr>
<tr>
<td>Autumn</td>
<td>3 (11) 11 (14) 20 (33) 37 (42)</td>
<td></td>
</tr>
<tr>
<td>Winter</td>
<td>15 (53) 36 (44) 9 (14) 7 (7)</td>
<td></td>
</tr>
<tr>
<td>Spring</td>
<td>9 (32) 28 (35) 17 (29) 8 (9)</td>
<td></td>
</tr>
<tr>
<td>Maternal demographics and health</td>
<td></td>
<td></td>
</tr>
<tr>
<td>and household demographics</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age in years</td>
<td>28 (24–30) 28 (23–32) 28 (23–32) 26 (21–31)</td>
<td>0.50</td>
</tr>
<tr>
<td>Ethnicity</td>
<td></td>
<td>0.008</td>
</tr>
<tr>
<td>European (E)</td>
<td>1 (4) 8 (10) 10 (16) 21 (24)</td>
<td></td>
</tr>
<tr>
<td>Māori (M)</td>
<td>4 (14) 18 (22) 15 (25) 25 (28)</td>
<td></td>
</tr>
<tr>
<td>Pacific (P)</td>
<td>14 (50) 46 (57) 26 (43) 27 (30)</td>
<td></td>
</tr>
<tr>
<td>Other (all others not E, M, or P)</td>
<td>9 (32) 9 (11) 10 (16) 16 (18)</td>
<td></td>
</tr>
<tr>
<td>Education</td>
<td></td>
<td>0.96</td>
</tr>
<tr>
<td>Primary</td>
<td>5 (18) 11 (13) 7 (11) 16 (18)</td>
<td></td>
</tr>
<tr>
<td>Secondary</td>
<td>8 (29) 24 (30) 18 (30) 24 (27)</td>
<td></td>
</tr>
<tr>
<td>Tertiary</td>
<td>15 (53) 46 (57) 36 (59) 49 (55)</td>
<td></td>
</tr>
<tr>
<td>Body mass index in kg/m² (n=257)</td>
<td>31 (26–38) 34 (28–40) 32 (27–38) 31 (25–37)</td>
<td>0.04</td>
</tr>
<tr>
<td>Doctor-diagnosed diabetes (n=256)</td>
<td></td>
<td>0.72</td>
</tr>
<tr>
<td>Yes</td>
<td>0 (0) 1 (1) 2 (3) 2 (2)</td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>28 (100) 77 (99) 59 (97) 87 (98)</td>
<td></td>
</tr>
<tr>
<td>Doctor-diagnosed hypertension</td>
<td></td>
<td>0.94</td>
</tr>
<tr>
<td>Yes</td>
<td>1 (4) 5 (6) 3 (5) 4 (4)</td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>27 (96) 76 (94) 58 (95) 85 (96)</td>
<td></td>
</tr>
<tr>
<td>Cigarette smoker pre-pregnancy (n=258)</td>
<td></td>
<td>0.70</td>
</tr>
<tr>
<td>Yes</td>
<td>10 (36) 37 (46) 27 (44) 34 (39)</td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>18 (64) 44 (54) 34 (56) 54 (61)</td>
<td></td>
</tr>
<tr>
<td>Number of people in house</td>
<td>4 (3–7) 5 (4–7) 4 (3–6) 4 (3–6)</td>
<td>0.27</td>
</tr>
<tr>
<td>Pregnancy health</td>
<td></td>
<td></td>
</tr>
<tr>
<td>First pregnancy</td>
<td></td>
<td>0.44</td>
</tr>
<tr>
<td>Yes</td>
<td>18 (64) 59 (73) 43 (70) 70 (79)</td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>10 (36) 22 (27) 16 (30) 19 (21)</td>
<td></td>
</tr>
<tr>
<td>Gestation in weeks (n=256)</td>
<td></td>
<td>0.68</td>
</tr>
<tr>
<td>28 (27–29)</td>
<td>27 (27–29) 27 (26–28) 27 (26–28)</td>
<td></td>
</tr>
<tr>
<td>Current cigarette smoker</td>
<td></td>
<td>0.13</td>
</tr>
<tr>
<td>Yes</td>
<td>2 (7) 19 (23) 8 (13) 20 (22)</td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>26 (93) 62 (77) 53 (87) 69 (78)</td>
<td></td>
</tr>
<tr>
<td>Dietary sources of vitamin D</td>
<td></td>
<td>0.80</td>
</tr>
<tr>
<td>Dietary vitamin D in ug/day</td>
<td>2.5 (1.7–3.5) 2.6 (1.7–4.2) 3.0 (1.9–4.0) 2.9 (1.6–3.8)</td>
<td></td>
</tr>
<tr>
<td>Vitamin D supplement (n=232)</td>
<td></td>
<td>0.70</td>
</tr>
<tr>
<td>Yes</td>
<td>1 (4) 3 (4) 4 (8) 3 (4)</td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>24 (96) 71 (96) 47 (92) 79 (96)</td>
<td></td>
</tr>
<tr>
<td>Sunlight exposure</td>
<td></td>
<td>0.004</td>
</tr>
<tr>
<td>Minutes/day outdoors past 4 weeks</td>
<td>31 (20–60) 49 (21–94) 45 (20–94) 77 (31–120)</td>
<td></td>
</tr>
<tr>
<td>Sunscreen if outside in summer</td>
<td></td>
<td>0.10</td>
</tr>
<tr>
<td>Yes</td>
<td>9 (33) 26 (32) 29 (48) 43 (48)</td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>18 (67) 55 (68) 32 (52) 46 (52)</td>
<td></td>
</tr>
<tr>
<td>Avoids sun exposure 10.00–16.00 hours</td>
<td></td>
<td>0.09</td>
</tr>
<tr>
<td>in summer</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>12 (43) 50 (63) 42 (63) 60 (67)</td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>16 (57) 30 (37) 19 (31) 29 (33)</td>
<td></td>
</tr>
<tr>
<td>Head covering worn (n=195)</td>
<td></td>
<td>0.38</td>
</tr>
<tr>
<td>No head covering or hat</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Head covering or hat</td>
<td></td>
<td></td>
</tr>
<tr>
<td>12 (86)</td>
<td>43 (86) 41 (85) 63 (76) 20 (24)</td>
<td></td>
</tr>
</tbody>
</table>

* Interquartile range
† From chi-Square, Fisher's Exact or Wilcoxon rank-sum test
‡ Includes scarf/head covering, burka, cap, winter pull-over beanie or cowboy hat/hat with rim
### Table 2: Unadjusted associations between participant characteristics and maternal serum 25-hydroxyvitamin D concentration during pregnancy.

<table>
<thead>
<tr>
<th>Variable</th>
<th>Associations with serum 25(OH)D &lt;50 nmol/L</th>
<th>P value*</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Odds ratio (95%CI)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>1.0</td>
<td>0.004</td>
</tr>
<tr>
<td>Enrolment season</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Summer</td>
<td>2.6 (0.3, 52.5)</td>
<td></td>
</tr>
<tr>
<td>Autumn</td>
<td>16.7 (3.2, 307.6)</td>
<td></td>
</tr>
<tr>
<td>Winter</td>
<td>9.9 (1.8, 184.7)</td>
<td></td>
</tr>
<tr>
<td>Spring</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Maternal demographics and health and household demographics</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age in years</td>
<td>1.0 (0.9, 1.1)</td>
<td>0.88</td>
</tr>
<tr>
<td>Ethnicity</td>
<td></td>
<td>0.06</td>
</tr>
<tr>
<td>European</td>
<td>1.0</td>
<td></td>
</tr>
<tr>
<td>Māori</td>
<td>2.7 (0.4, 53.6)</td>
<td></td>
</tr>
<tr>
<td>Pacific</td>
<td>5.5 (1.1, 101.6)</td>
<td></td>
</tr>
<tr>
<td>Other</td>
<td>10.0 (1.8, 189.7)</td>
<td></td>
</tr>
<tr>
<td>Education</td>
<td></td>
<td>0.90</td>
</tr>
<tr>
<td>Primary</td>
<td>1.3 (0.4, 3.6)</td>
<td></td>
</tr>
<tr>
<td>Secondary</td>
<td>1.1 (0.4, 2.6)</td>
<td></td>
</tr>
<tr>
<td>Tertiary</td>
<td>1.0</td>
<td></td>
</tr>
<tr>
<td>Body mass index in kg/m²</td>
<td>1.0 (1.0, 1.1)</td>
<td>0.06</td>
</tr>
<tr>
<td>Doctor diagnosed diabetes</td>
<td></td>
<td>0.35</td>
</tr>
<tr>
<td>Yes</td>
<td>0.4 (0.0, 2.4)</td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>1.0</td>
<td></td>
</tr>
<tr>
<td>Doctor diagnosed hypertension</td>
<td></td>
<td>0.76</td>
</tr>
<tr>
<td>Yes</td>
<td>1.2 (0.4, 3.7)</td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>1.0</td>
<td></td>
</tr>
<tr>
<td>Cigarette smoker pre-pregnancy</td>
<td></td>
<td>0.73</td>
</tr>
<tr>
<td>Yes</td>
<td>1.1 (0.7, 1.8)</td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>1.0</td>
<td></td>
</tr>
<tr>
<td>Number of people in house</td>
<td></td>
<td>0.13</td>
</tr>
<tr>
<td>7 or more</td>
<td>1.9 (1.0, 3.8)</td>
<td></td>
</tr>
<tr>
<td>4 to 6</td>
<td>1.1 (0.6, 2.1)</td>
<td></td>
</tr>
<tr>
<td>Less than 3</td>
<td>1.0</td>
<td></td>
</tr>
<tr>
<td>Pregnancy health</td>
<td></td>
<td></td>
</tr>
<tr>
<td>First pregnancy</td>
<td></td>
<td>0.40</td>
</tr>
<tr>
<td>Yes</td>
<td>0.8 (0.5, 1.4)</td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>1.0</td>
<td></td>
</tr>
<tr>
<td>Gestation</td>
<td>1.2 (1.0, 1.4)</td>
<td>0.09</td>
</tr>
<tr>
<td>Current cigarette smoker</td>
<td></td>
<td>0.90</td>
</tr>
<tr>
<td>Yes</td>
<td>1.0 (0.6, 1.9)</td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>1.0</td>
<td></td>
</tr>
<tr>
<td>Dietary sources of vitamin D</td>
<td></td>
<td>0.94</td>
</tr>
<tr>
<td>Dietary vitamin D ug/day</td>
<td>1.0 (0.9, 1.1)</td>
<td></td>
</tr>
<tr>
<td>Sunlight exposure</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Average time per day outdoors past 4 weeks</td>
<td></td>
<td>0.07</td>
</tr>
<tr>
<td>Less than 60 minutes</td>
<td>1.6 (1.0, 2.6)</td>
<td></td>
</tr>
<tr>
<td>60 Minutes or more</td>
<td>1.0</td>
<td></td>
</tr>
<tr>
<td>Sunscreen if outside in summer</td>
<td></td>
<td>0.01</td>
</tr>
<tr>
<td>Yes</td>
<td>0.5 (0.3, 0.9)</td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>1.0</td>
<td></td>
</tr>
<tr>
<td>Avoids sun exposure 10.00–16.00 hours in summer</td>
<td></td>
<td>0.08</td>
</tr>
<tr>
<td>Yes</td>
<td>0.6 (0.4, 1.1)</td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>1.0</td>
<td></td>
</tr>
<tr>
<td>Head covering worn</td>
<td></td>
<td>0.68</td>
</tr>
<tr>
<td>No head covering or hat</td>
<td>1.4 (0.4, 9.2)</td>
<td></td>
</tr>
<tr>
<td>Head covering or hat†</td>
<td>1.0</td>
<td></td>
</tr>
</tbody>
</table>

* From univariable logistic regression analysis
† Includes Scarf/head covering, burka, cap, winter pull-over beanie or cowboy hat/hat with rim
Table 3: Multivariable associations between participant characteristics and maternal serum 25-hydroxyvitamin D concentration during pregnancy.

<table>
<thead>
<tr>
<th>Variable</th>
<th>Associations with vitamin D deficiency as defined by a serum 25(OH)D &lt;50 nmol/L</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Odds ratio (95%CI)</td>
</tr>
<tr>
<td></td>
<td>P value*</td>
</tr>
<tr>
<td>Enrolment season</td>
<td></td>
</tr>
<tr>
<td>Summer</td>
<td>1.0</td>
</tr>
<tr>
<td>Autumn</td>
<td>2.2 (0.8, 6.3)</td>
</tr>
<tr>
<td>Winter</td>
<td>31.1 (11.9, 92.4)</td>
</tr>
<tr>
<td>Spring</td>
<td>13.5 (5.4, 38.2)</td>
</tr>
<tr>
<td></td>
<td>0.13</td>
</tr>
<tr>
<td></td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Ethnicity</td>
<td></td>
</tr>
<tr>
<td>European</td>
<td>1.0</td>
</tr>
<tr>
<td>Māori</td>
<td>2.8 (1.0, 8.3)</td>
</tr>
<tr>
<td>Pacific</td>
<td>5.8 (2.3, 15.8)</td>
</tr>
<tr>
<td>Other</td>
<td>5.3 (1.8, 17.2)</td>
</tr>
<tr>
<td></td>
<td>0.051</td>
</tr>
<tr>
<td></td>
<td>&lt;0.001</td>
</tr>
<tr>
<td></td>
<td>0.004</td>
</tr>
</tbody>
</table>

* From multivariable logistic regression analysis

Table 4: Diagnostic performance of screening tests for vitamin D deficiency in pregnant women based upon season or upon season and ethnicity.

<table>
<thead>
<tr>
<th>Screening test based upon season</th>
<th>Vitamin D deficiency*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Season when pregnant</td>
<td>Present</td>
</tr>
<tr>
<td>Winter/spring</td>
<td>88</td>
</tr>
<tr>
<td>Summer/autumn</td>
<td>21</td>
</tr>
<tr>
<td>Screening test performance</td>
<td>Absent</td>
</tr>
<tr>
<td>All ethnic groups</td>
<td>41</td>
</tr>
<tr>
<td>European</td>
<td>109</td>
</tr>
<tr>
<td>Māori</td>
<td>29</td>
</tr>
<tr>
<td>Pacific</td>
<td>121</td>
</tr>
<tr>
<td>Other</td>
<td></td>
</tr>
<tr>
<td>Screening test based upon season and ethnicity</td>
<td></td>
</tr>
<tr>
<td>Season when pregnant and maternal ethnicity</td>
<td>Vitamin D deficiency*</td>
</tr>
<tr>
<td>Winter/spring and non-European ethnicity</td>
<td>Present</td>
</tr>
<tr>
<td>Winter/spring and non-European ethnicity</td>
<td>79</td>
</tr>
<tr>
<td>Summer/autumn or European ethnicity</td>
<td>Absent</td>
</tr>
<tr>
<td>Summer/autumn or European ethnicity</td>
<td>29</td>
</tr>
<tr>
<td>Screening test performance</td>
<td>121</td>
</tr>
<tr>
<td>Sensitivity = 73%, specificity = 81%, PPV = 73%, NPV = 80%</td>
<td></td>
</tr>
</tbody>
</table>

* Serum 25-hydroxyvitamin D <50 nmol/L
PPV = positive predictive value
NPV = negative predictive value
There was increased odds of vitamin D deficiency associated with enrolment in women of Māori, Pacific or other ethnic groups (in comparison with European women); and winter or spring (compared with summer). A prediction model based on winter/spring seasons alone (Table 4) had comparable performance as a screening test for vitamin D deficiency as one that used both season and maternal ethnicity. In comparison with a model that included both season and ethnicity, the sensitivity for a model based solely upon season was 81% (95% CI 72–88) vs. 73% (63–81) and specificity 73% (65–80) vs. 81% (73–87).

Discussion

In this multi-ethnic, New Zealand-based pregnant cohort, the prevalence of vitamin D deficiency (defined as 25(OH)D concentration <50 nmol/L) was 42%. The only factors independently associated with vitamin D deficiency were ethnicity, with women of Māori, Pacific, and other ethnic groups all at increased risk compared with women of European ethnicity; and season with women tested during winter or spring being at increased risk compared with those tested during summer.

Our study, the third to describe vitamin D status in a pregnant population in New Zealand, is the largest and the only one that has enrolled an ethnically diverse population over the full calendar year and the first to assess the factors associated with vitamin D deficiency. Our findings confirm the higher prevalence of vitamin D deficiency in darker-skinned women, as reported in a study of 228 South Asian women living in Auckland,6 and the high prevalence in winter and spring as reported in the same paper6, and elsewhere.23–25 Vitamin D deficiency was also found to be prevalent (87%) in a study which enrolled a multi-ethnic sample of 90 pregnant women from a single primary care practice in Wellington city.1 Our study confirms that the vitamin D requirements in pregnancy cannot be met by the current vitamin D content of the New Zealand diet, particularly for Pacific and Māori women.26

We found no association between serum 25(OH)D levels and age, parity, smoking, BMI, or dietary vitamin intake. Whereas others have found associations between some of these factors and vitamin D deficiency in pregnancy,27, 28 these associations were not consistently present in studies performed in Australia.23, 29 For example, a study done in Canberra and Campbelltown identified four factors predictive of vitamin D deficiency: season; ethnicity; BMI; and vitamin D supplementation.23 Our study design prevented us from assessing the contribution of vitamin D supplement use to vitamin D status during pregnancy. In New Zealand, only 36% of pregnant women take any vitamin or mineral supplements, many of which are inadequate sources of vitamin D.30

Avoiding sunlight exposure in summer was not significant a predictor for the whole sample but it remained significant for the non-European participants (Table 2a and 2b), although this difference was no longer significant after adjusting for season and ethnicity. Although there is a general consensus that vitamin D levels increase with increased sunlight exposure,31 it is not possible to make a single recommendation32 and there is a variable response to UVB radiation, with some individuals having low serum 25(OH)D concentrations despite high levels of sun exposure.33

The associations we observed of season and ethnicity with vitamin D status are consistent with those described previously in New Zealand studies of women of child bearing age and of newborns.7, 9, 34 The New Zealand guidelines support the identification and supplementation of pregnant women at risk of vitamin D deficiency, based on the presence of specific factors: “dark skin, living in the lower regions of New Zealand in winter and completely avoiding sunlight.”8 The guideline did not identify ethnicity per se as a risk factor, nor is season emphasised except with reference to those living in more southern parts of New Zealand. Ethnicity defines groups of individuals who differ with respect to skin colour, socio-economic status and cultural behaviour, which in turn can determine the amount of sun exposure and the types of food consumed. Classifying skin pigmentation more simply as non-European ethnicity will simplify for women and for health workers the identification of those women at greater risk of vitamin D deficiency.
Routine measurement of serum 25(OH)D concentration is only recommended in symptomatic women during pregnancy in New Zealand, which differs from advice in a position statement for Australian and New Zealand infants which states, “pregnant women, especially those who are dark-skinned or veiled, should be screened” to prevent infant vitamin D deficiency. This statement reflects current clinical practice in Australia where women with risk factors have screening blood tests. A recent study from Australia had however advocated for change. Using only three predictor factors (non-European ethnicity, BMI >30kg/m$^2$ and all women in winter) it was shown that 91% of those with vitamin D deficiency would be identified and unnecessary testing avoided in 58%. 23

Supplementation based upon a simple predictor model using ethnicity (Māori, Pacific and Other) and season (winter and spring) (Table 4) would result in 72% of women with vitamin D deficiency being supplemented, but 19% of those who were vitamin D sufficient also being supplemented. Our preferred predictor model is for the supplementation of all pregnant women during winter and spring, which would result in 81% of those with vitamin D deficiency being supplemented and 27% of those who were vitamin D sufficient also being supplemented. The predictor model could potentially have an even higher predictive value (PV) amongst similar populations living at more southern latitudes in New Zealand. The predictive value of the model may not be as high in population areas where the majority of the population are European. Our prediction model, has a similar predictive value to that recently reported from Australia, but has a better PV to that of Jensen et al for a sample of pregnant women in Norway—perhaps reflecting the more limited dietary sources of vitamin D in New Zealand compared with Norway. A study that aimed to identify risk factors for vitamin D deficiency in children aged 12–22 months living in Dunedin (latitude 45°S) confirmed a strong seasonal variation but lacked the diversity of sample needed to investigate the relationship between ethnicity and vitamin D status.

Limitations of our study includes its modest sample size and enrolment from a single metropolitan centre, albeit of an ethnically and socioeconomically diverse sample. We did not seek to enrol a sample that was representative of the New Zealand maternity population, so caution is required when generalising from the study region to other New Zealand regions.

If pregnant women were to require vitamin D supplementation, a daily dose of 400 to 600 IU/day is recommended. However, a recent study had shown that a dose of 2,000 IU/day from 13 weeks gestation was needed to protect 98% (44 neonates) from vitamin D deficiency. We showed, in the randomised trial in which these women were enrolled, that daily vitamin D supplementary doses of 1,000 IU or 2,000 IU are safe as defined by serum calcium concentration measurement. Not all the vitamin preparations prescribed in pregnancy in New Zealand contain the recommended dose of vitamin D and not all women have access to the recommended supplements due to cost. Our findings support vitamin D supplementation for every pregnant woman in winter and spring. Even if issues of access to appropriate vitamin D supplementary doses were addressed, poor adherence to nutritional guidelines in pregnancy is common and may limit the success of any universal supplementation programme. We acknowledge that there are no data on the cost-effectiveness of supplementation without testing in winter.

Although missing 15% of those with severe vitamin D deficiency is a concern, the costs involved with measuring serum 25(OH)D levels on all pregnant women in New Zealand (as recommended in the position statement by Paxton et al 2013) is prohibitively expensive and acknowledged by the Ministry of Health as not being feasible. Our proposal for vitamin D supplementation of all pregnant women during 6 calendar months of the year (from June to November inclusive) is easier to remember and administer than current MoH guidelines, which make no clear recommendation on supplementation other than to identify groups of pregnant women, who—because of their skin pigmentation, sunlight avoidance
behavior or underlying conditions—will be at greater risk of being vitamin D deficiency. The current New Zealand MoH recommendations potentially miss 42% of vitamin D deficient pregnant women. Our recommendation does not remove the responsibility of the clinician caring for a pregnant women to acknowledge that she may be at higher risk of more severe vitamin D deficiency due to her skin pigmentation, lifestyle or presence of liver or kidney disease, and to manage this appropriately at an individual level, with such management likely to include measurement of 25(OH)D levels and potentially larger doses of vitamin D.

Conclusion

Vitamin D deficiency was present in 42% of this ethnically diverse sample of pregnant women living in Auckland, New Zealand. Winter/spring seasons and non-European ethnicity were the only independent risk factors for vitamin D deficiency. Given the high prevalence of vitamin D deficiency in our population and the limited number of factors associated with vitamin D deficiency, we recommend that a simple approach would be for all pregnant women to receive vitamin D supplementation during winter and spring, although it is acknowledged that data on costs and benefits of various options is lacking.

Competing interests:
The study was performed in South Auckland and the Department of Paediatrics, Faculty of Medical and Health Sciences, University of Auckland.

Author information:
Alec J Ekeroma, Department of Obstetrics and Gynaecology, Faculty of Medical and Health Sciences, University of Auckland, New Zealand; Carlos A Camargo Jr, Emergency Medicine, Massachusetts General Hospital, Harvard Medical School, Boston, 02114, USA; Robert Scragg, School of Population Health, University of Auckland, Auckland; Clare Wall, Department of Nutrition, University of Auckland, Auckland; Alistair Stewart, Epidemiology & Biostatistics, University of Auckland, Auckland; Ed Mitchell, Department of Paediatrics: Child & Youth Health, University of Auckland, Auckland 1142, New Zealand; Julian Crane, Department of Medicine, University of Otago, Wellington, New Zealand; Cameron C Grant, Department of Paediatrics: Child & Youth Health, University of Auckland, Auckland 1142, New Zealand.

Corresponding author:
Alec Ekeroma, c/o Pacific Women’s Health Research Unit, Department of Obstetrics and Gynaecology, Middlemore Hospital, University of Auckland, Private Bag 93311, Auckland, New Zealand
alec@pacifichealthresearch.org.nz

URL:

References:


The community pharmacy-based anticoagulation management service achieves a consistently high standard of anticoagulant care

Paul Harper, Ian McMichael, Dale Griffiths, Joe Harper, Claire Hill

ABSTRACT

AIM: To ensure that the Community Pharmacy-Based Anticoagulation Management Service (CPAMS) in New Zealand has continued to deliver a high standard of anticoagulant care as the service has grown to provide warfarin supervision to over 4,000 patients.

METHODS: A clinical audit of patients managed through CPAMS over two years from 1 January, 2013. Anticoagulant control was assessed by measuring the time in therapeutic range (TTR), proportion of high and low INR results and incidence of reported bleeds. Compliance with the service was evaluated by monitoring the frequency of testing and the interval between tests.

RESULTS: There has been only a modest change in the TTR from 76.4% to 74% during the audit period, despite the growth in patient numbers from 850 to 4,350. There was no change in the proportion of INR results above 4.0. Bleeding was reported in less than 4% of visits and 82% of bleeds were minor. 75% of patients attended for INR testing on the expected date, and only 3.3% were more than 2 weeks overdue. The interval between tests remained constant at approximately 19 days.

CONCLUSION: CPAMS provides safe reliable anticoagulant care with a consistently high level of anticoagulant control.

In New Zealand approximately 35,000 people regularly take warfarin and more than 80% have their treatment supervised by their own general practitioners. There is no standardised procedure for warfarin management, with no regular audit process or national reporting. The level of anticoagulant control achieved by general practitioners is unknown, but an audit in 2004 of a large cohort of patients managed through primary care showed that the INR was maintained within the therapeutic range only 55% of the time. International guidelines recommend the time in the therapeutic range (TTR) should be greater than 60%. In 2010, a proposal was put to Health Workforce New Zealand to pilot an alternative method of warfarin management supervised by pharmacists using near-patient-testing and decision support software (DSS). The aim was to reduce the general practitioners' workload by making use of other skilled health professionals and to see if this type of service could achieve a safe level of anticoagulant control.

The pilot study included 690 patients managed through 15 pharmacies over 9 months. It achieved a high level of anticoagulant control with the INR maintained in the therapeutic range at 78.6%. The study also received positive feedback from the patients, pharmacists and general practitioners involved. On the basis of these findings, a service funded by the Ministry of Health was introduced into approved pharmacies from late 2012.

Over the last 2½ years, the service has grown steadily, is now available in...
140 pharmacies and provides warfarin supervision for over 4,500 patients. One potential risk of expanding the service is that the level of anticoagulant control could fall. It is recognised that the outcome of pilot studies and clinical trials is not always maintained when the service is extended into more general use. In the Community Pharmacy Based Anticoagulation Management Service (CPAMS) pilot, the pharmacists involved were highly motivated, had a well-established relationship with their local general practitioners and were able to provide close supervision with appropriate collaboration with medical staff during the trial period; such close monitoring may not be possible in all pharmacies long-term. There was also potential for patient selection bias, as patients were referred at the discretion of the local general practitioners. Although the entry criteria for patients were wide and allowed for unstable patients to be included, there was the possibility that the more complex cases were not referred as this service was new and seen by some as experimental.

The aim of our audit was to see if the CPAMS service has continued to provide a high level of anticoagulant control as it has grown and to ensure that it maintains appropriate INR testing frequency and good adherence to testing on time.

Methods

Data for the audit were collected from the decision support software database (INR Online Ltd, Palmerston North, New Zealand). All patients on warfarin between 1 January, 2013 and 31 December, 2014, managed through CPAMS were included in the audit. To enable accurate calculation of TTR, the INR results from 1 November 2011 to 28 February 2015 were collected for the audit patients. The following data were recorded for each patient: date of birth; gender; reason for anticoagulant therapy; and length of treatment. The following data were collected each time an INR test was performed: date of the test; the INR result; the DSS recommended dose; the given dose; the DSS recommended date of the next test; and the pharmacists selected date of next test. At each test the patient was asked about missed medication, changes to medication, episodes of bleeding since the previous test and hospital admissions; this was recorded on the computer system. Since April 2014, the user has been able to record the severity of the bleed as minor (gum bleeding, spotting from the nose, minor bruising), moderate (blood in the bowel motions, haematuria, bruising >4cm) or major (bleeding requiring attention in hospital, intracranial bleeding, major gastro-intestinal bleed, major urinary tract bleed or any bleed requiring a blood transfusion). The service was supported with close collaboration between the pharmacist and the referring doctor. A mechanism was in place at each pharmacy to ensure that results outside the INR range 1.5 to 4.0 could be discussed with a supervising doctor at the patient's own general practice.

Assessment of anticoagulant control

Time in therapeutic range (TTR) was calculated using the method of Rosendaal,² which uses linear interpolation between successive INR values; the time in days above, within and below the therapeutic range was calculated for the total population for each month by calculating the sum of all results up to each time point. The TTR was also calculated for each patient using all their available INR results from November 2011 to February 2015.

The proportion of INR results between 4.0 to 4.5, 4.5 to 5.0, 5.0 to 5.5, 5.5 to 6.0 and above 6.0, and the proportion of INR result at 1.5 or lower were calculated each month, based on INR tests performed in that month. The number of episodes of bleeding reported by the patients was calculated each month and reported as a percentage of the total number of tests performed each month. From April, 2014, the severity of the bleed was also recorded.

Test intervals and adherence to testing

At each INR test the interval since the previous test was recorded and the mean interval calculated each month. Adherence to testing was calculated by measuring the difference between the recommended test date and the actual test date and recorded as on time, 1 to 3 days late, 3 to 7 days late, 7 to 14 days or more than 14 days late.
Statistical analysis
The assessment of trends for each parameter was measured using the Mann-Kendall test; p<0.05 was regarded as a significant trend. The comparison of the incidence of bleeding at various TTR ranges was calculated using chi-squared. The comparison of the mean time between intervals at various TTR ranges was evaluated using t-test. p<0.05 was regarded as significant.

Results
A total of 5,866 patients on warfarin have been managed through CPAMS during the audit period. The number of patients actively on treatment has grown steadily over the 2-year audit period, from 850 (January 2013) to 4,350 patients (December 2014). By December 2014, the service was provided in 126 pharmacies (Figure 1).

Demographics
The reason patients were taking warfarin is shown in Table 1. The most common indications for treatment were atrial fibrillation (63%), venous thromboembolic disease (DVT & PE) (17.2%) and mechanical heart valves (11.7%); 59% of patients were male.

The median age for males was 69.7 years (mean 67.3 years) and for females 71.6 years (mean 68 years). The mean age was higher in patients with atrial fibrillation than the other patient groups.

Assessment of stability of control
To assess the stability of control we measured the time in the therapeutic range, proportion of tests above 4.0 and below 1.5 and the incidence of reported bleeds each month.

Time in the therapeutic range: At the start of the audit period, 32 pharmacies were providing the service to 853 patients. The TTR for this population was 76.4% based on 17,000 INR results. As the size of the patient population increased there was...
Figure 2: The time above, within and below the therapeutic range each month.

Figure 3: Patients were grouped by deciles based on their TTR. The figure shows the number of patients in each group at the end of the audit period.

Figure 4: Percentage of tests with an INR above 4.0 each month.
**Figure 5:** Percentage of tests with an INR of 1.5 or less each month.

**Figure 6:** Proportion of tests where the patient reported bleeding since the previous test.

**Figure 7:** Relationship between the time in range (patients grouped in deciles based on TTR) and the reported incidence of bleeding. Bleeding rate falls significantly between TTR 50% and 100%; P<0.001.
Figure 8: Mean interval between INR tests + 1 SD.

Figure 9: Relationship between time in range (patients grouped in deciles based on TTR) and mean test interval (+ SEM).

Figure 10: Proportion of tests performed on the expected test date or later than the expected date.
a fall in the TTR to 74.8% (45,000 results) at 12 months and 74% (124,000 results) at 24 months (significant decreasing trend, p<0.05). The change in the TTR was largely due to an increase in the proportion of time below the therapeutic range, which increased from 12.6% to 16% (p<0.05). The proportion of time above the therapeutic range remained around 10% for the whole audit period (Figure 2).

The time in range was calculated for each patient at the end of the audit period. The distribution of results is shown in Figure 3; 75.4% of patients had a TTR greater than 60%.

Proportion of INR results outside the therapeutic range: Between 3% and 4.7% of INR results had a value of >4.0 each month. This did not change significantly over the audit period (no significant trend, Mann-Kendall test) (Figure 4). Between 4.1% and 6.3% of INR tests were less than or equal to 1.5 (Figure 5). The results show a significant positive trend.

Proportion of bleeds reported by the patient at each visit: The patient was asked about bleeding events since the previous test at each visit. The user could not proceed with the INR test until this had been answered on the computer system. The software was changed in April 2014 to allow the user to record the severity of the bleed. The proportion of tests where bleeding was reported, ranged from 2.1% to 4.9% each month. The trend was not uniform, with more bleeds reported during the months September to December. There is no significant trend during the first 15 months (only bleeding reported). The rate of reporting was higher after the pharmacists were able to report the bleed severity; 82.3% of bleeds are minor, 15.6% moderate and 2.1% major (Figure 6). Figure 7 shows the relationship between anticoagulant control and the incidence of bleeding calculated at the end of the audit period.

Assessment of stability of testing frequency and adherence to testing

Test interval: The mean interval between each test was calculated each month. This remained constant at approximately 19 days throughout the audit (Figure 8). The interval increased significantly as the INR control improved, with a mean of 23 days for patients with a TTR of 80 to 90% and 29 days with a TTR of 90 to 100% (Figure 9).

Adherence: Adherence to testing was assessed by monitoring the proportion of patients who attended for testing on the expected test date and the proportion who were late for testing. 75% of tests were performed on the expected date, a further 7.8% were only one day late. A total of 93.8% of tests were performed within a week of the expected test date and only 3.3% were more than 2 weeks late. Adherence remained stable throughout the audit period (Figure 10).

Discussion

The main finding of our audit is that community pharmacy-based anticoagulant service consistently delivers high quality anticoagulant care with the time in therapeutic range above 74%. This is in spite of the fact that the patient population has grown approximately five-fold during the audit period (Figure 1), and that the service is now supervised by more than 250 trained pharmacists. Our results also show that the frequency of testing remained remarkably constant, and patient adherence to testing is consistently high. However along with this growth, there has been a trend showing a modest fall in anticoagulant control, with the TTR dropping from 76.4% to 74% over two years.

The TTR is the most widely used measure of anticoagulant control, with several studies showing a correlation between the time in range and the incidence of both bleeding and thrombosis. A TTR around 75%, as achieved by the CPAMS programme, would be expected to achieve good clinical outcomes with a low incidence of warfarin complications. Two large clinical trials showed that patients on warfarin with good control (INR within range 75% of the time) had an annual mortality of 1.69% and major bleeding events of 1.58%, whereas the poorly controlled patients (INR within the therapeutic range <60% of the time) had an annual mortality of 4.2% and major bleeding of 3.85%. A TTR of 74% is significantly higher than the results from a meta-analysis of anticoagulant clinics in the USA (TTR 63%) and well above the level of control reported in this country.
Our results are similar to those achieved by a pharmacy-based service in Canada (TTR 73%).

Although the TTR is a useful measure of the quality of anticoagulant management, there is some evidence that the variability of INR results is also linked to adverse events. There is no standardised method of recording variability, but monitoring the proportion of INR results at the extremes of measurement can give an indirect assessment. Over the audit period we found no significant change in the proportion of INR results above 4.0 (Figure 4) and only a slight increase in INRs below 1.5. Although the trend reached statistical significance, the proportion of low INR results reported each month only increased by about 1% over the whole audit period (Figure 5).

The most direct measure of the complications of warfarin is the incidence of bleeding. In our audit we have tried to capture this by asking the patients about bleeds since their previous test. This has some limitations as it is dependent on the pharmacists asking the question and recording the answer on the computer system, however the software is designed to ensure that a question about bleeding must be answered before the INR test can be performed. During the first 15 months of the audit the software only allowed the user to record the presence of bleeding without giving details of the severity; during this period, the number of tests where bleeding was reported fluctuated from 2% to 3.5% each month with no overall trend. For the last 8 months, pharmacists were able to add details of severity and a slightly higher rate of bleeding was reported. It is difficult to know if this increase is clinically significant, as the different criteria for reporting may have influenced the pharmacists' decision to report a bleed. Anecdotally, pharmacists reported that not all minor bleeds were reported prior to the change. Of note, the rate of reported bleeds in our study correlates with the TTR supporting the hypothesis that there is a relationship between anticoagulant control and bleeding complications (Figure 7).

The gradual fall in the TTR over time could be due to a number of factors, including changes in the patient population, varied experience of the supervising pharmacists, and varied adherence to the decision support software. It is likely that the proportion of more complex cases has increased as the service has expanded. Patients were referred to the service at the discretion of their doctor, and in some practices only stable patients were submitted initially; only when the doctors were comfortable with the service were the more complex cases referred. The level of control fell most during the first 12 months of the audit, and stabilised during the second year—suggesting that control had reached a more steady state (Figure 2).

Another concern with an expanded service and a more diverse group of patients is that it could become less efficient, with patients requiring more frequent testing and worse adherence to the expected test dates. However, our results show that the interval between tests remains remarkably stable with mean interval of approximately 19 days with a similar distribution of results (Figure 8). The consistent test interval is, in part, due to the use of DSS as this recommends a test date at each visit and the pharmacists followed this 70% of the time. There is no recognised standard test frequency for warfarin management. International guidelines advise that testing every 4 to 6 weeks is appropriate for stable patients, but more frequent testing is necessary for those with less stable control. Studies have shown that more frequent testing improves control, however the benefit of frequent testing has to be balanced against the practicality of delivering a manageable service. We believe that a mean test interval around 20 days has been appropriate for our service, with the testing interval extended to around 4 weeks for well-controlled patients (Figure 9).

Another consistent finding is the adherence to testing, with 75% of patients attending for their INR tests on the expected date and only 3.3% more than 2 weeks overdue. The robust recall system which identifies patients overdue for testing and delivers automated e-mail reminders to the patients contributes to the high adherence rate.

The use of DSS for warfarin dosing, test dates and reminders has helped to maintain the consistent service but several other factors are likely to contribute to
the success of the programme. One key component is the streamlined process which enables patients to have an INR test, see their previous results, have a consultation with their pharmacist and get immediate treatment advice in a single visit. The feedback from patients is that this has made their warfarin management a simpler process and they feel more involved with their care. In conclusion, our results confirm that a community pharmacy-based anticoagulant service can deliver a safe and reliable service and further expansion would be appropriate to offer the same level of care to a larger number of patients on warfarin.

Competing interests:
Paul Harper reports he is a share holder and director of INR Online Ltd, a patient management system to assist in Anticoagulation Management. Dale Griffiths reports some funding from Health Workforce New Zealand during the conduct of the study and personal fees from Pharmaceutical Society of New Zealand, as a member of the Society’s National Executive, outside the submitted work. Joe Mr. Harper reports he is a shareholder and director of INR Online Limited, a patient management system to assist in Anticoagulation Management.

Author information:
Paul Harper, Clinical Haematology, Palmerston North Hospital; Ian McMichael, Pharmacist, Pharmacy 547, Hamilton; Dale Griffiths, Pharmacist, West View Pharmacy, Auckland; Joe Harper, INR Online Ltd, Auckland; Claire Hill, Devon Medical Centre, New Plymouth.

Corresponding author:
Paul Harper, Clinical Haematology, Palmerston North Hospital, Palmerston North, New Zealand.
paul.harper@midcentraldhb.govt.nz

URL:

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Prevalence of human papillomaviruses in the mouths of New Zealand women

Rebecca Lucas-Roxburgh, Jackie Benschop, Magdalena Dunowska, Matthew Perrott

ABSTRACT

AIM: Human papillomavirus (HPV) in the oral cavity has been retrospectively associated with an increased risk of developing HPV-positive head and neck squamous cell carcinoma (HNSCC). The aim of this study was to determine the prevalence of oral HPV infection in a local population of New Zealand women aged 18 to 25 years, including determination of HPV genotypes, and to assess potential risk factors for oral HPV infection using participant questionnaire responses.

METHODS: Oral brushings and questionnaire responses were collected from 234 women recruited from sexual health and student health centres. Questions covered age, ethnicity, sexual partners, alcohol consumption and smoking. PGMY primers were used for HPV detection by PCR, and results confirmed by sequencing and the cobas® 4800 HPV system.

RESULTS: The prevalence of HPV infection was 3.2% of 216 women (95% CI: 1.6%–6.5%). Samples from two women (0.9%, 95% CI: 0.3%–3.3%) contained oncogenic HPV, and another five (2.3%, 95% CI: 1.0%–5.3%) were positive for HPV 13. No significant associations were found between putative risk factors and the presence of oral HPV infection.

CONCLUSION: The prevalence of HPV in the oral cavity of New Zealand woman was comparable to results of other studies, but showed an unusual distribution of HPV types. The comparatively high detection rate of HPV 13 suggests that further work into clinical significance of oral HPV 13 infection is warranted.

Head and neck squamous cell carcinomas (HNSCCs) are the sixth most common cancers worldwide, with an estimated incidence of 405,000 cases and 200,000 deaths annually. These cancers comprise tumours of the oral cavity, oropharynx, hypopharynx, and larynx. Head and neck SCCs are a heterogeneous group of cancers showing two distinct pathways to malignancy. The first pathway involves smoking and alcohol as risk factors, and the second is mediated by infection with a high risk human papillomavirus (HPV) type. The incidence of HPV-positive HNSCC in developed countries has increased significantly in the past few decades. For example, data from the US have shown a 225% increase in cases of HPV-positive HNSCC between 1984 and 2004.

Although detection of HPV DNA in the oral cavity has been found to be associated with an increased risk of HPV-positive HNSCC, the pathogenesis of HPV-positive cancers of the oral cavity is not completely understood. Risk factors for HPV-positive HNSCCs include sexual behaviours, such as an increased number of sexual partners and practising oral sex. HPV-positive HNSCCs are most common in the oropharynx, and in particular the tonsils. HPV-positive HNSCCs appear to show some similarities with cervical cancer, including a pre-requisite for a persistent infection with a high-risk HPV type for a varied period of time before the development of cancer. As is the case with cervical HPV infection, only a very limited number of primary HPV infections persist and develop into malignancy.

The prevalence of HPV in the mouths of healthy individuals varied from 0% to 81% in overseas-based studies. Both low- and high-risk HPV types were detected.
High-risk HPV types, such as 16 and 18, have been shown to be associated with the development of oral cancer, with over 90% of HPV-positive HNSCC linked to infection with HPV 16. Infection with low-risk HPV types, such as 6 and 11, is causally associated with respiratory papillomatosis, a condition characterised by the growth of multiple papillomas, usually in the larynx.

There is currently no data on the prevalence on HPV in the oral cavity among New Zealanders. Thus, the aim of this study was to determine the prevalence of oral HPV infection in a local population of New Zealand women aged 18 to 25 years, including determination of HPV genotypes, and to assess potential risk factors for oral HPV infection using participant questionnaire responses.

Methods

Study design and recruitment
A cross-sectional design was used for this study. Eligible participants were women aged 18 to 25 years. Written consent was obtained from all participants prior to their participation. The study was approved by the Massey University Human Ethics Committee Southern A (approval 13/12). Recruitment took place between June and November, 2013, at sexual health and student health centres in the Manawatu region. All participants were asked to complete a questionnaire which encompassed demographic information and putative risk factors for oral HPV infection, including smoking, alcohol consumption, and the number of sexual partners. Information on whether the participants had been vaccinated with HPV vaccine Gardasil® was also collected. Alcohol consumption was measured in standard drinks per week, as defined by the New Zealand Health Protection Agency (330 mL can of beer, a 100 mL glass of wine, or a 30 mL glass of straight spirits). Being a current or previous smoker was defined as smoking more than 20 cigarettes in a lifetime. A sexual partner was defined as a partner of either sex, and the definition of sexual activity included vaginal, anal, and oral sex.

Sample collection and processing
After thorough explanation of the procedure by a registered nurse or the researcher, oral brushings were collected by self-sample. The left and right buccal surfaces and the base of the tongue were brushed using a cytobrush (Thermo-Fisher). Brushes were vigorously rinsed in ThinPrep® vials containing 20 mL Preservcvt® (CYTYC Corp). Samples were stored at room temperature until further processing. After mixing, 10 mL of each sample was centrifuged at 13,000xg for 10 minutes. The pellet was resuspended in 200 µL of phosphate buffered saline pH 7.0 (PBS), then transferred to a microtube for DNA extraction using High Pure™ PCR template preparation kit (Roche Diagnostics) as per the manufacturer’s instructions. The quality and quantity of extracted DNA was assessed using a NanoDrop™ spectrophotometer (Thermo Scientific).

Screening PCR with PGMY primers
Initially, PCR with PGMY09 and PGMY11 primers was used for detection of HPV DNA in test samples. Each 20 µL reaction contained 2 mM MgCl₂, 0.3 mM of each dNTP, 0.2 µM of each primer, one unit of Platinum® Taq, and 3 µL of template DNA in 1 x reaction buffer. The PCR was carried out using a SensoQuest® lab cycler (SensoQuest GmbH). An initial denaturation at 95 °C for 2 minutes was followed by 40 cycles of denaturation (95 °C for 5 seconds), annealing (55 °C for 5 seconds), and elongation (72 °C for 10 seconds for 30 cycles, increased to 30 seconds for the last 10 cycles), followed by a final elongation at 72 °C for 7 minutes. Positive (3 µL cobas® positive control, and 3 µL HPV 16 DNA that had been extracted from a cobas® HPV 16 positive cervical specimen) and negative (3 µL cobas® negative control, and 3 µL water) controls were included in each run. PCR products were visualised following electrophoresis through a 1.0% agarose gel containing 0.5 µg/mL ethidium bromide in 0.5% Tris-borate-EDTA (TBE) buffer at 100 volts for 45 minutes. Any sample that produced a 450 base pair band was considered a suspect positive.

Beta-globin PCR
The presence of amplifiable DNA in samples negative for HPV DNA by PGMY PCR was assessed by PCR targeting a human beta-globin gene using the PCO4 and GH20 primers. Each 20 µL reaction contained
1.5 mM MgCl₂, 0.2 mM each dNTP, 0.5 μM of each primer, 0.4 units of Platinum® Taq, and 3 μL of template DNA in 1 x PCR buffer. PCR was performed as described for the PGMY PCR. Positive (3 μL cobas® positive control) and negative (3 μL water) controls were included in each run. A sample was considered positive if a product of the expected size (268 bp) was visible on a gel. Samples that did not produce the expected band were removed from the analysis.

Roche cobas® 4800 testing

Suspect positives based on PGMY PCR were sent for testing using the Roche cobas® 4800 system, which detects 14 high-risk HPV types (16, 18, 31, 33, 35, 39, 45, 51, 52, 56, 58, 59, 66, and 68).

The remaining ~10 mL of oral brushings from each suspect positive was centrifuged at 13,000xg for 10 minutes, the pellet was then resuspended in 1.5 mL of oral brushings from each suspect positive was centrifuged at 13,000xg for 10 minutes, the pellet was then resuspended in 1.5 mL Preservcyt®, and this preparation was sent for cobas® testing at a commercial laboratory (MedLab Central, Palmerton North) according to standard protocols. Types 16 and 18 were reported individually while the other detectable HPV types were reported as ‘other high risk type/s detected’.

Confirmatory testing

All suspect positives that tested negative using cobas® system were re-tested using PGMY PCR. Samples that did not produce the expected band on re-testing were considered negative for HPV DNA. The identity of the 450 base pair bands produced by the remaining samples was confirmed by sequencing. DNA was purified from the gel using a freeze-squeeze procedure. Briefly, the excised band was placed in a 1.5 mL microtube on the top of a filtered pipette tip, which had been cut short to fit into the tube. The tube was snap-frozen in liquid nitrogen, then centrifuged at 13,000xg for 3 minutes. The filtrate containing DNA was used for sequencing, either directly or after cloning into a pCR4-TOPO vector using TOPO TA cloning kit for sequencing with Top10 competent cells (Life Technologies Inc.), according to the manufacturer’s instructions.

The colonies were screened for the presence of the 450 bp insert using PCR with M13 primers. Up to 10 colonies were randomly picked into 10 μL Luria Bertani (LB) broth containing 50 μg/mL ampicillin, and incubated at 37 °C for approximately 3 hours. DNA from PCR reactions that produced product of the expected size (616 bp) was prepared using ExoProStar™ (GE Healthcare, Life Sciences) as per the manufacturer’s instructions, and sent for sequencing using the Big Dye Terminator 3.1 chemistry at the Massey Genome Service (Massey University). Initially, two colonies were sequenced from each ligation reaction. If neither of these two colonies contained HPV sequences, an additional three colonies were sequenced, for a total of 5 colonies. The sequences were compared with other sequences available in GenBank using Basic Local Alignment Search Tool (BLAST).

Data analysis

Initial exploration of data was by summary statistics, tables and plots. Descriptive analysis was performed for each variable using statistical software R 3.0.2 (R development core team 2011, R foundation for statistical computing, Vienna, Austria). Categories were collapsed for analysis to avoid issues associated with data scarcity for the variables ethnicity, alcohol consumption, and number of sexual partners. Associations between categorical variables and the detection of HPV were explored using univariable logistic regression. Variables were allowed to enter a multivariable model if the Likelihood Ratio Test (LRT) was statistically significant at a p-value ≤0.20.

Results

A total of 234 participants were recruited as part of this study. Participants were from sexual health (n=55) and student health (n=179) centres. Each participant provided an oral brushing and at least partially filled in the questionnaire.

A summary of the results obtained at each stage of the testing process is shown in Figure 1. A total of 49 samples were considered suspect positives from the initial PGMY PCR. Of the 185 PGMY negative samples that were subjected to the betaglobing PCR, 18 samples were excluded due to a lack of amplifiable DNA. This resulted in 216 samples for inclusion in the analysis.

After all confirmatory testing was completed, seven of 216 samples were
considered positive for HPV. Thus, the prevalence of oral HPV infection among sampled women was 3.2% (95% CI: 1.6%–6.5%). An oncogenic HPV type was found in two samples (prevalence: 0.9%; 95% CI: 0.3%–3.3%), and HPV 13 was found in five samples (prevalence of 2.3%; 95% CI: 1.0%–5.3%).

A summary of questionnaire responses is shown in Table 1. Questions one to three were answered by all participants. Question four was only applicable to those answering yes for question three ($n=134$). This question had eight missing responses. Questions five to seven had 10, 9, and 11 missing values, respectively.

Of the 216 study participants, 196 (91%, 95% CI: 86%–94%) were eligible for the free Gardasil® immunisation based on their date of birth. Of those eligible, 68 (35%, 95% CI: 28%–42%) were not vaccinated. The majority ($n=122$) of the vaccinated women had completed the course of three injections, while 12 participants received one or two injections. Around two thirds ($n=82$) of the vaccinated women received the vaccine before becoming sexually active. The remaining third ($n=44$) were vaccinated after they had commenced sexual activity. No significant associations (at $p<0.2$) were found between putative risk factors (smoking, alcohol consumption, and the number of sexual partners) and the presence of oral HPV infection (including all types, an oncogenic type, or type 13) were found.

**Discussion**

The oral HPV prevalence obtained in this study, although comparable to results of other published studies, showed an unusual distribution of HPV types—namely the comparatively high prevalence of HPV 13 and the lack of any HPV 16 among HPV-positive samples. The latter has been reported as the most prevalent HPV type in a number of other oral HPV prevalence studies of healthy individuals. Our study found no associations between previously reported risk factors for oral HPV—namely smoking, alcohol consumption, and the number of sexual partners—and the detection of oral HPV. The lack of association may be due to the low oral HPV prevalence seen in this study.

HPV 13 is typically transmitted through oral contact, and the shared use of objects contaminated with saliva. HPV 13 is considered an non-oncogenic HPV type, as infection with this type is not associated with malignancy. However, detection of HPV types 13 and 32 in the oral cavity have been linked to development of focal

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**Figure 1:** Flow chart of testing methods and results obtained from each step.

1 High risk type from cobas® testing was a non-16/18 and could be any of the following high risk types; 31, 33, 35, 39, 45, 51, 52, 56, 58, 59, 66, or 68.
Table 1: Questionnaire responses from study participants.

<table>
<thead>
<tr>
<th>Question number</th>
<th>Variable</th>
<th>Level</th>
<th>Overall number (%)</th>
<th>HPV-positive number (%)</th>
<th>HPV negative number (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Age</td>
<td>Born before 1990</td>
<td>20 (9)</td>
<td>0</td>
<td>20 (100)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Born during / after 1990</td>
<td>196 (91)</td>
<td>7 (4)</td>
<td>189 (96)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Missing</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>2</td>
<td>Ethnicity</td>
<td>NZ European</td>
<td>153 (71)</td>
<td>4 (3)</td>
<td>149 (97)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Māori</td>
<td>38 (18)</td>
<td>1 (3)</td>
<td>37 (97)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Other</td>
<td>25 (11)</td>
<td>2 (8)</td>
<td>23 (92)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Missing</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>3</td>
<td>Vaccination status</td>
<td>Not vaccinated</td>
<td>82 (38)</td>
<td>3 (4)</td>
<td>79 (96)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Fully vaccinated</td>
<td>122 (56)</td>
<td>4 (3)</td>
<td>118 (97)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Partially vaccinated</td>
<td>12 (6)</td>
<td>0</td>
<td>12 (100)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Missing</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>4</td>
<td>Vaccine and sexual debut¹</td>
<td>Before sexually active</td>
<td>82 (61)</td>
<td>1 (1)</td>
<td>81 (99)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>After sexually active</td>
<td>44 (33)</td>
<td>3 (7)</td>
<td>41 (93)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Missing</td>
<td>8 (6)</td>
<td>0</td>
<td>8 (100)</td>
</tr>
<tr>
<td>5</td>
<td>Smoking</td>
<td>Never smoked</td>
<td>157 (73)</td>
<td>6 (4)</td>
<td>151 (96)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Current smoker</td>
<td>28 (13)</td>
<td>1 (4)</td>
<td>27 (96)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Previous smoker</td>
<td>21 (10)</td>
<td>0</td>
<td>21 (100)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Missing</td>
<td>10 (4)</td>
<td>0</td>
<td>10 (100)</td>
</tr>
<tr>
<td>6</td>
<td>Alcohol consumption</td>
<td>Doesn’t drink</td>
<td>47 (22)</td>
<td>2 (4)</td>
<td>45 (96)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>1-5 drinks per week</td>
<td>128 (59)</td>
<td>5 (4)</td>
<td>123 (96)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>&gt;6 drinks per week</td>
<td>32 (15)</td>
<td>0</td>
<td>32 (100)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Missing</td>
<td>9 (4)</td>
<td>0</td>
<td>9 (100)</td>
</tr>
<tr>
<td>7</td>
<td>Sexual partners</td>
<td>0-5 partners</td>
<td>135 (63)</td>
<td>3 (2)</td>
<td>132 (98)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>6-10 partners</td>
<td>34 (16)</td>
<td>2 (6)</td>
<td>32 (94)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>&gt;11 partners</td>
<td>36 (17)</td>
<td>2 (6)</td>
<td>34 (94)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Missing</td>
<td>11 (4)</td>
<td>0</td>
<td>11 (100)</td>
</tr>
</tbody>
</table>

¹Question only applicable to those answering yes for initial vaccination question (n=134)
epithelial hyperplasia (FEH) or Heck's disease.\textsuperscript{24} Although FEH lesions are benign, they can persist for many years leading to cosmetic problems, which to date have limited treatment options.\textsuperscript{24} FEH is characterised by numerous painless papules on the lips, tongue, and buccal mucosa.\textsuperscript{24} Heck's disease has been described predominantly in people of the Eskimo, American Indian, and Latin American ethnicity, and is strongly associated with poverty and poor living conditions.\textsuperscript{25} FEH and Heck's disease are usually seen in children or adolescents.\textsuperscript{25} It is unclear what proportion of oral HPV 13 infections progress to FEH or how prevalent HPV 13 is in healthy adults. We have identified five cases of HPV 13 infection among 216 healthy females. By comparison, the prevalence of oral HPV 13 infection among 689 Dutch men with high-risk sexual behaviours was 0.1 \% (95\% CI: 0\%–0.8\%).\textsuperscript{26} Thus, it seems that the prevalence of HPV 13 infection in our study (2.3\%) was comparatively high. There are several possible reasons for the differences between our data and the Dutch data, based largely on differences in the study populations. The majority of our study subjects were university students, who were therefore likely to be living in student flats or hostels, both of which could be considered inferior living situations. Although the living conditions for the Dutch participants were not specified, the comparatively high prevalence of HPV 13 among subjects of the current study may fit with the reported association between FEH and poor living conditions.\textsuperscript{25} Secondly, our sampling population consisted exclusively of females, in contrast to the Dutch study, where the population consisted exclusively of males. Although there are no data available for HPV 13 prevalence among woman from other countries, FEH was reported to be more common in females than in males.\textsuperscript{24} Lastly, our study population may have included females genetically predisposed to HPV 13 infection. A genetic predisposition among selected non-European populations for FEH has been described by others.\textsuperscript{24,25} Published data on FEH in Māori and Pacific people are limited to a case report of Heck's disease in a Polynesian child in 1966.\textsuperscript{27} In our study, three of the five HPV 13 cases were of non-European decent (one Guatemalan, one Pacific Islander and one New Zealand Māori), even though non-Europeans constituted only 29\% of the study participants. The two remaining HPV subtypes detected in the study were from New Zealand Europeans. However, given the low numbers of HPV 13 positive samples, the apparent predisposition to HPV 13 infection among non-Europeans should be interpreted with caution. In addition, as we did not perform an oral examination, it is unclear if any participant had visible oral lesions suggestive of FEH.

The detection of oral HPV in this study employed a multi test approach. Of the 49 suspect positives in the initial PGMY PCR, only five turned out to contain HPV sequences. This is likely a reflection of the degeneracy of HPV primers and low annealing temperature employed in the assay. While both are necessary for detection of multiple HPV types, they also facilitate non-specific amplification in samples negative for target HPV sequences. Our results underscore the importance of confirmatory testing when assessing PCR data, particularly if they have been generated using degenerate primers.

The prevalence of oral HPV is also of interest with regard to the prevention of HPV-positive HNSCC through vaccination.\textsuperscript{28,29} The quadrivalent cervical cancer vaccine (Gardasil\textsuperscript{®}) was introduced in New Zealand in 2008 and was initially offered free to any female born after 1990. The vaccine protects against HPV types 16, 18, 6 and 11\textsuperscript{28} and is now routinely offered to 12 year old girls as part of the national immunisation schedule. However, coverage rates are variable and the vaccine's introduction was controversial, largely due to the sexually transmitted nature of HPV.\textsuperscript{30} Results of a Costa Rica-based case control study showed that vaccination with Gardasil\textsuperscript{®} resulted in a 93\% (95\% CI: 63\%–100\%) reduction in oral HPV infection between the test and control groups.\textsuperscript{29} We were not able to assess the effect of the Gardasil\textsuperscript{®} vaccine on oral HPV infection among New Zealand woman due to the low prevalence of oral HPV infection with only one sample positive for HPV vaccine type (HPV 18) detected in the current study. The HPV 18 positive sample was obtained from a
woman who had received all three doses of the Gardasil® vaccine, but after the onset of sexual activity. Although this is only a single case, the finding supports the importance of vaccination prior to exposure to HPV.

The vaccine coverage in the current study population was 56% (95% CI: 50%–63%) which is consistent with between 48% and 52% coverage for the same age group reported nationally. Thus, one of the challenges for successful immunisation with Gardasil® may be achieving the desired coverage of at least 70% as used in models of vaccine effectiveness and cost efficiency. The results from this study have provided initial data on oral HPV infection among young women in New Zealand. The comparatively high detection rate of HPV 13 suggests that further work to determine the clinical implications of this infection is warranted, especially in the Māori and Pacific Islander groups who tend to be over represented with respect to poverty-associated diseases.

Competing interests: Nil
Acknowledgements: We wish to thank Massey Medical, UCOL Student Health, Radius Medical, and The Sexual Health Centre Palmerston North Hospital for their involvement in participant recruitment and sample collection. Thank you also to the study participants. We would also like to acknowledge LabPlus Auckland for the donation of the PGMY primers, MedLab Central for the donation of clinical samples, Gavin Thomas for performing the cobas® testing, and Roche Diagnostics for the discount on DNA extraction and cobas® testing kits.

Author information:
Rebecca Lucas-Roxburgh, PhD student, Institute of Veterinary, Animal and Biomedical Sciences, Massey University; Jackie Benschop, Senior Lecturer, Molecular Epidemiology and Public Health Laboratory, Institute of Veterinary, Animal and Biomedical Sciences, Massey University; Magdalena Dunowska, Senior Lecturer, Institute of Veterinary, Animal and Biomedical Sciences, Massey University; Matthew Robert Perrott, Senior Lecturer, Institute of Veterinary, Animal and Biomedical Sciences, Massey University.

Corresponding author:
Rebecca Lucas-Roxburgh, PhD student, Institute of Veterinary, Animal and Biomedical Sciences, Massey University, Palmerston North, New Zealand.
R.Lucas-Roxburgh@massey.ac.nz


REFERENCES:


Analysis of the Auckland 2014 measles outbreak indicates that adolescents and young adults could benefit from catch-up vaccination

Gary Reynolds, Cassandra Dias, Simon Thornley, Ronald King, Anne Morrison, Angela Matson, Richard Hoskins

ABSTRACT

AIM: To analyse the epidemiology, serology and vaccine effectiveness in a recent New Zealand measles outbreak that started in Auckland, from December, 2013 to June, 2014, to guide further preventive measures.

METHOD: Cases had a clinically compatible illness, which was either confirmed by PCR or serology, or were linked to a laboratory confirmed case.

RESULTS: A total of 113 cases with 3,113 contacts were traced and managed in the Auckland region. Thirteen overseas acquired cases, produced a total of 98 locally acquired secondary cases, (plus two cases with unknown travel history). The majority of cases occurred in adolescents and young adults; 68/113 cases (60.1%) were aged 10 to 19 years. Among cases, 38.9% (44/113) were unimmunised, and 31.8% (36/113) had unknown immunisation status. A further 15.0% (17/113) of cases had received one or two doses of measles, mumps, rubella (MMR) vaccine. Of the contacts who underwent serological testing for immunity (n=735), the lowest levels of serological immunity were observed in people aged 10 to 24 years. Vaccine effectiveness was calculated for the 15–24 year age cohort at 92% (95%CI; 82–97).

CONCLUSION: Results suggest that an adolescent catch-up immunisation programme would prevent further outbreaks of imported measles.

Measles is a highly contagious viral exanthem that historically—before the introduction of the vaccine in 1969—infected 95–98% of children by age 18 years. Despite 46 years of an effective vaccine, measles and its complications continue to cause global mortality and morbidity. The burden of disease is largely in developing countries, where measles is the most common vaccine-preventable cause of paediatric death. The incidence of disease in the western world has declined markedly in association with mass vaccination campaigns. Many countries have eliminated indigenous cases of measles using a two-dose measles-mumps-rubella (MMR) vaccine regime. While Australia was declared “measles free” by the World Health Organization (WHO) in March 2014, New Zealand has not yet attained this milestone. Measles became notifiable to public health authorities in New Zealand in 1996.

The MMR vaccine has high efficacy in clinical studies. Since a live vaccine requires no formal boost, the second dose is added to improve efficacy from 90 to 95%. Measles vaccine was introduced in 1969 to New Zealand, with the second dose added in 1992. Under the New Zealand national immunisation schedule, children receive MMR vaccine at 15 months and 4 years. The rationale for this timing is to minimise interference by circulating maternally-derived anti-
bodies in the infant, with published reports indicating that vaccine effectiveness increases steadily after 6 months, reaching its maximum of 95–98% at 15 months when the vaccine is given. High coverage levels are required for the prevention of outbreaks, with modelling studies showing a vaccine uptake of over 95% to eliminate the disease. Historically, the MMR vaccine has suffered from unjustified controversy about its safety (starting in 1998), so a large cohort of adolescents are likely to be partially or completely unimmunised.

Many measles outbreaks continue to occur in New Zealand and the western world, which are usually the result of imported disease. In New Zealand, 248 cases were notified in 2009 and 597 cases in 2011. The most recent New Zealand outbreak started in Auckland in December, 2013, then spread to the Waikato and ended June, 2014. This study analyses the epidemiology, immunology and vaccinology of this measles outbreak to identify factors that may help to restrain further outbreaks.

### Methods

**The setting:** Auckland city has a population of 1.4 million, with port and airport connections to the rest of the world. Previous analysis of the Auckland Regional Public Health Service (ARPHS) database (unpublished results) demonstrated an indigenous measles-free population, with most cases imported from Asia.

**The method:** All measles notifications to the ARPHS were processed direct from the laboratory or via telephone contact with hospitals, emergency departments (ED), and general practitioners (GP). Each notification was assigned to a public health nurse (PHN) for the collection of all clinical information (diagnosis and clinical course) and missing details (immunisation history and status). Each notification was assessed for case status, as “confirmed”, “probable” or “not a case”, using the criteria in Table 1. A confirmed case required either a clinically compatible illness with links to a confirmed case, or the isolation of measles virus from clinical specimen, such as nasopharyngeal or throat swab polymerase chain reaction (PCR), or serological presence of measles immunoglobulin M (IgM), or rise in measles immunoglobulin G (IgG) antibody titre between acute and convalescent sera. A “probable” case had clinically compatible illness with no laboratory testing. All notified suspect cases that did not fulfil these criteria were classified “not a case”.

The outbreak coordinator initiated case management, contact tracing and management for households, and identified high-risk contacts of cases. Contacts were identified from ED, and GP waiting rooms, institutions such as schools and sports clubs, air travel and other significant sources of exposure. Quarantine and self-isolation was recommended until serology or PCR results could be assessed and post exposure prophylaxis was given for high-risk household contacts where vaccine was contraindicated or pregnant contacts.

**Laboratory analysis:** Clinically compatible measles illness was confirmed by laboratory PCR testing if symptoms had arisen within the previous five days. Thereafter, anti-measles IgM and IgG serology were used to confirm measles illness (Table 2). Serology was also obtained for exposed contacts to

<table>
<thead>
<tr>
<th>Confirmed</th>
<th>Probable</th>
<th>Not a case</th>
</tr>
</thead>
<tbody>
<tr>
<td>Laboratory results consistent with measles</td>
<td>Fever ≥38°C and a generalised maculopapular rash and:</td>
<td>No clinically compatible illness or</td>
</tr>
<tr>
<td>or</td>
<td>and cough or</td>
<td>Laboratory results not consistent with measles infection or</td>
</tr>
<tr>
<td>Fever ≥38°C and a generalised maculopapular rash and:</td>
<td>cough or</td>
<td></td>
</tr>
<tr>
<td>• cough or</td>
<td>conjunctivitis or</td>
<td></td>
</tr>
<tr>
<td>• coryza or</td>
<td>Koplik’s spots</td>
<td></td>
</tr>
<tr>
<td>• conjunctivitis or</td>
<td>Note:</td>
<td></td>
</tr>
<tr>
<td>• Koplik’s spots</td>
<td>• No link to confirmed case</td>
<td></td>
</tr>
<tr>
<td>and link to confirmed case</td>
<td>• No relevant laboratory results</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Confirmed</th>
<th>Probable</th>
<th>Not a case</th>
</tr>
</thead>
<tbody>
<tr>
<td>Laboratory results consistent with measles</td>
<td>Fever ≥38°C and a generalised maculopapular rash and:</td>
<td>No clinically compatible illness or</td>
</tr>
<tr>
<td>or</td>
<td>and cough or</td>
<td>Laboratory results not consistent with measles infection or</td>
</tr>
<tr>
<td>Fever ≥38°C and a generalised maculopapular rash and:</td>
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<tr>
<td>• cough or</td>
<td>conjunctivitis or</td>
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</tr>
<tr>
<td>• coryza or</td>
<td>Koplik’s spots</td>
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</tr>
<tr>
<td>• conjunctivitis or</td>
<td>Note:</td>
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</tr>
<tr>
<td>• Koplik’s spots</td>
<td>• No link to confirmed case</td>
<td></td>
</tr>
<tr>
<td>and link to confirmed case</td>
<td>• No relevant laboratory results</td>
<td></td>
</tr>
</tbody>
</table>

Note:

• No link to confirmed case
• No relevant laboratory results

Table 1: The criteria for measles diagnosis for “confirmed” and “probable” cases. All others were deemed “not a case”.

establish their immune status. Serological analysis was qualitative, an optical density result below 0.9 was negative, between 0.9–1.09 equivocal and a result over 1.10 considered positive and "serologically immune". Where possible, at least one sample from each of the linked chains of transmission was genotyped at the National Measles Reference Laboratory to identify measles strains.

Statistical analysis: Exploratory data analysis was carried out in R (version 3.1.2). The ‘lattice’ and ‘ggplot2’ libraries were used to produce the plots. The ‘binom’ package exact method was used to calculate 95% confidence intervals. Age-specific incidence rates were calculated by ethnic group from the Statistics New Zealand 2013 estimated resident population, derived from census data. Vaccine effectiveness (VE) was calculated using the screening method, where the odds ratio is calculated to compare the proportion of cases that are vaccinated with the proportion in the general population (this approximates to the relative risk). The difference between 1 and the odds ratio is the vaccine effectiveness:

\[
VE = 1 - \frac{\text{P(vaccinated = YES| case = YES)}}{\text{P(vaccinated = YES| case = NO)}}
\]

Where:

\(P(\text{vaccinated = YES| case = YES})\) is the probability of being vaccinated against measles, among cases.

\(P(\text{vaccinated = YES| case = NO})\) is the probability of being vaccinated against measles, in the general population.

Results

The measles outbreaks started on 17 December, 2013, with the last case occurring on 2 June, 2014. The first reported case was an 18-year-old, who had recently visited Sydney, and the measles strain was later genotyped and linked to a fellow traveller at the same dance event from the Philippines. Soon after this, on 27 December, the next case became ill—a 12-year-old from the Philippines visiting an international camp. Overall, 113 cases were reported, 13 of which were imported from overseas and 9 were associated with travel to the Philippines. Of the 18 (16%) local cases that did not appear to be directly linked to imported cases, 16 (89%) were later linked to known imported cases by genotyping. Two cases were not linked by contact or genotyping to known cases, with one genotype unknown and one different genotype to any known imported case. While the remainder (n=82; 73%) were linked to imported cases, a total of 98 (88%) were locally acquired (Figure 1). The numbers of cases peaked in March, 2014, with a temporal association of local cases with cases acquired overseas.

The majority of cases occurred in adolescents and young adults, with 41/113 cases (36.3%) occurring in 15 to 19 year olds, and 27/113 (23.4%) cases among 10 to 14 year olds (Figure 2). The majority of the cases self-identified as New Zealand European (58/113; 51%), with Asian (19/113; 17%), Pacific (14/113; 12%) and Māori (13/113; 12%) also affected. Age- and ethnic-specific incidence rates (Figure 3) showed the highest population levels of illness in Europeans (or other ethnicity) aged 15 to 24 years (n=30), and Pacific children aged 0 to 4 years (n=7). In the Pacific children aged 0 to 4, 6 of 7 cases occurred in infants aged less than 1 year of age.

Among the cases, 44/113 (38.9%) occurred in the unimmunised, 36/113 (31.8%) had unknown immunisation status, 16/113 (14%) occurred in infants too young to receive the vaccine, and 17/113 (15%) had received one or two doses of the vaccine, yet still developed the disease (16/113 had both vaccine doses; 14%). Of note, Māori rates of disease were lower than European and other groups, except children aged under 4 years.

<table>
<thead>
<tr>
<th>Day</th>
<th>Symptoms</th>
<th>Investigation timing</th>
</tr>
</thead>
<tbody>
<tr>
<td>-5</td>
<td>Prodrome (5 days)</td>
<td>PCR or serology</td>
</tr>
<tr>
<td>-4</td>
<td>Prodrome (5 days)</td>
<td>PCR</td>
</tr>
<tr>
<td>-3</td>
<td>Prodrome (5 days)</td>
<td>PCR</td>
</tr>
<tr>
<td>-2</td>
<td>Prodrome (5 days)</td>
<td>PCR</td>
</tr>
<tr>
<td>-1</td>
<td>Prodrome (5 days)</td>
<td>PCR</td>
</tr>
<tr>
<td>0</td>
<td>Prodrome (5 days)</td>
<td>PCR</td>
</tr>
<tr>
<td>1</td>
<td>Rash onset</td>
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<td>2</td>
<td>Rash (5 days)</td>
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<td>3</td>
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<tr>
<td>4</td>
<td>Rash (5 days)</td>
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Table 2: Measles ten-day infectious periods and timing of investigations.
Figure 1: Histogram which illustrates the number of measles cases overseas and locally acquired, by date of notification. A local peak is highlighted in March, 2014. There is a temporal association of local cases from people travelling to New Zealand from overseas.

Figure 2: A histogram, illustrating the numbers of confirmed and probable measles cases overseas and locally acquired by age, showing peaks in the under 1 and adolescent age groups.
Of the total number of cases, almost a quarter of cases (23%; 26) required hospital treatment. The majority (about two-thirds; 63/113) of the cases occurred in the Waitemata District Health Board catchment (North and West Auckland), with one-fifth (21/113) occurring in Auckland District Health Board and one-quarter in Counties Manukau (29/113).

The secondary cases linked by contact arose primarily at one school (n=37), and from household (n=29), healthcare (n=8; 3 from primary care and 5 from hospital) and social contacts (n=8).

During the outbreak, 3,113 contacts of the 113 cases were traced by ARPHS and quarantined from school, work or large-scale social events. Of the contacts who had their immune status determined either by history of MMR vaccination or serology (n=2,594), non-immune status was highest in under 1 year olds (68/75; 90.7%) and the 20 to 29 year group (60/325; 18.5%). Adolescents aged 10 to 14 and 15 to 19 years also had high rates of non-immune status (22/149; 14.8% and 28/186 15.1%, respectively).

Of the contacts, who underwent serological testing for immunity (n=735), those who tested negative (median age: 28.8 years; n=81) or equivocal (median age: 26.6 years; n=57) were generally younger than those who tested positive (median age: 34.0 years; n=597). Lowest levels of serological immunity were observed in people aged 10 to 24 years (Figure 4).

VE was calculated from the following information: Of the total number of cases, 60/113 (53%) were unimmunised with 16 aged less than 15 months (too young to immunise) and 44 known not to be immunised, with 36 having an unknown vaccine status. If the unknowns are assumed vaccinated, the prevalence of vaccination among cases is estimated at 53/113 (47%). Statistics New Zealand estimates that current immunisation coverage levels are 92% at 2 years; however, in the sample of contacts available to ARPHS during this outbreak, in which serology was tested, 83/737 (11%) had negative serology, indicating no, or inadequate, vaccination. If the prevalence of vaccination is assumed to be 90%, then the VE is conservatively estimated at 89% (if the 36 with unknown vaccination status are assumed to be vaccinated). If the unknown vaccine status group are instead assumed to be non-vaccinated, then the VE calculates...
as 98%, making the true value likely to lie between 89 and 98%.

Since it is recommended that age-specific VE is calculated, the 15 to 24 year age group was selected for this analysis. This cohort accounts for the majority of cases and likely to have statistical power. Other age groups had small numbers of cases, with little precision to undertake this calculation. The VE for this age group was calculated, using the immune status of contacts as a proxy for population immune status. Among the 122 contacts who were serologically tested in this age group, 84% (106/122) were immune. Among cases of this age, immune status was known in 33/50 individuals. In this restricted group, 22/33 reported being unimmunised. Based on these counts, the VE for this age group was 92% (95% CI: 82–97%).

Discussion

These results confirm the highly contagious nature of measles in New Zealand, with the appearance of a series of small outbreaks contributing to the 2014 cases. While the index case contracted measles at an international dance event in Sydney, many cases in this series of outbreaks were associated with a single high school in Auckland’s North Shore, where the case had visited the Philippines and returned to school while contagious. Genotype data confirms the Auckland outbreaks to be the result of a series of suboutbreaks with 2 prevalent measles strains. Any connection with the recent prolonged Sydney outbreak was not confirmed, with different predominant genotypes (B3) in Auckland and (D8) in Sydney. While New Zealand has exported a relatively unimmunised adolescent cohort to Sydney, it has clearly not exported measles.

The vast majority of cases were unimmunised or had unknown immune status, although there was a 14% rate of measles in cases having two documented MMR vaccinations. While the apparent vaccine failure rate appears high, the VE calculation confirms a high overall level of vaccine effectiveness in the adolescent cohort (92%, CI: 82–97%). These results suggest the reason for rapid expansion of cases were the unimmunised, low adolescent immunity and the highly contagious nature of the disease. The majority of contacts of cases were exposed at school, at home or socially, with reassuringly few exposed in primary care, hospitals, the workplace, early childcare centres or while on flights.

The VE results should be treated with caution, as the method relies on a number of assumptions, such as a sufficiently large proportion of the population being unvaccinated for the disease to propagate, so that there is a lack of herd immunity effect.
The method also assumes that vaccine coverage is relatively stable, and is subject to information bias and confounding, as with all observational studies.

**Measles elimination in New Zealand**

Elimination of measles requires the maintenance of a very low reproduction number ($R_0$) at $<1$ rather than the typical measles $R_0$ of 12–18, as likely occurred in this outbreak—predominantly at the single high school. Maintaining a low average number of secondary infections produced by an infective person reduces rapid spread of measles. If $R_0$ is maintained below 1, the number of cases will decrease and all endemic chains of transmission will eventually succumb. To achieve this sustained measles elimination requires very high immunity levels. There are many examples of immunisation programmes that have controlled measles transmission to the point of elimination. Mathematical models showed herd immunity and eventual elimination of disease for industrialised countries requires between 91 to 94% vaccine coverage for adults and 95% for secondary school age cohort. Models of disease transmission for New Zealand suggest that coverage of greater than 90% for both MMR doses would eventually eliminate outbreaks. The coverage in New Zealand is currently 93% for the first dose of MMR, although historically it has been significantly lower. A national coverage survey in 1991 demonstrated that less than 60% of children were fully immunised by two years of age, including only 42% of Māori children and 45% of Pacific children. Gains, albeit slow, were made over the following years, so that by 2005, 77% of children were fully immunised by two years of age, including 69% of Māori and 85% of Pacific children. This has left a significant legacy cohort, in their current adolescent or young adult years, unprotected from measles.

**Adolescent immunity to measles**

As shown by previous studies, adolescent populations are most at risk of disease, with the highest burden in teenagers aged 10 to 19 years. The reasons for this are uncertain but might reflect:

1. Sustained historic low coverage due to the controversy about the MMR and its safety through the late 1990 and early 2000s.
2. Waning immunity has been previously reported. In a community with low incidence or in elimination stage of measles, vaccine-induced immunity decreased with time to below protective levels without natural boosting.
3. In New Zealand, systemic organisational issues of the previous vaccine schedule resulted in suboptimal coverage:
   - i) The shift of MMR2 from 11 years to 4 years of age in 2001, despite a school-based catch-up programme for 5–10 year old children.
   - ii) Compromised vaccine quality, as this cohort predated an effective cold chain in New Zealand established in 2004.

The elimination of measles is a priority and part of the New Zealand schedule strategy. This data lends weight to a catch-up programme to improve coverage in the adolescent and young adult cohort.

**Vaccine catch-up campaigns**

This study was consistent with other measles outbreaks around the world. An outbreak of measles occurred in East Sussex, UK, from December, 1992, to February, 1993, with 66/96 cases at the local school. The majority of cases occurred in the 11 to 17 year age group (78%) with 74% of the students attending the school fully immunised. VE was high and estimated at 92%. Low vaccine uptake and waning antibody levels in this age cohort contributed to the outbreak and reinforced the need for catch-up immunisations to reach this susceptible group of adolescents.

In April 2013, a large outbreak was reported from Wales with 693 cases in the Swansea area. The highest number of cases was noted in the 10 to 14 year old age group, and a MMR catch-up programme was implemented. Seroprevalence of immunity to measles infection increased by 5 to 10% after the adolescent
Vaccine failure

While natural infection confers life-long immunity, vaccination gives protection against measles transmission for a prolonged time. MMR has been demonstrated to be protective for over 20 years and thought to be lifelong. While antibody levels decline over time, secondary vaccine failure due to waning protection is relatively rare. A UK study showed 3% of children who received MMR vaccine between 12 and 18 months of age were seronegative after 4 years. In Canada, 3.6% and 12% of children, vaccinated by different vaccine strains between 12 and 15 months of age, were found to become seronegative after 5 to 6 years of follow-up. This outbreak showed a failure rate of 14% among cases with two documented MMR vaccinations, though it was not possible to determine if the failure was due to the vaccine (primary failure) or due to waning immunity (secondary failure).

In the spring of 1985, an outbreak of measles occurred among adolescents in Corpus Christi, Texas, even though vaccination requirements for the school attendance were strictly enforced. Only 4.1% of the students at this school (74/1806) lacked detectable antibody to measles and more than 99% had records of vaccination. Of the seronegative students, all of the 14/74 who contracted measles had been vaccinated. This demonstrates that outbreaks can occur in secondary schools even when more than 99% of students have been vaccinated and more than 95% were immune.

Conclusion

Careful analysis of the New Zealand outbreak suggests European adolescent and young adults, with a historically low immunisation coverage, are most at risk of measles. Along with prompt reporting of measles to initiate timely action and the quarantine of students without documented histories of immunisation during school outbreaks, the New Zealand population and elimination effort could benefit from a comprehensive catch-up programme in this age group.

Competing interests: Nil

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Author information:

Gary Reynolds, Auckland Regional Public Health Auckland District Health Board; Cassandra Dias, Auckland Regional Public Health Auckland District Health Board; Simon Thornley, Auckland Regional Public Health Auckland District Health Board; Ron King, Public Health Intelligence Team, Auckland Regional Public Health Service; Anne Morrison, Auckland Regional Public Health Auckland District Health Board; Angela Matson, Auckland Regional Public Health Auckland District Health Board; Richard Hoskins, Auckland Regional Public Health Auckland District Health Board.

Corresponding author:

Gary Reynolds, Auckland Regional Public Health, Auckland District Health Board
garyr@adhb.govt.nz

URL:

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Rethinking the conceptual toolkit of organ gifting
Rhonda M Shaw

ABSTRACT
Organ transplantation is often spoken of as a “gift of life”. However, the concept of the “gift of life” has been subject to scrutiny over the course of the last two decades within social sciences and bioethics for failing to reflect the complexities of tissue and organ exchange. I suggest a new ethical model of organ donation and transplantation is needed to capture the range of experiences in this domain. The proposed model is both analytical and empirically oriented and draws on research findings linking a series of qualitative sociological studies undertaken in New Zealand between 2007 and 2013. The studies were based on document analysis, field notes, and 127 semi-structured in-depth interviews with people from different cultural and constituent groups directly involved in organ donation and transplantation. The aim of this viewpoint article is to disseminate to a New Zealand audience of healthcare professionals published research promoting an expanded conceptual toolkit of organ donation. The toolkit, which includes the concepts of unconditional gift, gift relation, gift exchange, body project and body work, is designed to provide an explanatory framework for organ donors and transplant recipients and to assist the development of ethical guidelines and health policy discourse.

Organ transplantation is often spoken of as a “gift of life”, particularly where the sale of body tissue and organs is illegal. However, over the course of the last two decades, the concept of the “gift of life” has been subject to critique. In light of such criticism, I suggest that a new ethical model is needed to capture the multivalent phenomenon of organ gifting and to incorporate the range of experiences in this domain. The model I propose is based on an expanded toolkit of concepts that include unconditional gift, gift relation, gift exchange, body project, and body work. In short, these ways of framing organ donation and transplantation can be defined as follows: an unconditional gift refers to a one-way altruistic act; the gift relation refers to dyadic relationships between intimates or people who are familiar to one another; gift exchange is an anthropological concept that emphasises the social significance of giving, receiving, and reciprocating; body project is a term used by sociologists to refer to the use of one’s body as integral to the process of identity-construction; and body work, a corollary sociological concept, refers to physical and therapeutic work undertaken on one’s own body and the bodies of others. Aside from contributing to social science knowledge about organ donation, the aim of the toolkit is to help patients and families involved in organ transfer procedures make better sense of their experiences, to aid healthcare professionals when communicating information about organ donation and transplantation experiences to prospective donors, donor families, and recipients and recipient families, and to assist in the development of ethical guidelines and policy discourse.

The proposed model is both analytical and empirically oriented, and links a series of qualitative sociological studies, all of which received research ethics approval (VUW 2-2007-SACS; MEC/08/03/027; AUTEC 08/179; VUW 16628/4/06/09; MEC/11/EXP/089). These studies were informed by debates in sociology and anthropology about gift theory and phenomenological accounts of organ exchange. The objective of the studies was to examine how research participants make moral decisions about bodily exchanges, and to investigate the degree to which participant experience...
aligns with existing moral vocabulary to describe the meanings of organ donation and transplantation from a first-hand perspective. As such, study participants were invited to consider the salience of altruism and the metaphor of the gift as tools for making sense of their experiences. Where vocabulary was out-of-step with participants’ accounts, the aim was to rethink it.

The project

The studies were undertaken in New Zealand and are based on document analysis, field notes, and 127 semi-structured in-depth interviews of 1 to 2½ hours duration, conducted between 2007 and 2012. Three studies were undertaken by the author and examined the views of 19 living directed kidney donors, six living non-directed kidney donors, nine members of deceased donor families, and 27 transplant recipients of kidneys, lungs, and hearts. Fifty-one background interviews with expert academics, stakeholders and healthcare professionals (HCPs) support the project. These interviews include discussions with 15 intensivists and donor and recipient coordinators, and 11 transplantation specialists (nine surgeons and nephrologists and two nurses). Study participants primarily self-identified as New Zealand European or Pākehā and were interviewed by the author. Fifteen living organ donors, organ recipients and whānau, 12 of whom identified as Māori, were interviewed in a connected study by an associate investigator. This paper is an abridged version of a much longer article by the author.

7 The rationale for a summary version of the article is to promote readership among a New Zealand HCP audience. For an extended discussion of the research this paper draws on, and for details about study methods and supporting references see the publications listed below.1-7

Unconditional gift

In this description, organ donation is conceptualised as a gift, given freely and without remuneration or external reward. The gift is assumed to have a clear-cut meaning affixed to altruism, which is regarded as a disinterested one-way act. The donated organ is given unconditionally by the living organ donor or deceased donor family. Some proponents of this account maintain that there should be no relationship between the donor and recipient or their respective families. Various HCPs, including transplantation specialists and surgeons, support the view of organ donation as an unconditional gift. Some use the term gift to distinguish deceased and live donation from commercialisation. They contend that gift language transmits the positive message that donation is a noble and morally worthy...
The term gift is thus an important part of their linguistic toolkit. It is useful for educational and promotional purposes, it can be used (in the right circumstances) with deceased donor families to thank them for their donation, and in conversation with transplant recipients in the clinical context.

In addition, some HCPs maintain that highlighting the magnitude of the gift serves to encourage transplant recipients to value the donated organ, and to show gratitude to the donors by taking responsibility for looking after themselves post-transplant. Viewing the gift as a one-way altruistic act enables transplant recipients to accept the donated organ as their own, rather than thinking about the organ as an alien body part from a foreign body. Being able to integrate and accept the newly donated organ is beneficial for the post-operative emotional and psychic wellbeing of transplant recipients.

Gift relation

In this understanding, the gift relation involves face-to-face gift giving, often of an asymmetric nature, between people who have prior personal or intimate relationships with one another. In organ exchange the archetypal gift relation occurs between a parent and child, although it may extend to living organ donation by donors who are biologically or emotionally related to the recipient (sibling, spouse, or friend). This relation is unlike anonymous donation to a stranger, in that non-directed donation entails a cognitive recognition of the other and detached reflection on the other's suffering.

If organ donation occurs as part of a gift relation, the donated organ often goes unrecognised as a gift by the donor and recipient. In other words, the motivation that prompts organ donation within some family and kinship groups, and between close friends, is not articulated in the deliberate language of moral decision-making. This is because biologically and emotionally related donors often do not see their donation as a gift because they feel they get something back from donating an organ, such as alleviating the suffering or saving the life of a family member or loved one, or improving the recipients' health and thereby making life better for the whole family, themselves included.

Gift exchange

In jurisdictions where organ commerce is prohibited, lay accounts of organ donation and transplantation often come closest to a gift exchange model. In this understanding, for social and cultural reasons, people often feel morally obligated to reciprocate the gift of an organ in a meaningful way. A gift or gift exchange relationship is based on giving, receiving and reciprocating; it is not to be confused with pure altruism, which is a one-way transaction.

Persons who subscribe to a gift exchange model of social life may encounter difficulties in a closed donation system governed by a social-organisational imperative of confidentiality and anonymity. For some transplant recipients, the need to express gratitude to the donor, donor family, or to the health system is linked to strong affects. The desire for contact with the donor or donor family can range from curiosity, to desire for knowledge about the donor, a desire to meet the donor, or a desire to establish a relationship. For some transplant recipients, for whom integrating an organ from another person feels like incorporating a part of the donors’ genetic makeup and personhood, making connection with the donor or donor family is important.

Anxiety and ambivalence around donation and transplantation can be exacerbated when donation occurs across different kinds of body-subjects (eg, from male to female or young to old), or between persons who subscribe to different belief systems and worldviews. For some cultural groups, such as the indigenous peoples of Aotearoa New Zealand, Australia, and North America, connection may be especially important, as the sharing of biological matter such as body parts implicates entire kin networks, and has ramifications beyond its effect on individual donors and recipients. Organ donation and reception not
only creates intersubjective bonds between people, it entails ongoing responsibilities to those people and their families. To fail to make connection with a donor or their family, in the form of gratitude or some kind of reciprocity, would be considered disrespectful and socially unacceptable. A gift exchange framework may therefore be preferred by some donors and recipients, because it emphasises the interconnectedness between persons who give and receive body parts, and foregrounds the impact bodily exchanges can have for relational ontologies spanning beyond the interpersonal to the cosmological.

Body project

An alternative way of understanding living organ donation is to think about it as a body project. Classifying organ donation as a body project refers to the way people purposively use and transform their bodies in a variety of ways to communicate and express different ideas, values and beliefs. While living organ donors are not concerned to transform their bodies to enhance appearance and body image—as is the case with most late twentieth and twenty-first century projects that involve work on the body—they focus on what their body can do and how it can be used to facilitate wellbeing for other people. In donative body projects, the donor makes an individual decision to transform his or her body for the benefit of another person, with the help of biomedicine and technology.

This description is in keeping with the perspective that many living non-directed donors hold. While the desire to donate an organ is performative of the donors’ moral identity and sense of social responsibility, insofar as it is an action that is directed toward others, the donative decision may also be experienced by the living organ donor as self-defining. From the non-directed donors’ perspective, organ donation is an extreme example of civic-mindedness and is consistent with a donation mindset. Although improved self-esteem may be a consequence of donation, studies show that this is not a primary motivator. Living organ donors may give time, blood, money, and offer services to others, and often on a regular basis.

As with all projects, organ donation is something that the living donor plans. The intention to donate an organ, which may or may not be coherently expressed as part of an altruistic value system, is carefully deliberated; from the first inquiry about donation and the decision to donate, through to the medical tests donors are required to undergo and the eventual surgery. For non-directed donors who do not have an established relationship with their recipient, the donation event has a finite end. That is, despite their view that organ donation is a gesture of shared humanity, the matter of kinship and relatedness through the bio-medically engineered transfer of their kidney to the body of another person is not a key concern for them.

Body work

Body work refers to work undertaken on one’s own body and to work performed on the bodies of others. Organ donation is body work that is embedded in a network of caring relationships that involve HCPs, numerous stakeholders, donors, transplant recipients, families, and friends.

Organ donation requires the interventions of a hierarchy of HCPs, who work on the bodies of deceased donors, living organ donors, and transplant recipients. This work includes the activities of healthcare assistants who mediate between patients and nurses to provide a range of services in hospital, through to ICU physicians, specialists and transplantation surgeons, who literally engage with and operate on the physical bodies of patients in their care.

Body work involves work on the body-self by donors and recipients to prepare for and recover from organ transplantation. To donate and receive organs, donors and recipients have to be relatively fit and healthy, as well as being able to demonstrate to relevant HCPs the capacity to act autonomously. Complying with clinical and psycho-social assessment criteria takes effort. Living donors must learn the requisite communicative and moral repertoires to convey their donative conviction to HCPs. Being able to articulate altruistic intent, in terms of “gift of life” rhetoric, is part of that package. Likewise, transplant recipients must adhere to extensive self-
care routines by taking responsibility for their diet, medication, and lifestyle, as part of their new postoperative health regimen. Body work also involves the activities of non-remunerated caregivers: a network of invisible others made up of family members and friends, who help the living donor and transplant recipient recover and heal postoperatively. This work includes emotional, psychological and moral support, accompanying family members and friends to hospital visits, and providing care during convalescence (ie, housework, dependent care, and miscellaneous daily activities).

Body work is important to consider because it links all the participants involved in organ transplantation procedures. No matter which of the previous concepts donors, recipients, and HCPs prefer to use to conceptualise organ transfer procedures, there is no question that they will all be involved in body work of some kind or another. The danger of sentimentalising organ transplantation as altruistic is that it can conceal the mundane, physical and bodily aspects of this work and the value associated with it.

Body work not only focuses on HCPs' expertise, it acknowledges transplant recipients' activities of self-care, and the social care management and welfare of donors, those they care for, and those who care for them. It thus accounts for the complex relational and material aspects of organ donation and transplantation that involve labour on the body, without losing sight of its important metaphysical and value dimensions.

Furthermore, the concept of body work may permit consideration of some of the indirect costs associated with transplantation that are currently hidden because they involve nonpaid labour. This labour is increasingly outsourced to the home as a consequence of health philosophies and programmes supporting self-management and due to economic reforms in the formal health sector. The body work concept enables us to take into account the costs incurred by home productivity losses associated with organ donation and transplantation, which need to be considered when evaluating the economic effects of organ transfer for patients and those who care for them.

Body work thus goes beyond the gift-commodity binary to permit discussion around compensation for organ donors, recipients, and their respective families.

Conclusion

The expanded conceptual toolkit presented here sketches different conceptions of organ donation and transplantation, based on theoretical analysis and empirical data drawn from sociological research. The author's view is that gift terminology in the context of organ donation and transplantation is useful, but has limitations. Principally, it does not take socio-cultural and economic context into account, or different permutations of exchange relations between donors and recipients and their respective biographies. In contrast, the proposed toolkit incorporates some of the nuanced meanings that donors and recipients attribute to their decision-making and experiences, as well as including the perspectives of HCPs and analysts that may prove useful in the provision of pre- and postoperative care and informed consent procedures in both the clinical context and policy development.
COMPETING INTERESTS: Nil

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Author information:
Rhonda Shaw, Senior Lecturer, School of Social and Cultural Studies, Victoria University of Wellington, New Zealand.

Corresponding author:
Dr Rhonda Shaw, School of Social & Cultural Studies, Victoria University of Wellington, PO Box 600, Wellington 6140, New Zealand.
rhonda.shaw@vuw.ac.nz

URL:

REFERENCES:
CLINICAL CORRESPONDENCE

Conjunctival squamous cell carcinoma
Ali Mahdavi Fard, Leili Pourafkari, Nader D Nader

A 69-year-old farmer presented with a growing non-tender lesion in his right eye. He first noticed the lesion two years earlier, but hadn’t sought medical attention. He was previously a smoker, but his past medical history was otherwise unremarkable. His visual acuity was 6/12 on the right eye and 6/9 in the left. On examination, a raised fleshy, papillomatous elevated growth involving interpalpebral fissure and extending beyond the limbus to upper and lower parts of cornea was present (Figure 1). Conjunctival congestion was present and corkscrew-like vascular loops were evident (Figure 2). Cytopathological examination from incisional biopsy showed squamous cell carcinoma. Magnetic resonance imaging with intravenous contrast enhancement did not show gross orbital involvement. Surgical excision and topical mitomycin therapy was discussed with the patient, but he refused surgical treatment.

Figure 1: Slit-lamp examination of the right eye showing the large mass
Figure 2: Slit-lamp examination of the lesion, corkscrew-like vessels are present

Competing interests: Nil

Author information:
Ali Mahdavi Fard, Assistant Professor of Ophthalmology, Tabriz University of Medical Sciences, Tabriz, Iran; Leili Pourafkari, Assistant Professor of Cardiology, Cardiovascular Research Center, Tabriz University of Medical Sciences, Tabriz, Iran; Nader D Nader, Professor of Anesthesiology, University at Buffalo, Buffalo, NY

Corresponding author:
Nader D Nader MD, PHD, FACC, Professor of Anesthesiology, University at Buffalo, Buffalo, NY
nadernd@gmail.com

URL:
A case of perforated chronic idiopathic megacolon
Benjamin Cribb, Rukshan Ranjan, Nigel Henderson

A 61-year-old male, with long-standing abdominal distension, presented with generalised abdominal pain, shortness of breath, and marked abdominal distension. The patient reported increasing abdominal distension over a 6-week period with associated infrequent bowel motions. No other significant medical or surgical history of note.

X-ray and CT imaging showed extensive colonic distension and a large volume pneumoperitoneum (Figures 1 and 2). There was also marked elevation of the right hemidiaphragm with associated volume loss of the right lung.

He proceeded acutely to theatre. An attempt at pre-oxygenation prior to induction of anaesthesia resulted in respiratory distress with oxygen desaturation. Needle decompression of the abdomen was required to relieve the tense pneumoperitoneum. At laparotomy, the patient was found to have a massively distended colon (see Figure 3), and a large amount of free intra-peritoneal gas without gross faecal contamination. Colonic micro-perforation was suspected and subtotal colectomy with end ileostomy performed. Histopathological analysis showed stercoral ulceration in the descending colon (the presumed area of micro-perforation). There was no evidence of aganglionosis or other intrinsic neuromuscular abnormality.

The patient had a protracted post-operative course due to respiratory failure, which necessitated tracheostomy insertion and ventilatory assistance. This gradually improved and the patient made a full recovery.

The causes of chronic megacolon can be divided into congenital, acquired and idiopathic causes. In general, chronic megacolon develops from refractory constipation from any cause. Idiopathic megacolon is a rare and poorly understood condition. This condition has many similarities with other conditions associated with chronic megacolon, such as Hirschsprung’s disease, chronic idiopathic intestinal pseudo-obstruction and idiopathic megarectum. However, idiopathic megacolon is unique in that the onset of symptoms can occur in early or late childhood or in adult life. The aetiology of this condition may be different between those patients with an early onset of symptoms and those with a late onset. The symptoms of idiopathic megacolon also differ between these two groups. Patients with an adult onset do not always complain of constipation, though it is the most common symptom. Abdominal pain, abdominal distension, palpable abdominal mass, irregular bowel habit and sometimes overflow diarrhoea are the other most common symptoms in patients with an adult onset of idiopathic megacolon. Faecal impaction is uncommon. Colonic perforation is a rare complication in association with idiopathic megacolon. Only one other case could be identified from the literature. Pathological features of idiopathic megacolon are thickening of the enteric smooth muscle, but with an intact enteric nervous system.

Conservative management of patients with idiopathic megacolon is frequently ineffective. For the majority of patients with an onset of symptoms later in life, medical treatment is unsuccessful.
Surgery is reserved for those who fail conservative management or who develop a complication necessitating urgent surgical intervention, such as perforation or ischemia. The surgical options for idiopathic megacolon in the elective setting have previously been evaluated.\textsuperscript{3,6} Subtotal colectomy with ileorectal anastomosis appears to be the optimum procedure in patients with a non-dilated rectum.\textsuperscript{4,6} In patients with a dilated rectum, restorative proctocolectomy with ileal pouch reconstruction is recommended.\textsuperscript{3,6} However, in the acute setting of perforation there are few surgical options available, other than subtotal colectomy with end ileostomy formation, as performed in this case.

Although faecal impaction with stercolar perforation is not uncommon, this case report of perforated idiopathic megacolon is a rare complication of this interesting condition.

\textbf{Figure 1:} Axial computed tomography image of the abdomen demonstrating a massive pneumoperitoneum with the abdominal viscera pushed posteriorly. Note the marked wasting of the anterior abdominal wall.

\textbf{Figure 2:} Coronal computed tomography image demonstrating the marked colonic distension with associated elevation of the right hemidiaphragm and reduced right lung volume.

\textbf{Figure 3:} The resected specimen demonstrating the generalised distended colon.
CLINICAL CORRESPONDENCE

Competing interests: Nil

Author information:
Benjamin Cribb, Department of general surgery, Taranaki Base Hospital, New Plymouth, New Zealand; Rukshan Ranjan, Department of general surgery, Taranaki Base Hospital, New Plymouth, New Zealand; Nigel Henderson, Department of general surgery, Taranaki Base Hospital, New Plymouth, New Zealand.

Corresponding author:
Nigel Henderson, Department of general surgery, Taranaki Base Hospital, New Plymouth, 123 Vivian St, New Plymouth 4310, New Zealand.
Nigel.Henderson@tdhb.org.nz

URL:

REFERENCES:

Benjamin Riordan, Tamlin Conner, Jayde Flett, Damian Scarf

Andy Ellis’s kick found touch in the 80th minute to win the 2011 Rugby World Cup final. Four years on and rather than kicking alcohol into touch, our government continues to pass legislation that keeps it in the field of play. Case in point is the recent amendment made to the Sale and Supply of Alcohol Act (2012), that will allow licensed premises to open and sell alcohol during the Rugby World Cup 2015 matches. Far from sneaking through, and despite a large number of submissions from individuals in the health sector (eg, New Zealand Medical Association, Public Health Association of New Zealand, The National Public Health Alcohol Working Group), and various other groups (eg, Alcohol Action Tai Tokerau, National Community Action on Youth and Drugs, Waitakere Anti Violence Essential Services, Women’s Refuge), the bill passed with overwhelming support (99 For vs 21 Against). Specifically, the bill allows bars, pubs, and licensed clubs to open and sell alcohol an hour before the start of a match, during the match, and for half an hour after the match ends. On nights with multiple matches played in succession, licensed premises will be able to continue selling alcohol between matches, provided that the second match starts less than an hour after the first. This will allow licensed premises to open well outside of normal operating hours and may lead to an increase in both alcohol use and alcohol-related harm. The aim of the current piece is to lay out in clear detail how wrong-footed the government’s game plan really is.

In their submission, the New Zealand Medical Association made it clear that restricting trading hours is one of the few measures that reduces alcohol use and the harms associated with it. Indeed, in a review of the literature, Hahn, et al (2010), demonstrated that increasing trading times by just 2 hours led to a significant increase in alcohol-related harm. But, even small changes appear detrimental. For example, in central Amsterdam, extending trading hours from 4am to 5am led to a 34% increase in ambulance attendances for alcohol-related harm. A similar increase in Norway led to a 16% increase in violent crime. Conversely, and closer to home, reducing trading hours in parts of Australia led to a decrease in assaults. To add to the concern, and in contrast to the studies mentioned above, our government’s relaxed trading hours coincide with our country’s major sport event. While the government appears to think that this is the perfect time to relax trading hours, one could argue it is the perfect time to do the exact opposite. Unsurprisingly, events are associated with an increase in alcohol use and alcohol-related harm. Although we are unaware of any research focusing on the increase in New Zealander's drinking during the World Cup, there was a marked increase in alcohol-related emergency
department presentations during the 2011 World Cup. In other event-related contexts in New Zealand, we have found that individual's consume around 200% more alcohol during events relative to the amount they drink during a standard drinking session. To conclude, the government's previous inaction with regard to alcohol reform was concerning enough, the fact that their most recent action may increase alcohol use and alcohol related harm, is nothing short of alarming.

Competing interests: Nil
Author information:
Benjamin Riordan, Department of Psychology, University of Otago, Dunedin; Tamlin Conner, Department of Psychology, University of Otago, Dunedin; Jayde Flett, Department of Psychology, University of Otago, Dunedin; Damian Scarf, Department of Psychology, University of Otago, Dunedin.

Corresponding author:
Dr Damian Scarf, Department of Psychology, University of Otago, P.O. Box 56, Dunedin, 9054 damian@psy.otago.ac.nz

URL:

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Accident Compensation Corporation claim status and benefit type is associated with low back pain outcomes

Jon Cornwall, Achim Elfering, Rebecca J Crawford, Markus Melloh

Compensation schemes for injury and injury recovery are important, as there is an association between compensation-related factors and poorer health outcomes following injury.¹ There are few previous data investigating outcomes of low back pain sufferers in relation to the support received from the Accident Compensation Corporation (ACC), or social welfare system in New Zealand, and no studies specifically examine low back pain (LBP) outcomes by benefit type. Recent publications have shown that some injury or illness outcomes are worse where the ACC do not provide financial support,²,³,⁴ while another reports no difference in outcomes between ACC and non-ACC supported patients receiving lumbar spinal fusion surgery.⁵ For LBP treated non-surgically, our previous study reports a negative correlation between ACC claim status (accepted, or not) and benefit status (on a benefit, or not); poorer outcomes were shown for individuals receiving a benefit and without an accepted ACC claim.³ What was unclear is whether specific benefit type (sickness [SB], unemployment [UB], invalids [IB], domestic purposes [DPB]) is predictive of outcome in LBP patients without an accepted ACC claim; we therefore examined the relationship between benefit type and LBP outcomes for those without accepted ACC claims for LBP.

Details on our methodology have been published previously.⁶ In brief, a prospective cohort study of patients presenting with a new episode of LBP was undertaken. The study was approved by the Lower South Regional Ethics Committee (LRS/08/03/008). Patients attending primary care practitioners were recruited across New Zealand, and sent questionnaires at weeks zero, three, six and twelve, then six months. Questionnaires were based on the Multinational Musculoskeletal Inception Cohort Study statement addressing risk factors for the development of persistent LBP.

Variables of interest included function (Oswestry Disability Index), pain (visual analogue scale), physical and mental health (Physical and Mental Component Scale Short Form 12 Health Survey Questionnaire), fear-avoidance beliefs (Fear-Avoidance Beliefs Questionnaire), and helplessness (pain catastrophising scale). Patients were grouped into those having a LBP ACC claim accepted, and those that did not. In total, 124 ACC claim-accepted patients, and 188 ACC claim-not-accepted were included; 168 patients completed all surveys. ACC-claim-not-accepted patients were further grouped by benefit groups (on or not on benefit), including DPB (n=12), SB (n=11), UB (n=6), and IB (n=4). Mean time on benefits (baseline) was 423 in DPB, 203 days in SB, 216 days in UB, and 304 in IB. Numbers were not adequate to allow significance testing between groups; drop-out accounted for a reduction in benefit participants from 33 to 18 (55%) at three months, and to 13 over six months.
Despite the small group numbers, some trends in LBP outcomes were apparent across the different time frames for those in different benefit classes. Specifically, trends highlighted the performance of UB who were either worse or unchanged for all measures at six months, while every other group improved across most measures. UB were the only group to worsen over time for functional limitation, mental health, pain, and helplessness; at 6 months they were unchanged in fear avoidance beliefs about work and physical activity, and were worse for physical health (with SB). The best results over six months were observed for DPB (the only ones to improve in FABQ Physical Activity) while SB and IB improved in most assessed categories.

A possible explanation for UB poor performance compared to other benefit groups may include a lack of motivation for improvement; previous studies have indicated that work participation and resource provision have positive effects and are predictive of outcomes for LBP recovery, with musculoskeletal disorders being more difficult to cope with for those with fewer resources, like money or secure social frameworks. Without work as a stimulus, motivation may be low to actively engage in seeking and facilitating improvement. Further, there are many factors that influence recovery from LBP, including management of resources such as social support, employment, and treatment; lack of work prospects may also have contributed to UB patients poorer performance.

Even though study numbers were limited, the existence of trends between the different benefit groups points to a pressing need to examine LBP outcomes in non-ACC supported individuals to more closely determine modifiable risk factors for poor outcome in those individuals on benefits. In particular, the UB category, because of the trends observed suggesting their performance is worse than other benefit groups. Further data are required to support these preliminary findings, and to explore the relationship between LBP outcome and benefit type for those people with and without accepted ACC claims for their injury.

Competing interests: Nil

Author information:
Jon Cornwall, Senior Lecturer, Graduate School of Nursing, Midwifery and Health, Victoria University of Wellington; Achim Elfering, Professor, Department of Work and Organizational Psychology, Institute for Psychology, University of Bern, Switzerland; Rebecca J Crawford, Senior Research Fellow, Centre for Health Sciences, School of Health Professions, Zurich University of Applied Sciences, Switzerland; Markus Melloh, Professor, Centre for Health Sciences, School of Health Professions, Zurich University of Applied Sciences, Switzerland.

Corresponding author:
Jon Cornwall, Senior Lecturer, Graduate School of Nursing, Midwifery and Health, Victoria University of Wellington.
jon.cornwall@otago.ac.nz

URL:
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Fluoxetine-induced phenytoin toxicity: a clinical reminder about the perils of polypharmacy

Sean Lance, Ian Ternouth

Case report

JS is a 62-year-old patient who was admitted to a secondary care hospital from resthome care with progressive reduction in her Glasgow Coma Score (GCS). She had been commenced on fluoxetine 20mg OD (once daily) 11 days prior by the GP for low mood. Her other medical history includes difficult-to-control epilepsy, for which she takes phenytoin 300mg OD, clobazam 20mg BD (twice daily), and levetiracetam 1g BD. Including these, she was taking 19 different medications for a number of other medical problems.

Examination was consistent with phenytoin toxicity, with a markedly elevated plasma phenytoin level of 244 umol/L (reference range 40–80 umol/L). With no other reasons for a supratherapeutic level, it was concluded that the commencement of fluoxetine was the likely cause for the grossly elevated phenytoin level.

Fluoxetine and phenytoin were withheld, and she showed slow improvement in her neurological state over the following three weeks. This correlated with a gradual decline in her plasma phenytoin levels over this period. She was subsequently discharged at her baseline, with the plan to restart phenytoin alone, once the levels were back within the normal range.

We discuss the interaction between these two commonly prescribed medications, along with wider discussion regarding polypharmacy.

Discussion

Phenytoin’s unique pharmacokinetic profile leads to problems associated with dosing and drug interactions. Following non-linear kinetics, its half-life is widely variable, dependent on dose, absorption, saturation of metabolic pathways, and enzyme induction/inhibition. Metabolism is via the liver microsomal cytochrome P450 (CYP450) enzymes. Consequently, a number of drugs interactions exist. Along with this, phenytoin is a potent CYP450 inducer, specifically CYP3A4 and CYP2C19. It is predominantly protein-bound, so when saturated, small changes in doses produce large variations in levels of the free drug (contributing to toxicity).

Fluoxetine is similar, in that it is largely protein-bound (95%), and metabolised by CYP450 enzymes (predominantly CYP2C19 and CYP2D6). The active form (norfluoxetine) has a long half-life (approximately 9 days).

The first report of an interaction between phenytoin and fluoxetine was in 1992 by Jalil, who described two patients who developed phenytoin toxicity after having had fluoxetine added. In 1997, Schmider et al further detailed this with in vitro testing of liver tissue from six healthy volunteers. This revealed the interaction was via inhibition of CYP2C9-mediated metabolism of phenytoin.

Spina and Perucca outlined the clinically relevant pharmacokinetic interactions of SSRIs, citing the aforementioned research regarding the interaction between fluoxetine and phenytoin via inhibition of CYP2C9. They also noted that the clinical consequences are compounded by the long half-life of fluoxetine.

This case also highlights the dangers of polypharmacy—something that has been previously well demonstrated in elderly
and residential care patients, where polypharmacy results in higher numbers of adverse reactions and complications.\textsuperscript{6,7}

This case demonstrates the vast potential for drug interactions, and highlights the need for consideration of drug choice, along with drug monitoring when prescribing new medications. It also serves to highlight the caution needed when prescribing in patients already on multiple medications and should serve as a clinical reminder of such.

\textbf{Competing interests:} Nil

\textbf{Author information:}

Sean Lance, Medicine, Taranaki Base Hospital, New Plymouth; Ian Ternouth, Cardiology, Taranaki Base Hospital, New Plymouth

\textbf{Corresponding author:}

Sean Lance, Medicine, Taranaki Base Hospital, New Plymouth.

Sean.Lance@tdhb.org.nz

\textbf{URL:}


\textbf{REFERENCES:}


New Zealand’s growing thirst for a sugar-sweetened beverage tax

Gerhard Sundborn, Simon Thornley, Bodo Lang, Rob Beaglehole

Findings from two large-scale, nation-wide surveys indicate that the majority of New Zealanders are now supportive of a tax on sugar sweetened beverages.

A significant shift has occurred in New Zealanders’ appetite for a tax on sugar-sweetened beverages (SSBs), if the funds collected are to be used to prevent childhood obesity.

Two polls, 18 months apart, show a strong increase in support of a tax on sugary drinks. The first poll, from February, 2014, found that 44% of respondents supported a tax on sugary drinks. The second poll, carried out in June 2015 (funded by the National Heart Foundation and the Cancer Society of Auckland), showed that support had risen to 52%, provided funds be used to address childhood obesity—this represents an eighteen percent rise in favour of a tax.

Interestingly, there was an even stronger drop in those who opposed such a tax. Opposition to a SSB tax dropped by 35% from 49% in February 2014 to 32% in June 2015 (Table 1).

These findings indicate a significant shift in public attitude towards the taxation of SSBs, because a quarter of respondents have moved to a more supportive, or less opposed, stance about the introduction of an SSB tax.

The speed at which public opinion has shifted (in favour of a SSB tax) indicates that New Zealanders are increasingly aware of the harms SSBs pose to health, and that of children especially. Strong media attention around SSBs may have facilitated this change. Over the last two years, the harm that SSB intake poses to health, and the notion of a tax on SSBs, have been regularly profiled in mainstream media. The public support for an SSB tax is also echoed by public policy makers in recent research. A study conducted by Signal et al, interviewed key health policy and decisions makers, including politicians, bureaucrats, food industry and key stakeholders about the acceptability and feasibility of a number of fiscal policies aimed at improving nutrition. Out of six policy options (that included either a fat tax; salt tax; removal of GST from fruit and vegetables; a combined fat, salt, GST removal type policy; and an SSB tax), an SSB tax was most frequently selected by respondents as the most feasible and acceptable option.

There is also strong political support for the need to address SSBs by political parties outside of government. A policy brief, written by the New Zealand Beverage Guidance Panel titled Options to reduce sugar sweetened beverage consumption in New Zealand, outlined 20 initiatives relating to how SSB intake could be reduced, with a

Table 1: Horizon Research polls relating to public opinion for a sugar-sweetened beverage tax, comparing results obtained in 2014 and 2015.

<table>
<thead>
<tr>
<th></th>
<th>2014</th>
<th>2015</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Revenue use not mentioned</td>
<td>Revenue used for childhood obesity prevention</td>
</tr>
<tr>
<td>Support SSB tax</td>
<td>44%</td>
<td>48%</td>
</tr>
<tr>
<td>Oppose SSB tax</td>
<td>49%</td>
<td>35%</td>
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LETTER

20% excise tax included. This document was received on parliament grounds on 19 June, 2014, and formally endorsed by the Green, Labour, and Māori parties.9

A refreshing initiative that Minister Coleman recently introduced is the mandate that hospitals and district health boards (DHBs) lead public policy to restrict SSB intake. A blanket ban on sugary drinks in all hospitals and DHBs has recently been announced under the leadership of the Director-General of Health and Chief Executive, Chai Chuah. We congratulate Mr Chuah for this bold initiative and Minister Coleman for creating an environment in which such decisions can be made. The exclusion of sugary drinks from hospitals will be a positive legacy for these leaders.10

However, SSBs present a problem that requires a more urgent and larger-scale solution. New Zealand has the third highest rate of childhood obesity in the developed world, and a recent study has found that high sugary drink intake is conservatively attributed to 561 deaths in Australasia per year.11,12 Equivalent to 40% of the annual road toll. Thus, New Zealand urgently needs a policy that will address such health issues in a manner that benefits all New Zealanders, particularly those who are most vulnerable.

The increasing public dissatisfaction from greater awareness of the effect of SSBs on our children's health is shared by policy makers and several political parties. This makes the political acceptability of introducing an SSB tax a likely reality in the future.

The introduction of an SSB tax would be another positive step toward addressing childhood obesity, making a strong statement that New Zealanders, as a society, value child health over corporate profits. Whether the current Minister of Health will extend his legacy to include the introduction of a SSB tax, or not, remains to be seen. It seems inevitable, however, that an SSB tax will be a major part of reclaiming our children's health, considering the growing public support for its implementation. The only question that remains is when.

This paper has been prepared by FIZZ (Fighting Sugar in Soft-drinks) New Zealand; a public health advocacy group established by researchers to reduce the consumption of sugar sweetened beverages in New Zealand to zero by 2025.

Competing interests: Nil
Author information:
Gerhard Sundborn, Epidemiology and Biostatistics, University of Auckland; Simon James Thornley, Consulting Epidemiologist, Auckland; Bodo Lang, Department of Marketing, Business School, University of Auckland; Rob Beaglehole, Principal Dental Officer, Nelson Marlborough District Health Board.
Corresponding author:
Dr Gerhard Sundborn, Epidemiology and Biostatistics, University of Auckland, Auckland, New Zealand
g.sundborn@auckland.ac.nz
URL:

REFERENCES:
LETTER


Is our focus on pharmaceutical company influence too narrow?
Lance Gravatt

The 4 September issue of the Journal reports the findings of accuracy and bias in pharmaceutical industry advertising in New Zealand, and is accompanied by an editorial by Toop and Mangin.¹

We would like to see the suggested transparency of the commercial relationship by the medical profession and the pharmaceutical industry extended to include the medical-device industry. This does however beg the question is there any evidence to suggest that we should be concerned about any commercial relationship between the medical profession and medical-device companies.

In 2014, the US federal government reported that drug and medical-device makers gave nearly USD $6.5 billion to US doctors and teaching hospitals. What is not made clear is how much of this was paid by medical-device companies.²

In 2006, a renowned spinal surgeon appeared before the US Senate Committee seeking funds for research into a bone-graft device made by Medtronic, which was granted. What the surgeon did not disclose was that his trip to Washington was paid by Medtronic, and he had been on the Medtronic payroll for several years—to the tune of USD $1.14 million. Medtronic would directly benefit from the funding.³

In 2007, five medical-device companies (dePuy Orthopaedics, Zimmer, Biomet, Stryker and Smith & Nephew) entered into a USD $311 million settlement with the Department of Justice to settle allegations of violating the law prohibiting kick-backs and inducement agreements with orthopaedic surgeons.⁴

In 2015, NuVasive Inc settled a false claims case regarding certain spinal surgery devices with a USD $13.5 million federal payment.⁵

This type of direct financial benefit is relatively obvious. However, there is a less obvious, indirect benefit that may be just as influential on the medical profession. In the period 1990–1996, US physicians held 5,051 medical-device patents, which represented nearly 20% of all medical device patents granted during this period. More than 60% of the doctor-inventors were practicing healthcare practitioners.⁶ The authors of the research presented evidence that doctor-inventors demonstrated bias in their publications.

New Zealand doctors are encouraged to practice an arm’s length, transparent, relationship with the pharmaceutical industry, but should we be broadening our approach to include the medical-device industry too?

We do not have to look too far for reason to be potentially concerned. While transparent, it is surprising to see that the University of Auckland School of Medicine Foundation Trustees include the CEO for the Medical Technology Association of New Zealand, which is the peak industry body for the medical device companies in New Zealand. I ask myself how comfortable the medical profession would feel if the CEO for Medicines New Zealand was a member of the HRC?

New Zealand is one of the least corrupt countries in the world, and let’s work to keep it that way. Making one group the scapegoat for the ills of a profession is not constructive. The bullying and sexual harassment reported by our junior doctors is not industry-made and yet needs attention. Let us all expect integrity and transparency, not just from the pharmaceutical industry, which, as it happens, is a mere remnant in New Zealand.
LETTER

Competing interests: Nil

Author information:
Lance Gravatt, Chairman, Te Arai BioFarma Ltd

Corresponding author:
Lance Gravatt, Chairman, Te Arai BioFarma Ltd
gravatt@ihug.co.nz

URL:

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LETTER

Comment on: Getting serious about protecting New Zealand children against unhealthy food marketing

Katherine Rich

Dear Editor,

This Viewpoint suggests that an evaluation of the “degree of exposure of New Zealand children to unhealthy food marketing” is required. We welcome such an evaluation, but suggest the Viewpoint is seriously outdated. The current situation, which has been extant for five years and is set to continue into the future, is as follows.

Advertising in all media (print, radio, television, cinema, and websites) in New Zealand is subject to oversight by the Advertising Standards Authority (ASA). This is the agency that provides industry self-regulation of advertising for New Zealand. It is unique in world terms in that its membership comprehensively includes all major New Zealand advertising, media and broadcaster organisations. The ASA develops codes of practice and maintains compliance with the codes through voluntary commitments and a public complaints process.

In 2010, the ASA published the Children’s Code for Advertising Food 2010 as a companion to the Code for Advertising Food and the Code for Advertising to Children. There is an explicit recognition in the Children’s Code for Advertising Food of the need to protect children, of the need to support the food and nutrition policies of Government and the Ministry of Health Food and Nutrition Guidelines and the need to protect the health and wellbeing of children.

A selection of requirements in the codes reflects the measures applied: advertisements should not undermine the role of parents in educating children to have a balanced diet and be healthy individuals; advertisements for treat food, snacks or fast food should not encourage children to consume them in excess; the quantity of the food depicted in the advertisement should not exceed serving sizes that would be appropriate for consumption by a person or persons of the age depicted; benefits of foods for a nutritious diet should not be exaggerated and should not imply that a single food should replace a healthy diet, nor undermine the importance of consuming a variety of food; children should not be urged in advertisements to ask their parents, guardians or caregivers to buy particular products for them; and advertisements soliciting responses incurring a charge should state, “Children ask your parents first” or similar words.

In this context, all major publishers and broadcasters require advertisements to show evidence of assessment for compliance with the Codes and will publish only in line with the Codes.

In order to assess compliance, the ASA invites complaints from the public (consumers, competitors, representative organisations etc), assesses the complaints and publishes its determinations. ASA decisions are available in a searchable database on the ASA website. There have been 9 complaints about advertising food to children in the past 5 years, representing around 0.2% of complaints received over that period (there are around fifty complaints a year received by the ASA relating to food and beverages...
of around 700–800 complaints annually). The grounds for complaint about advertising food to children covered sexism (boys only), nutrition related, disturbing to children, timing of advertisement and trade name. None were upheld.

Television watching in New Zealand for children aged 5–14 years is decreasing, evidenced by reporting by the Ministry of Health. The Ministry reports that while nearly half of children aged 5–14 years (53 percent) usually watched two or more hours of television a day in 2011/12, this was down from 57 percent in 2006/07. The measures applied by Free-to-Air Television broadcasters’ in their policies and voluntary rules include no advertising in specific preschool television programming times and limited advertising in school-age children’s television programming times. The times variously cover 0600–0950 and 1400–1700. This, and several developments in the past two decades, render research such as by Wilson, 1999, as of historical interest only. Work by the same authors and others in 2014 show that 67% of selected packaged food manufacturers and soft drink manufacturers in New Zealand had a publicly available policy related to marketing to children on their company website.

It is of particular interest that the recently adopted Health Star Rating system (HSR), which has been developed and endorsed by joint Australian and New Zealand Governments, rates over 30 different breakfast cereals from Kellogg’s, Sanitarium and Hubbard’s with 4.5 stars (out of 5 stars), a number that increases to 70 different cereals rating 4 stars or more. As well, a number of products from a range of fast food outlets rank with 4 or more stars.

What is disappointing is that voluntary agreements, such as those signed by major soft drinks companies not to sell into schools, are being circumvented by ‘third parties’ and the schools themselves for continuing to accept soft drinks for sale. Support from Government for healthy eating programmes in schools, and greater promotion of the Heart Foundation’s Fuelled4Life programme, would be welcomed by industry.

Overall, this Viewpoint creates the false impression that self-regulation has failed. In our view, self-regulation is very effective and increasingly so in terms of driving measures, such as limited food advertising to children, reformulating foods and conveying the healthfulness of foods to consumers.

Yours sincerely,
Katherine Rich

Competing interests: Nil
Author information:
Katherine Rich, Executive, New Zealand Food & Grocery Council
Corresponding author:
Katherine Rich, Executive, New Zealand Food & Grocery Council
katherine.rich@fgc.org.nz

URL:
LETTER

REFERENCES:


OBITUARY

Sir Patrick William Eisdell Moore
(17 March 1918—18 June 2015)
Otolaryngologist, Head and Neck Surgeon, Kt., OBE, MB. ChB, DLO (Eng), FRCS, FRACS

Patrick Moore was born in Bristol on 17 March 1918. His father, Arthur Eisdell Moore (“Eisdell”), was in England on a post-War surgical appointment. Eisdell had met Pat's mother, Alice, a nurse from Yorkshire, in 1915 when Eisdell was serving as a field surgeon with the RAMC on the Western Front. Patrick was the first child of three—two sons and a daughter—and although christened William Ernest Moore, the infant had been nicknamed “Pat” while still in utero in anticipation he (or she) would be born on St Patrick’s Day. The name stuck when that prediction proved correct. It was not until he reached the age of 21 that he formalised his adopted name by deed poll, and also changed Ernest to Eisdell.

After the war, Eisdell returned to New Zealand with his new family and set up consulting rooms as a general surgeon in Symonds Street, Auckland. This was where Pat’s lifelong interest in, and love for, horses was first kindled. He was fascinated by the variety of draught horses operated by the local merchants who lived in the neighbourhood. It was also a time when the first stirrings of artistic talent took form, as he drew and sketched on any blank or receptive surface—often to the chagrin of his parents.

Pat commenced his secondary education at Auckland Grammar as an 11-year-old. While his love of literature and the classics led him to top the country in English in his matriculation year, he struggled with mathematics. After a year at Auckland University College, Pat continued his studies at Otago University. For his first
four years in Dunedin, Pat was a resident at Selwyn College, and was elected the house presidency for the last of these years. As a medical student, he played on the wing of the university senior rugby team. He supplemented his meagre student allowance by selling his sketches, cartoons, caricatures, short stories and poems to various publications, including Punch. At student parties, his musical talents as a pianist were in great demand, although he did occasionally lament his popularity on the keys by reason of the restrictions it necessarily imposed on his ability to socialise more widely.

After leaving Selwyn College, Pat moved to a boarding house in Cargill Street, where he met fellow resident Beth Beedie—a final year physiotherapy student from a medical family in Dannevirke. After qualifying, she was posted to Hawke’s Bay and Pat moved to Auckland for his final year of medical studies. Their courtship flourished, albeit remotely. Pat graduated in 1943, and he and Beth married, commencing life together in a small flat near Auckland Hospital. Pat worked as a house surgeon to obtain full registration and eligibility to re-enlist in the army. As a medical student, he had been commissioned in the Otago University Medical Corps, and in his final year worked as a resident army medical officer in the Auckland region. After obtaining full registration, he wasted no time in enlisting with the 2nd NZEF and was posted overseas, leaving Beth and their infant son, Anthony.

Once overseas, he single-mindedly set about joining the 28th (Māori) Battalion, with whom he served throughout the Italian campaign, rising to the rank of Captain. Tall, freckled and red-haired, he was the only Pākehā in the Battalion. Culturally immersed, he became fluent in Te Reo and Tikanga Māori, making lifelong friendships with his comrades and developing a sophisticated understanding, even at that early time, of how a bicultural New Zealand should look. He actively applied those principles of biculturalism throughout the rest of his life.

During the Battle of Faenza he was badly wounded. His right arm was saved from amputation at considerable risk to his life, only because the surgeon was aware of Pat’s surgical ambitions. On leaving the Battalion at the cessation of hostilities, he was farewelled by the Commanding Officer with the words: “You were not the most academic takutia (doctor) we had. You may not necessarily have been the most brave, but you were, definitely, the most Māori.” He was subsequently made Patron, and a life member of the 28th Battalion, a recognition which meant the world to him.

In 1946, he returned to Auckland Hospital. A 3-month rotation in eye and ENT surgery kindled an interest which, in 1947, led him to become an eye and ENT registrar. During this year, he was greatly influenced by the country’s foremost ENT consultant, James Hardie Neil, and Pat decided on a career in ENT.

In 1948, after a year working as an anatomy demonstrator in Dunedin, Pat, Beth, and their two sons, sailed to London, where he spent two years working and demonstrating at the Middlesex, training at the Royal National Throat, Nose and Ear Hospital in Grey’s Inn and studying at the College of Surgeons. He passed his primary and, at his first attempt, his English fellowship examination and subsequently the DLO. He then obtained a very busy ENT registrar post in Northampton for two years, under ex-patriot Australian, Charles Gledhill.

In 1952, Pat and the family returned to Auckland where he set up rooms as an ENT consultant in Symonds Street, and the family was expanded by the addition of two more sons. Pat was appointed junior ENT surgeon at the recently opened department at Greenlane Hospital. He rapidly rose to head of department. Under his leadership and innovation, the department grew quickly. Facilities expanded as did the number of staff, to include a team of GPs and specialists in related disciplines, including allergy, oral surgery and voice therapy. He pioneered the use of microsurgery in New Zealand, encouraged the innovative use of homo-grafts and was the first in the world to transplant appropriately prepared and sterilised tympanic membranes, initially in animals and later in human beings. Building on this research, he established the Deafness Research Foundation in 1962, an organisation specifically created to assist clinicians undertaking research into hearing and deafness-related problems.
Between 1965 and 1977, his continuing engagement with Māori led him to make regular voluntary visits to the East Coast of the North Island, where ear disease and resulting hearing loss was endemic, particularly amongst children. Through his energies, he sourced sophisticated surgical equipment and instructed local doctors and nurses in its use. These efforts were rewarded by a remarkable reduction in the incidence of ear disease on the East Coast. Encouraged by these results and conscious of the common and understandable reluctance on the part of many parents to take their children to hospital, Pat's natural flair for innovation led him to raise funds for the development of mobile ear clinics, which took clinical services into the community under the banner of the Deafness Research Foundation. Following success from this initiative in Northland, it was adopted in Auckland and then, through the generosity of the Variety Club, a fleet of mobile ear clinics allowed similar services to be extended across many other regions.

Pat also encouraged research into the pharmacological treatment of tinnitus, the inclusion of ear and hearing problems in the Dunedin multi-disciplinary study, and he investigated the effects of hearing loss on prison inmates. He led the first ENT teaching programme in the Auckland Medical School and supported the establishment of a dedicated tertiary degree course for the training of audiologists.

As President of the then Otolaryngological Society of New Zealand, Pat organised the first joint conference with the Australian society, with in excess of 100 attendees from either side of the Tasman. This inaugural meeting was New Zealand's first ENT international conference.

By the mid-1970s, Pat appreciated that hearing research was moving its focus from the external and middle ear to the inner ear. At the same time he realised the activities of the Deafness Research Foundation required a higher and more sustained level of scientific input and engaged a postgraduate scientist, Peter Thorne, to build a research team. Pat also monitored the evolution of cochlear implants and, once a multi-channel device had been perfected, persuaded benefactors to support the introduction of a cochlear implant programme in New Zealand: initially for adults and later for children. He was quick to acknowledge the need for specialist auditory verbal training for implanted children and persuaded philanthropists and friends to support the establishment of the now highly successful Hearing House.

Pat's interests were not simply limited to deafness and hearing. He served on the Council of Auckland University, helped establish Riding for the Disabled and the Coeliac Society. He was Master of the Pakuranga Hunt for nine years and President and Emeritus Member of the New Zealand Hunts Association.

His mastery of prose, verse and sketching has left an enduring literal and pictorial record in the annals of the many institutions with which he has been involved. Perhaps the best known is his brilliant water colour caricature; a montage of the 1940 professors of the Otago Medical School. This remarkable drawing, which has been reproduced in numerous publications, now hangs outside the Dean's office. In 2004, his autobiography was published. The title, So Old, So Quick, was coined from a quote by Ogden Nash and the book's flowing literacy style, humour and self-deprecation earned it universally positive reviews.

Pat's vision, enthusiasm and selfless contribution to medicine and the wider community was recognised by the Queen in the 1982 Royal Honours, with the award of an OBE, and in 1992 he was knighted for his services to medicine and the community. Auckland Grammar honoured him in 2005, with an Augusta Fellowship as a distinguished old boy. In 2007, Selwyn College elected him an Honorary Fellow.

Pat's funeral, in a packed St Mary's-in-Trinity, was a moving and evocative tribute to an extraordinary New Zealander. His plain coffin, draped in a New Zealand flag, was adorned by a magnificent korowai (feathered clock) woven by the widows of the Battalion, in its colours of red, black and white. To the haunting strains of a karanga (call of welcome) he was carried in by representatives of the Battalion, various iwi and representatives of longstanding friends. At the end of the service, a rousing haka—performed by the Auckland Grammar kapa haka group—paid a final farewell.
Sir Patrick is survived by his beloved wife Beth, their four sons, Anthony (a pathologist practising in Australia), Tim (a radiologist practising in North America), Simon (a High Court Judge), Chris (a leading commercial property lawyer), 12 grandchildren and eight great-grandchildren.

Author information:
Ron Goodey FRACS, Simon Moore, Chris Moore

URL:
Magnetic resonance and the prediction of dementia

Dementia risk prediction has conventionally been based on sociodemographic, neuropsychological, health, lifestyle, physical function, and genetic variables. This report concerns a population-based cohort study which considers whether magnetic resonance imaging (MRI) would improve prediction of dementia.

The study involved 1,721 men and women without dementia who underwent MRI at baseline and had known dementia status over 10 years of follow-up. During follow-up, 119 (6.9%) of the participants progressed to dementia. The researcher’s conclusion was that MRI did not improve the prediction of dementia.

In an editorial on the topic, it is noted that as dementia cannot be reversed, stopped or slowed down, its early diagnosis may not be helpful.


Ezetimibe added to statin therapy after acute coronary syndromes

Statin therapy reduces low-density lipoprotein (LDL) cholesterol levels and the risk of cardiovascular events, but whether the addition of ezetimibe, a nonstatin drug that reduces intestinal cholesterol absorption, can reduce the rate of cardiovascular events further is not known.

This randomised trial was designed to elucidate the issue. Over 18,000 patients who had been hospitalised with an acute coronary syndrome within the last 10 days were involved. They were randomised to receive simvastatin 40mg and ezetimibe 10mg or simvastatin alone. The primary end point was a composite of several unfavourable cardiovascular events or non-fatal stroke.

At a median follow-up of 6 years, the LDL cholesterol levels were significantly lower in the combination group. There was also a significant lowering of cardiovascular events in the combination group, although it was modest with an absolute risk difference of 2%. Adverse events causing discontinuation of treatment occurred in approximately 10% in each group.


Risk of serious infection in biological treatment of patients with rheumatoid arthritis

Biological drugs are a new class of disease-modifying treatment options for rheumatoid arthritis that have been reported to show large clinical and radiographic improvements compared with traditional disease-modifying antirheumatic drugs (DMARDs), such as methotrexate.

Such drugs include the Tumour Necrosis Factor Inhibitors etanercept, infliximab and adalimumab. Although they may be useful in the management of rheumatoid arthritis, there is concern that they may be associated with an increased risk of serious infection compared with DMARDs.

This review of the topic includes data from 106 trials which involved the use of the biological treatments and compared the rates of serious infections between their use and the use of traditional DMARDs. The conclusions were that standard-dose and high-dose biological drugs (with or without traditional DMARDs) are associated with an increase in serious infection in rheumatoid arthritis compared with traditional DMARDs, although low-dose biological drugs are not. Clinicians should discuss the balance between benefit and harm with the individual patient before starting biological treatment for rheumatoid arthritis.

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Measles in adults
Farquhar Matheson, M.R, Glasgow, House Surgeon, Wellington Hospital

Measles is so frequently a disease of childhood that it is not often one sees many cases in adults. Since the commencement of the war, a number of adult cases have been admitted to Wellington Hospital, most of them being members of the Expeditionary Forces. An examination of these cases shows that the course of the disease is essentially the same in adults as in children. The rash stage was usually attended with a high temperature, readings of 104 to 105 degrees F. being common. This often terminated by crisis, the pulse rate, too, showing a remarkable fall. During the febrile stage epistaxis was a very common symptom, fairly persistent in some cases, but never alarming, and usually terminating without treatment. There was one case with gastro-intestinal symptoms lasting for 24 hours.

As one would expect, complications affecting the respiratory tract were most frequently met with. Practically every case had bronchitis and laryngitis to a varying degree. There was one death from pneumonia. In this case, we had not merely the ordinary lobar type due to the pneumococcus; but there was a secondary infection, probably streptococcal, which made the case hopeless from the beginning. Another case developed pneumonia during convalescence, but he ran a normal course with a crisis on the eighth day. Apart from these, there were no cases which caused one any anxiety.

With regard to the laryngitis and bronchitis, in many cases these were very distressing: coughing being incessant. We depended on the hospital linctus, containing tr. camp. co.,
squirils and tolu, and on glyco heroin to control the coughing, but the results were not as satisfactory as one could wish. An experiment was made with guiacol carbonate gr. v. doses t.d.s., six patients being put on this treatment when admitted. The results were most gratifying; cough and laryngitis were markedly less in these cases. One hesitates to draw conclusions from such a small number of cases, but taking everything into consideration, guiacol seems to have been of real benefit in those cases in which it was tried. Further experience with this only seems to bear out its value in such cases.

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In an earlier version of the paper, 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? by Alison Ma and Lianne Parkin (NZ Med J 128:1421; 22-29), a publication error occurred in the competing interests section, which read: “Richard Milne reports personal fees from Fisher Paykel Healthcare during the conduct of the study and personal fees from Fisher Paykel Healthcare outside the submitted work.” Richard Milne was not involved in the production of that paper, and an editorial oversight occurred. This has been remedied.