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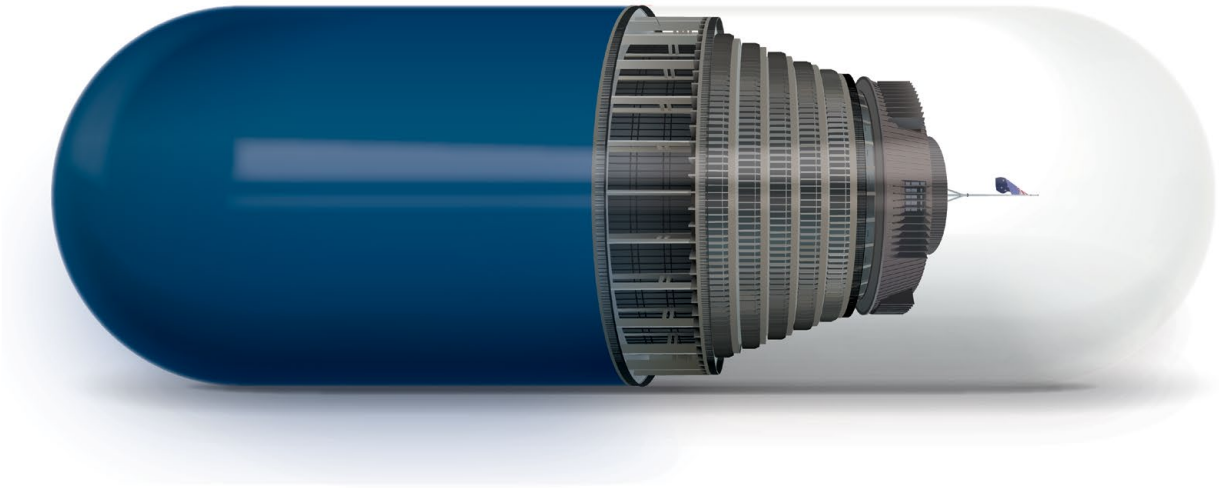

Politics and Medicine in Aotearoa

- Exploring the medical professional's role and responsibility in political issues related to health
- Narrative reviews exploring determinants of health in the Pacific Islands
- *New academic series:* Clinical Pearls
- Original research exploring predictors of response to immune checkpoint inhibitors
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EDITORIAL

Editors' welcome

Nicky Dunn, Sameer Bhat

Kia ora koutou katoa and welcome to Issue 32 of Te Hautaka o Ngā Akongā Rongoā, the New Zealand Medical Student Journal (NZMSJ). The theme of this issue is "Politics and Medicine in Aotearoa", an important topic for medical students and health professionals. We are proud to share a range of thought-provoking and high-quality articles by medical students, clinicians, and academics from Aotearoa and abroad.

The unprecedented events of the coronavirus disease 2019 (COVID-19) pandemic have brought the tightly intertwined relationship between politics and medicine to the forefront of society's attention. From public health and social measures to reduce the spread of the disease, to the vaccine rollout, the Government's pandemic response has been guided by the latest scientific research and the voices of expert health professionals and scientists. This interface was also highlighted by the public debates on cannabis and euthanasia laws and subsequent referenda held alongside the 2020 General Election. Many doctors, both locally and internationally, have been the impetus for political change on a range of health-related issues. This role of doctors is encouraged by national and international medical organisations, including the New Zealand Medical Association (NZMA), who outline in their Code of Ethics: "*Doctors should accept a share of the profession's responsibility toward society in matters relating to the health and safety of the public, health promotion and education, environmental issues that have a bearing on the health of individuals and populations, and legislation affecting the health or well-being of the community.*"[1]

As a result, we believe medical students and doctors are essential voices at the table of political discussions, and this has therefore motivated the theme of NZMSJ Issue 32.

An overview of this issue's articles

We are proud to have outstanding editorials from three experts who explore different aspects of politics and medicine in Aotearoa. Dr Ashley Bloomfield discusses the interface between medicine and politics with examples of the challenges and successes he has experienced whilst navigating this political landscape. Dr Bloomfield outlines how this interface is an imperative, and an opportunity which should be used responsibly. Dr Jonathan Coleman explores the roles and responsibilities that medical professionals have in relation to political issues. Dr Coleman provides interesting examples and insights into politics, including some of the challenges and caveats which may be encountered. Professor Boyd Swinburn discusses the causes of policy inertia and the implications of these on disease prevention in Aotearoa. Professor Swinburn also outlines the role of civil society organisations, such as non-governmental organisations, in driving change in our disease prevention policies. He suggests the need to take a "COVID-19 approach" to addressing the social inequities which are driving poor health outcomes in some of our communities. These editorials each provide important messages for medical students and doctors alike. We are very grateful to Dr Bloomfield, Dr Coleman, and Professor Swinburn for their valuable contributions to NZMSJ Issue 32.

In this issue, we have two articles related to the COVID-19 pandemic. Firstly, in a letter to the editor, Leah Sarah Peer describes how virtual volunteerism has been a silver lining of the COVID-19 pandemic and an accomplishment for medical students around the globe. Secondly, in a feature article, Dr Shibu Sasidharan explores the associated challenges with undergraduate medical education and lessons gained from the COVID-19 pandemic, with examples from the Democratic Republic of Congo.

We are fortunate to also include our two regular feature series. In this issue's Māori Health Review, Nadine Houia-Ashwell explores how the pandemic challenged Māori assertion of *Tino Rangatiratanga* (self-determination) within the tertiary education sector and by *iwi*. We are also grateful to include our regular statistics primer, written by Dr Ari Samaranayaka et al., from the University of Otago Biostatistics Unit. Issue 32's primer focuses on sample size consideration at the time of conceiving and designing a study, and the importance of sample sizes in health research and the overall research process.

This issue includes an impressive selection of academic articles from medical students and clinicians. We are proud to share the first of the NZMSJ's new academic series, "Clinical Pearls." This issue's clinical pearl, by Dr Kaveshan Naidoo and Dr Subaschandra Shetty, explores Eagle's Syndrome as a differential diagnosis in patients with odynophagia. Muhammad Luthfi Adnan explores the potential antihypertensive activity of probiotic bacteria *Lactobacillus casei* through gut microbiota modulation, through a narrative literature review. Tim Bridgman carried out a study examining potential predictors of response to immune checkpoint inhibition in patients with metastatic melanoma treated at Christchurch Hospital. We also have two interesting narrative reviews investigating broader determinants of health in the region of the Pacific Islands. The first, by Thomas Swinburn et al., reviews the impact of climate change and food security on health outcomes in Pacific Island countries and territories. The second, by Tahirah Moton et al., explores factors driving noncommunicable diseases in the Pacific region, with a focus on the island of Niue. Dr Oliver Lyons describes a case report of a patient who was managed with an antibiotic desensitisation procedure in order to treat a *Streptococcus gallolyticus* bacteraemia in the context of a penicillin allergy. We are proud to publish two dermatology essays, by Jamin Kim and Christopher Mayo, who each explore the disability burden of skin diseases. These essays were both awarded the 2020 Wilson-Allison Memorial Prize in Dermatology, sponsored by the New Zealand Dermatological Society Incorporated (NZDSI). This issue also includes the 2020 Bachelor of Medical Sciences with Honours (BMedSc(Hons)) abstracts from University of Auckland students who have undertaken the intercalated BMedSc(Hons) research year.

Finally, we would like to congratulate the winners of our Issue 32 Creative Arts Competition: Emi Frost, Ria George, and Hannah S.Y. Kim.

This competition is an ongoing collaboration with the New Zealand Medical Students' Association (NZMSA) to showcase our fellow medical students' creative and artistic talents. This year's three winning pieces are strongly connected with the theme of mental health and wellbeing. Emi and Ria both submitted powerful poems related to grief and post-partum depression, respectively, whilst Hannah painted a special moment between two children, symbolising our need for maintaining social connection in times of physical distancing.

Acknowledgements and conclusions

The NZMSJ Editorial Board would like to thank the Universities of Auckland and Otago for their financial and academic support for the journal. We would like to thank the Medical Assurance Society (MAS), the Royal Australian and New Zealand College of Psychiatrists (RANZCP), the Auckland Radiology Group, Specialty Trainees of New Zealand (STONZ), the Goodfellow Unit, and the NZDSI for their generous funding. We would also like to thank Catherine's Creations, Medisave, Medshop, and the Royal Australasian College of Surgeons (RACS) for sponsoring the prizes for our Researcher Spotlight initiative, and the Royal Australian and New Zealand College of Obstetricians and Gynaecologists (RANZCOG) for sponsoring our new RANZCOG Blog Post Award for the best student-authored blog post published on the NZMSJ Blog this year. Not least of all, the Editorial Board are indebted to Professor Frank Frizelle for his ongoing financial support for the Verrall Award. The winner of this year's Verrall award will be chosen from the academic articles included in the NZMSJ issues published this year, and will be announced at the end of the year. We would like to acknowledge the New Zealand Medical Students' Association (NZMSA) for their ongoing support, and our Advisory Board members for their continued advice and guidance. Finally, the authors would like to thank the Editorial and Commercial Boards and our student and expert peer reviewers for their exceptional work behind the scenes to enable this issue to be published.

We hope NZMSJ readers will enjoy the wide variety of interesting articles included in Issue 32. We would like to congratulate all of the authors who have contributed, and encourage all readers to submit their work to NZMSJ in the future.

"The real question now is not whether young physicians should have a voice in politics, but just how loud it will become."[2]

References

1. NZMA. Code of Ethics [Internet]. Wellington: NZMA; 2020 Jun [updated 2020 Aug]. Available from: https://assets-global.website-files.com/5e332a62c703f6340a2faf44/5fbd645fe15640fa981fa469_Code%20of%20Ethics%20Redesign%202020%20version%204.pdf

2. Frank E, Nallamothu BK, Sen S. Is there a place for politics in medicine? 2019 Dec 9 [cited 2021 March 30]. In: BMJ. BMJ Opinion [Internet]. [place unknown]: BMJ. 2004-. Available from: https://blogs.bmj.com/bmj/2019/12/09/is-there-a-place-for-politics-in-medicine/

INVITED EDITORIAL

The interface between medicine and politics; an imperative and opportunity that should be used responsibly

Ashley Bloomfield

On a baking hot Sunday in February 2019, I joined then Associate Minister of Health Honourable Jenny Salesa and Children's Commissioner Andrew Becroft at a Weetbix TRYathlon in Point England, Auckland. At this event, the Minister announced the government's intention to legislate banning smoking in motor vehicles carrying children and teens under the age of 18.

I made a special effort to be present at this announcement for two reasons. Firstly, it was an important additional step in our ongoing efforts to reduce the impact of tobacco on health in Aotearoa New Zealand. Secondly, it had been around 15 years since the Ministry of Health had first provided advice to the government on introducing such a ban, and I wanted to mark the achievement and the tenacity of all involved. While the evidence for the benefits of such a ban had not changed over that time, the point had been reached where there was sufficient "social licence" to implement a ban: the political "window of opportunity" had opened to literally let in the fresh air.

For anyone who has worked in tobacco control, or indeed, public health more broadly, this will be a familiar story. All the changes in tobacco control that I have been involved with or observed over many years have required dedication and persistence on the part of many people to successfully navigate the political landscape. Public health, and medicine more generally, frequently operate at the political interface—in this case, the interface was with national politics, but it is just as likely in a workplace, professional organisation, local government body, or community.

This is hardly surprising, and indeed, not unique to medicine and public health. My personal definition of politics is that it is "what happens when you have two or more people in a room." In other words, politics is about the contest of ideas, beliefs, and opinions—it is part of our everyday human experience in homes and with wider whānau and friend groups, in workplaces, community organisations, neighbourhoods, etc.

The relationship between medicine and politics was astutely described by German pathologist and politician Rudolf Virchow in the 19th century:

> *"Medicine is a social science, and politics nothing but medicine at a larger scale. Medicine as a social science, as the science of human beings, has the obligation to point out problems and to attempt their theoretical solution; the politician, the practical anthropologist, must find the means for their actual solution."*[1]

Despite being a pathologist by training, Virchow is often described as the "founder" of social medicine—now more commonly known as public health, population health, or community health. His fundamental notion was that whole populations can be sick, or at risk of becoming sick, and that political action is sometimes needed to improve population health.[2]

What I find interesting in Virchow's quote is his comment about the role of politicians—that is, to "find the means for their actual solution." This resonates with the oft-quoted description of politics as "the art of the possible." It is one thing to point out the problems (easy—we are all experts at this) and have great ideas about how to solve them (also relatively easy), but much harder for politicians to successfully get people on board, and then ensure solutions are successfully implemented!

I've certainly found Virchow's description of politics very helpful over the last 20-plus years that I have worked in the wider public service. It explains how sustainable progress is made; often, the outcome of political negotiation is an agreement that is no single stakeholder group's full preference, but one that all stakeholders can live with *and* that can be successfully implemented. Compromise is not capitulation. A key point here is that politicians have a difficult job, and, as I've also learnt over the years, they all set out to make the best decisions that lead to the best possible outcomes.

Central to the work of public health is understanding the role of the broader environmental, social, cultural, and economic determinants of health and wellbeing. These determinants include access to safe water, education, income, employment, housing, access to cultural resources including land and language, safe neighbourhoods, and opportunities for active transport. All of these determinants are influenced by national and local government decision-making, policies, and funding. So, it is hardly surprising that public health action frequently lies at the political interface and can be seen as political in nature.

Addressing these determinants may bring public health professionals into conflict with powerful social and economic interests. Three of the biggest risk factors for non-communicable diseases, which account for much of the burden of disease globally, are tobacco consumption, harmful use of alcohol, and overconsumption of foods high in salt, sugar, and fat.[3] Private sector actors, including large, multinational companies that manufacture and market these products, have an interest – indeed an obligation to their shareholders – in maintaining or continuing to grow the market for their products.

Public health professionals working in advocacy have a different role to play in addressing the impact of these risk factors from those working in government roles. The latter must provide balanced and evidence-based advice on options to reduce the impact of these risk factors, while taking into account the wider costs and benefits of policy and regulatory change.

For those working in advocacy roles, championing public health causes is, at times, not for the faint-hearted. Public health professionals can find themselves provoking reaction and confrontation with other interested stakeholders. While social media present an opportunity to deliver public health messages and campaigns, they also provide a readily accessible platform for campaigns to counter, and even attempt to discredit, those seeking changes to improve public health.

Public health legislative or regulatory interventions sometimes impinge on people's rights and freedoms and there can be fierce debate as they pass through the parliamentary process. Yet, soon after their introduction, people can wonder why it took so long to implement them! One example, which I was involved with early in my career, was the introduction of Smokefree workplaces, including bars, clubs, cafes, and restaurants, in December 2004. Most of you won't have any knowledge of what it was like to come home reeking of smoke after an evening out; imagine what it was like for bar and waiting staff working there. As the (then) Ministry of Health lead for this area, I recall being quizzed by reporters as to who would "police" venues to ensure that smokers didn't light up inside once the new law came into effect. Of course, once the day arrived, smokers just went outside to smoke, and within a short period of time, most people—including smokers—strongly supported the new law.

Effective communication is essential to building "social licence" for change that requires political action. One of the most successful public health interventions during 2020 (and perhaps for some years) was open and clear communication with New Zealanders from the outset of the emergence of coronavirus disease 2019 (COVID-19) globally. Political and other leaders played a key role in supporting and championing a science-based response, and the clear and consistent communication of the government's decisions helped to build the trust and confidence needed to successfully implement radical interventions, not least a national "lockdown." A key piece of feedback I have received from the public was that people trusted the response in large part because those responsible for it didn't claim to have all the answers, and were honest when things didn't go right, or when they had changed their minds as new evidence emerged. This lesson is highly relevant to communication between health professionals and patients as well.

More broadly, medical and public health practitioners have played (and continue to play) a key role in advocating for changes to improve health and wellbeing and address inequities, especially between Māori and non-Māori. The understanding of people—individuals, families, and communities—that is a core part of the work of health professionals is highly relevant to the political process, as a key role for governments is to protect and improve the wellbeing of all people.

Medical practitioners are also often involved in the delivery of services where ideas and values are contested. Topical areas include taking a harm reduction rather than prosecutorial approach to drug addiction; the delivery of abortion services and the pending implementation of the outcome of the End of Life Choice referendum; and, of course, asking people to stay at home for weeks to help control the spread of COVID-19!

Finally, medical professionals have the privilege in New Zealand of receiving a medical education and training that are (still) largely publicly funded. With that privilege also comes a degree of political power (whether we seek it or not) and responsibility (whether we like it or not). A key responsibility is to ensure that the political power wielded by individual practitioners and professional medical organisations such as unions, colleges, and associations is used fairly and wisely. It can be used simply to commandeer resources for a service, specialty, or organisation, or it can be used for the wider good; keep in mind that "the only appropriate use of power is to empower others."

References

1. Ackerknecht EH. Rudolf Virchow: Doctor, Statesman, Anthropologist. Madison: University of Wisconsin Press; 1953. Quoted in Semenza JC, Giesecke J. Intervening to reduce inequalities in infections in Europe. Am J Public Health. 2008 May[cited 2021 Jan 20];98(5):787-92. Available from: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2374832/pdf/0980787.pdf

2. Mackenbach JP. Politics is nothing but medicine at a larger scale: reflections on public health's biggest idea. J Epidemiol Community Health. 2009 Mar [cited 2021 Jan 20];63(3):181-4. Available from: https://jech.bmj.com/content/63/3/181

3. World Health Organization. Global Action Plan for the Prevention and Control of Non-Communicable Diseases: 2013-2020. Geneva: WHO; 2013. https://apps.who.int/iris/bitstream/handle/10665/94384/9789241506236_eng.pdf;jsessionid=763EFC484B8EB76C922C9FEE232A34A0?sequence=1

About the author

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INVITED EDITORIAL

Shifting the policy inertia on prevention

Boyd Swinburn

We could do disease prevention really well. We are a small, smart country, and if we invested some political will and a small slice of the health budget into promoting health and preventing diseases, we could really shift the dial on some of our appalling health statistics, especially in relation to health equity.

One-third of our health loss (measured in terms of disability-adjusted life-years lost) is directly caused by three harmful, commercially-available products—tobacco, alcohol, and unhealthy food.[1] This is a huge overall toll, but just as stark are the inequities that lie beneath the national figures. The heaviest burden of preventable diseases is almost always borne by Māori, Pasifika, and disadvantaged communities.[2]

The never-ending stream of health inequity statistics we hear about are the visible symptoms of structural unfairness in our society. Examples of this include the neglect of our Te Tiriti o Waitangi obligations; allowing commercial interests to dominate public health interests; and abandoning already-disadvantaged communities to the predatory influences of cheap booze, junk food, cigarettes, and pokies which line the streets in those neighbourhoods.

We largely know what needs to be done in terms of policies, funding and action—you only have to look at the dozens of evidence-based recommendations from many national and international authoritative reports. When we don't enact those recommendations, this is called "policy inertia."[3] The Law Commission report on alcohol,[4] the World Health Organization (WHO) report on childhood obesity,[5] and the WHO Best Buys for reducing non-communicable diseases[6] are all good examples of reports which have been largely ignored by successive New Zealand (NZ) Governments.

What is the cause of policy inertia? First and foremost, when it comes to tobacco, alcohol, and unhealthy food, it is the commercial lobbying power of the businesses profiting from these harmful products that creates political inaction. Alcohol and food businesses in NZ are powerful forces that very few politicians to date have shown a willingness to confront.

While tobacco companies have less legitimacy and access to the government, they readily fund other groups, such as shopkeepers, to lobby on their behalf.[7] For example, if the government proposes measures to restrict the number of tobacco outlets in its renewed efforts to reach SmokeFree2025, the tobacco industry will likely fund "astroturf groups" (i.e. artificial grassroots groups)[7] claiming to represent the interests of small shop owners arguing on behalf of the tobacco industry.

The second major cause of policy inertia is government reluctance to implement recommended public health policies. This might be because they actually dismiss the expert recommendations and believe that education and market solutions will make a difference to complex problems like obesity. Alternatively, it might be because of government corruption, which is common internationally, but thankfully not an issue with the NZ Government. But inertia always exists primarily because enacting policies like tax increases or regulations on marketing always results in huge battles against powerful industries.

The NZ Government's leadership during the acute coronavirus disease 2019 (COVID-19) crisis has shown the way forward for dealing with other major, albeit chronic, crises such as obesity, diabetes mellitus, and health inequities in general.

We could characterise the "COVID-19 approach" as: prioritising public health above commercial interests, aiming for long-term economic benefits, looking closely at the scientific evidence, listening to experts, implementing bold policies, communicating and disseminating them clearly to the population, and adapting rapidly in response to emerging local and international evidence. The corollary of this, as evidenced by the 2020 election result, is that the public typically values this decisive, pro-health approach. Bold political actions in the interests of public health can, indeed, be a real vote-winner.

The third major cause of policy inertia is the insufficient demand for change from the public and civil society organisations. People, as consumers, voters, or advocates, can only muster sufficient power to influence the major players (governments and the private sector) when they are coordinated and organised.

I consider civil society organisations (i.e. non-governmental organisations (NGOs), professional associations, and academic groups) to be the "sleeping giants" in the power dynamic for creating better disease prevention policies.[8] Awakening the giant to create a greater demand for stronger public health policies and capacity is probably the best way forward for overcoming policy inertia.[3]

Bloomberg Philanthropies has developed a successful approach to mobilising civil society organisations to demand, support, and evaluate key food policies. Their Food Policy Program began by working with Mexico to achieve a tax on sugary drinks and unhealthy food.[9] Based on the success in Mexico, they then extended the support for civil society action and robust policy evaluation in seven other countries. Their commitment is now over $435 million (United States Dollar) to low- and middle-income countries worldwide.[10]

The approach taken by Bloomberg Philanthropies is to support NGOs to conduct agenda-setting communications campaigns; researchers to provide the evidence for policies, in terms of their need and impact; and social lobbyists to work with legislators and their officials to secure regulatory or taxation changes. Bloomberg Philanthropies funds the building of this triumvirate of capacity and expertise, but with very specific policy targets in mind. The main policies they are currently seeking to achieve are: taxes on sugary drinks, front-of-package warning labels, and restrictions on unhealthy food marketing to children.

Funding the evaluation process is especially important, because the impact of these policies is always highly contested, especially by large, multinational food companies. The Bloomberg-funded evaluation studies, which have demonstrated the impact of food policies,

are incredibly valuable for other countries seeking to achieve action on similar policies.[11–13]

Apart from in the United States, Bloomberg Philanthropies is not funding this work in high-income countries, so what options do we have to apply such a model in New Zealand? A couple of years ago, a group of NGOs and academics met to create a similar approach, but covering tobacco and alcohol as well as unhealthy foods—the major commercially-available harmful products suffering from policy inertia.

Thus, Health Coalition Aotearoa was created.[11] It is an incorporated society with charitable status, and at present, it has about 60 organisational members, in addition to many other individual, committed members. It aims to improve health and health equity through reducing harm from tobacco, alcohol, and unhealthy food. The Coalition developed a Prevention Brief[12] of the priorities for action ahead of the 2020 NZ General Election and is now seeking to have those policies implemented.

Can this collective voice overcome the last decade or more of policy inertia on regulating harmful commercial products? The political environment is theoretically conducive to creating bold policies, given the current government's priorities include improving equity and wellbeing; indeed, it is moving early in its second term to get SmokeFree2025 back on track. The fact that it has no current plans to address childhood obesity or the environments which promote the consumption of unhealthy food and alcohol is a clear gap in its ambitions to improve child wellbeing and health inequities across the board.

Strong policies to reduce harm from tobacco, alcohol, and unhealthy food consumption are very popular among New Zealanders. For example, two-thirds of New Zealanders support regulations to restrict unhealthy food marketing to children.[13] The public is supportive of stronger prevention, but they may be surprised that less than 3% of the health budget is spent on population health prevention measures[14]—this small slice of funding covers all infectious disease control, disease screening programs, and health promotion. Just how inadequate this investment is has been graphically exposed in NZ, and indeed in most countries, by the COVID-19 pandemic.

By international standards, New Zealand has a very good "disease management" system (i.e. our healthcare system receives about 97% of the health budget), but our "prevention system" is weak, underfunded, and falling far short of its potential to improve our health status. About 80% of our health status and 90% of our health equity status is determined by factors outside of the healthcare system,[15] and these factors would be the central focus of a fully-functioning prevention system—ensuring that systems involved in education, taxation, benefits, consumer protection, justice, local government, food, water, and so on are oriented, as much as possible, towards health, and certainly away from creating ill-health.

Taking a "COVID-19 Approach" towards harmful products will provide the foundations for the prevention system that NZ desperately needs.

References

1. Institute of Health Metrics and Evaluation. GBD Compare (tobacco, alcohol, high BMI, dietary risks, and malnutrition for New Zealand). Available from: https://vizhub.healthdata.org/gbd-compare/

2. Ministry of Health. Annual Update of Key Results 2019/20: New Zealand Health Survey [Internet]. [place unknown]: [publisher unknown]; 2020 Nov 19. Available from: https://www.health.govt.nz/publication/annual-update-key-results-2019-20-new-zealand-health-survey

3. Swinburn BA, Kraak VI, Allender S, Atkins VJ, Baker PI, Bogard JR, et al. The Global Syndemic of Obesity, Undernutrition, and Climate Change: The Lancet Commission report. Lancet. 2019 Feb 23;393(10173):791–846.

4. New Zealand Law Commission. Alcohol in our lives: curbing the harm. Wellington: New Zealand Law Commission; 2010 Apr. Report No. 114.

5. World Health Organisation. Report of the commission on ending childhood obesity [Internet]. Geneva: [publisher unknown]; 2016. Available from: https://www.who.int/end-childhood-obesity/en/

6. World Health Organisation. Tackling NCDs: 'Best buys' and other recommended interventions for the prevention and control of noncommunicable diseases [Internet]. Geneva: [publisher unknown]; 2017. Available from: https://apps.who.int/iris/handle/10665/259232

7. Savell E, Gilmore AB, Fooks G. How does the tobacco industry attempt to influence marketing regulations? A systematic review. PLoS ONE. 2014;9(2):e87389

8. Swinburn B. Power dynamics in 21st Century food systems. Nutrients 2019 Oct 22;11(10):2544

9. Donaldson E. Advocating for sugar-sweetened beverage taxation: A case study of Mexico [Internet]. [place unknown]: Johns Hopkins Bloomberg School of Public Health; 2015 Jun 18. Available from: https://www.jhsph.edu/departments/health-behavior-and-society/_pdf/Advocating_For_Sugar_Sweetened_Beverage_Taxation.pdf

10. Bloomberg Philanthropies. Food Policy Program [Internet]. [place unknown]: [publisher unknown]; [date unknown]. Available from: https://www.bloomberg.org/program/public-health/food-policy-program/#progress

11. Health Coalition Aotearoa. Available at https://www.healthcoalition.org.nz

12. Health Coalition Aotearoa. Prevention Brief [Internet]. [place unknown]: [publisher unknown]; 2020. Available at https://www.healthcoalition.org.nz

13. Castles B. Unhealthy food marketed to kids. Consumer [Internet]. 2021 Feb 9. Available from: https://www.consumer.org.nz/articles/marketing-food-to-children

14. Minister of Health. Vote Health [Internet]. [place unknown]: Treasury; 2019. Health Sector B.5 Vol.6. Available from: https://treasury.govt.nz/sites/default/files/2019-05/est19-v6-health.pdf

15. New Zeland Health and Disability System. Health and Disability System Review/ Pūrongo Whakamutunga [Internet]. Wellington: [publisher unknown]; 2020 [last updated 2020 Jun 16]. Available from: www.systemreview.health.govt.nz/final-report

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INVITED EDITORIAL

The roles and responsibilities of students and clinicians in political issues related to health

Jonathan Coleman

New Zealand has just experienced a year like no other in its history. Throughout 2020 and now into the new year, health has been thrust to the forefront of public and political affairs in a manner unprecedented in living memory. We are, of course, in an extremely fortunate position with regard to coronavirus disease 2019 (COVID-19) relative to nearly every other nation in the world. Politically, the stance on the Government's management of COVID-19 has been largely united, although there has inevitably been a range of views on some of the details about how the crisis should have been managed.

What has been interesting throughout the pandemic is that the voices of doctors have been heard in the media in a way that doesn't usually occur to any great extent. At various points in the crisis, governments have been urged to take whatever steps have been deemed appropriate by expert opinion. We've seen examples of prominent individuals from the medical profession stating their views, most notably immediately before the first lockdown in March 2020. Statements by Sir David Skegg, Sir Peter Gluckman, and Professor Michael Baker have all helped shape the Government response at crucial points.

COVID-19, of course, provides a striking example of an issue on which medical voices absolutely need to be heard, but it raises the wider question of the extent to which the medical profession should involve itself, either individually or collectively, in political issues containing a health dimension. Some would argue that the perspective of a medical professional carries an obligation to speak out on issues that go beyond health. Indeed, many would say that the health of an individual and population is inextricably entwined within the context of wider societal issues.

There are a range of ways in which it is possible for the medical profession to play a political role, and of course, individual doctors will have vastly differing levels of interest in politics (not to mention differing political beliefs). At times, though, the absolute urgency of the situation pushes doctors who would normally shun political involvement to leave their comfort zone and speak out. Right throughout 2020, doctors in the United States felt compelled to speak up in the face of Federal Government denial of the extent of the COVID-19 crisis. The human toll of the pandemic confronted them every day in the course of their medical duties, and issues like access to personal protective equipment (PPE) compounded the danger that frontline health professionals were facing. Without taking a stand and speaking out, many of those issues around COVID-19 may have slipped by with little pressure on officials to address them.

Prior to diving into political waters, it is of value to understand a little of the nature of politics itself, as it is a field with its own unique characteristics, and a potentially brutal field on which to play. There are no particular rules, but there are definitely skills which can be applied to achieve a desired political outcome.

At the level of national politics, just because your argument may be morally correct (at least in your view) you still may not win the debate. Formal political structures are not a true meritocracy, either. Many a thoroughly decent and competent person has struggled in politics because their face doesn't fit, they lack the natural charisma, or maybe they've made too many enemies along the way to gain support for their ideas. Yes, politics is a very unforgiving game.

Politics is essentially about the art of compromise, and this inevitably comes as a disappointment to idealists and purists. It's never easy to drive through all of your agenda in the form that you might like (unless, of course, you are running a military dictatorship). Frequently, there are tradeoffs, in an effort to gain the support necessary for any given initiative.

In government, there is always an opportunity cost in the delivery of any particular initiative—spending public money on one thing inevitably means that there is less money to be spent on another. As a politician, you always receive less money than you would like for your initiatives, because, of course, your colleagues have portfolio priorities that require funding as well. There is never a limitless pot of money, and this is an aspect of government decision-making that many members of the public struggle to accept. This is no more keenly illustrated than in the area of pharmaceutical funding.

This is a key point. When you strip it all away, politics comes down to decisions about the allocation of resources. The health portfolio in government is, in many ways, a function of the finance portfolio; more effective allocation of resources, driving for productivity, and finding new ways to do things will take a health system to a certain point in terms of improvement. However, beyond this, increased funding is required to keep up with health inflation, population growth, and demographic change.

In short, as one former Prime Minister used to say, "if you are seeking perfection, you won't find it in politics" (meaning, effectively, that for all the reasons listed, it is very hard to achieve everything you would like to, in the manner that you envisaged).

Given these caveats, what role should the medical profession play in political debate, and how can doctors influence policy outcomes for the public good?

The most direct and obvious role is for more doctors to seek to enter Parliament. Currently, there are record numbers of medical doctors in our parliament, on both sides of the House. This brings a breadth and depth of experience which will be invaluable in informing debate. Certainly, to successfully negotiate the health portfolio, one needs a prolonged period during which to study the portfolio (usually as a health spokesperson in opposition), or some degree of clinical background. Given that I became Minister of Health after six years in other portfolios (although with a 3-year stint as an associate Health Minister), I found it invaluable to be able to draw on my medical background as I dealt with the notoriously tricky portfolio.

Obviously, we can't have a parliament full of only doctors, and most clinicians would express very little interest in heading into the

parliamentary setting. All political parties have doctors as members, which is a great way for individuals to help shape the policy of their chosen party. It also provides direct access to senior politicians, and is a way to make a behind-the-scenes contribution. Parties often welcome the input of experts as they look for new ideas and ways of meeting the challenges of providing a sustainable public health system.

Doctors are also able to play an important role in raising public awareness on matters of vital public interest related to health, and this is probably where the most value is able to be added to the public debate. To speak out effectively, it is important to have some understanding of the media, because they are the conduit for transmitting your message to a wider audience. Don't fret though—the basics of media communications are fairly common sense and can certainly be learnt up to a certain level. The rest comes with experience.

Of course, pandemics are (thankfully) rare events; more often, the medical profession's role is to highlight gaps in public policy or an area of social or medical need that needs to be urgently addressed. The late Professor Diana Lennon advocated strongly for some of the most vulnerable in the community during her career, including children from socioeconomically disadvantaged backgrounds, constantly highlighting the links between poverty and ill health.

Medical training, and the privilege of working with people at their most vulnerable, affords doctors a perspective on health issues that no other profession holds. Many would argue that this creates a responsibility to speak out on issues that are a matter of public interest. This is not only to raise awareness on key issues, but also to help shape the decision-making of governments. Informed comment on cancer rates and treatment from medical experts has helped keep cancer care in the public eye and created political pressure for increased funding for new treatments.

Speaking out in such circumstances will seem intuitive to some doctors, although many will prefer to stay out of the spotlight. What may be less clear-cut is where the limits of a doctor's responsibility lie with regard to wider, yet no less important, issues. For instance, should doctors, either singularly or collectively, be taking a stance on climate change initiatives? At what point does an issue acquire a health-related dimension? It could be said that any political issue ultimately has a health-related consequence for individuals and populations. With the emergence of climate change as a political issue, more doctors are speaking out on this issue, as they perceive a very real threat to public health, and a range of wider social issues that may result.

Indeed, a number of medically-related bodies internationally have issued position statements on the issue. Some would see it as a presumption for any professional body to make a statement that professes to represent the views of all its members; others would argue that some issues are so clear and pressing that a stake has to be put in the ground. What is clear is that claiming to represent the unified views of all one's members risks disenfranchising a significant minority at the very least. It would seem that stances on political issues are best taken on an individual basis, although numbers always add heft to any argument.

While many of us in the profession may be clear about the role we wish to play with regards to political involvement, some may have less clarity about the extent of responsibility they desire. Many would see protests and the raising of issues as the totality of that responsibility, but perhaps that requires more careful examination. Raising issues is the easy part—developing constructive and implementable solutions is where the real difficulty lies.

There were many times during my tenure as Minister of Health when I would have liked to have instantly pushed the "yes" button in response to the case for funding new treatments and services. An excellent example was the campaign for the funding of Keytruda for metastatic malignant melanoma in 2016; I absolutely had the deepest sympathy for the patients involved, and it was clear that the drug delivered outstanding results for many patients. It was a compelling case, but the money still had to be found either within the PHARMAC budget, or via a new injection of Government money. Both involved tradeoffs, as of course the money would not be available for other projects. I was conscious too that delays in public funding would have very real consequences for those people whose survival depended on it. Further complicating this was the independence of PHARMAC, and the (somewhat opaque) processes that it follows. A Keytruda equivalent was funded by PHARMAC, and sometime thereafter, Keytruda itself became publicly available.

The medical profession, through the Cancer Society, played a role in raising the profile of this issue, and it was absolutely right that that happened. Many would argue that finding the solution is not within the medical profession's remit, and indeed, that is what politicians are paid to do. That is certainly a valid viewpoint, but there does need to be some understanding of the choices that have to be made whenever decisions around health funding are taken.

The Government's budget is limited, and there are myriad pressures on it; each year in May, the spending decisions for the year ahead are announced by the Minister of Finance at the Budget. Arriving at those decisions is a complex process, involving negotiations between Ministers as they each lobby for the portfolio interests for which they are responsible. Those discussions are always held behind closed doors, and the public have very little line of sight on the nature of what is said. Let me assure you that Ministers of whatever party that happens to be in power always face difficult decisions on where to invest the public purse.

Fortunately, health is consistently the biggest winner in terms of money allocated at budget time, but even within the Health portfolio, there are always tradeoffs. Increasing investment in primary care makes absolute sense as we try to move to a system that deals with problems earlier and takes pressure off hospitals. However, the combination of population growth, an ageing population, and increasing costs of technology and medicines means that the amount of money required for hospital system operations is increasing year-on-year. The result is that new money needs to go into both of these annually.

Raising awareness about an issue in Parliament is not even half the work done—constructive engagement on the solution is where real progress is made.

What is the role of medical students in political issues? Students have traditionally been a voice for change in society. Many decades of life stretch before you, and political decisions taken now may affect your lives in a range of dimensions for years to come. It's important to take an interest in the issues of the day, and in the political environment in general. Students, as with the rest of society, will vary in their degree of interest in political issues, but keeping informed is important. Political views may change over the course of a lifetime, but engaging in debate, rather than just complaining in private, is the most productive approach.

Students are also free of many of the encumbrances that people sometimes feel limit their ability to get involved in issues and speak out in later years. It's a chance to express strong views and brave opinions, while of course staying within the law. Student voices (and those of younger people in general) are especially important to ensure that the interests of future generations are properly considered in the decision-making equation. Policy makers need to be forced to look forward, beyond the horizon of their own life span, and the involvement of younger people keeps up the pressure to do so.

In the end, the extent of any individual's involvement in political issues is of course a judgment call. What one person perceives to be a crucial matter might be met with indifference by another. It is not easy to define the point at which one must get involved and speak out; on some issues, it will be clear that action needs to be taken; and on others, the distinction is not so clearly defined.

What is clear, though, is that doctors have much to constructively add to the debate on a wide range of political issues relating to health and beyond. The onus is on the individual to exercise their own judgment on when to step up and take action.

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LETTER TO THE EDITOR

Virtual volunteerism: The impetus for connection in the time of COVID-19

Leah Sarah Peer

Dear Editor,

In the wake of the coronavirus disease 2019 (COVID-19) pandemic of cancelled clinical rotations and in-person classes, while medical students felt uncertain and ill-equipped to serve directly on the frontline, many rose as leaders. Driven by the passion to overcome obstacles, and the desire to contribute towards the cause, students joined forces virtually, to volunteer their time.

One such initiative was born when a casual tweet from a medical student spiralled off a chain of responses that led to the creation of the movement now known as #Students_Against_COVID, or SAC. As a multi-disciplinary online platform defying the boundaries of space and time, students and allies from around the world have connected to address the major challenges of these trying times. Metro Detroit, a sub team within SAC, assisted with drives calling for personal protective equipment (#PPE), while others helped in the curation of a clinical resources database for frontline health professionals caring for COVID-19 patients. At the heart of the movement, students have united to share ideas on medical education, research, and global health. One core objective is fighting the "infodemic" of the century. As such, different health campaigns created by public health guidelines from the Centres for Disease Control and Prevention (CDC) and the World Health Organization (WHO) were translated into over 40 languages by volunteers aiming to disseminate accurate, evidence-based information. Ensuring that scientific knowledge is accessible and comprehensible to the general public is of utmost importance, particularly during a pandemic. Additionally, students started a research mentorship program, formed a conference taskforce, and sought to elevate each other's voices.

In the past few months, SAC has encouraged members to explore different skill sets and strengthen existing ones, and has transformed them into resilient leaders, engaging in acts of goodness. These innovative forms of collaboration during the crisis provided students with a sense of purpose, connection, and fulfilment, all the while opening up avenues for leadership and inspiration as advocates for change. As compassionate members of society, the movement enhances the zest for a better world by encouraging social accountability within members in order to make a tangible difference.

Although COVID-19 has engendered many downfalls, one of the biggest accomplishments that this pandemic will be remembered for is the power of collective thinking, innovation, and the courage possessed by students to converse and unite on virtual platforms. Serving as the impetus for connection, virtual volunteerism has paved the way for meaningful relationships and friendships that may not have been possible otherwise.

About the author

Leah Sarah Peer (BSc), is a second-year medical student at Saint James School of Medicine. She is passionate about global health, social justice, and accessibility of medical care for underserved communities across the world, and is the recipient of the Anne C. Carter Global Health Fellowship by the American Medical Women's Association (AMWA).

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ACADEMIC: CLINICAL PEARL

Eagle's syndrome as a differential diagnosis in odynophagia

Kaveshan Naidoo, Subhaschandra Shetty

History

Eagle's syndrome was first comprehensively described in 1937, by Watt Eagle.[1] However, stylohyoid ligament ossification was described as early as 1652 by Pietro Marchetti of Padua.[2] In 1870, Lucke described pain associated with this anatomical variation.[3] The first surgical excision of the styloid process to treat symptoms was in 1872 by Weinlechner of Vienna.[4] The incidence of an elongated styloid process amongst the general population ranges between 4–18.2%. However, the incidence of true Eagle's syndrome is highly controversial, ranging between 0.16–17%.[5,6]

Anatomy

The styloid process is a cylindrical, bony projection of the temporal bone and is derived from the second pharyngeal arch (Reichert's cartilage). It is located between the internal and external carotid arteries and the internal jugular vein, and lies anteromedially to the stylomastoid foramen. Three muscles are attached to the styloid process: styloglossus, stylopharyngeus, and stylohyoid; these extend to the tongue, pharynx, and hyoid bone, respectively. The two ligaments attaching to the styloid process are the stylomandibular and stylohyoid ligaments, associated with movements of the mandible, hyoid bone, tongue and pharynx.[7–9] The styloid process length ranges between 0.1 and 8 cm[10,11]; a styloid process greater than 3 cm is widely accepted as being elongated.[12]

Clinical presentation

Radiological evidence suggests that styloid process elongation is usually bilateral. However, symptoms are almost always unilateral.[13,14] Eagle's syndrome has been shown to occur more often in women than men, and a greater incidence has been noted in elderly women, which is thought to be associated with menopause.[15,16] Calcification of the styloid process is attributed to the deposition of calcium salts, and has been shown to be associated with renal disease; causing abnormalities in vitamin D, calcium, and phosphorous metabolism.[17,18]

Eagle's syndrome typically presents with persistent unilateral pharyngeal pain that worsens with swallowing. The pain may also be referred to the ear, resemble a foreign body sensation, or be accompanied by painful trismus.[4,19] Eagle described two forms of the syndrome: a vascular form associated with impingement of the internal carotid artery by the styloid process, and the form associated with scar tissue development around the tip of the styloid process after tonsillectomy. The vascular form may cause transient ischaemic attacks or strokes when turning the head.[20,21]

Case

A 44-year-old female presented with a two-week history of painful swallowing following the ingestion of chicken. She was subsequently referred to the otorhinolaryngology/head and neck service for further investigation. No chicken bone was noted on fibre optic nasoendoscopy. However, elongation of the styloid process was noted on x-ray (Fig 1.). Following administration of non-steroidal anti-inflammatory drugs (NSAIDs), her pain resolved and further management was not indicated.

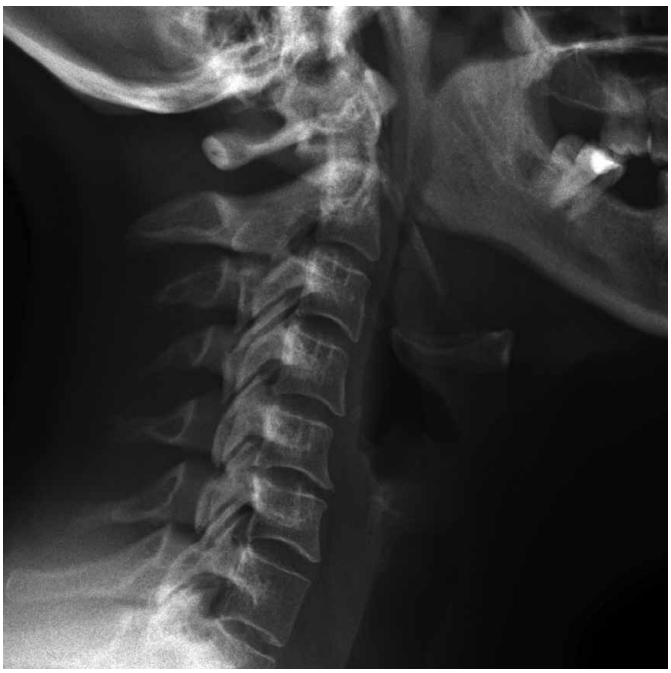

Figure 1. Lateral x-ray showing of elongation of the styloid process.[22]

Diagnosis

The diagnosis of Eagle's syndrome is based on symptomatology; digital palpation of the styloid process in the tonsillar fossa; radiographical evidence of calcification or elongation of the styloid process on x-ray or computed tomography of the neck; or a positive local anaesthetic infiltration test, whereby symptoms are relieved following injection into the anterior tonsillar pillar.[23] Treatment of Eagle's syndrome may be conservative or surgical. Conservative management involves injecting steroids into the lesser cornu of the hyoid or the inferior aspect of the tonsillar fossa. NSAIDs may also have a role in conservative and post-operative management.[9,14] Surgical management is deemed appropriate when conservative management fails. Excision of the elongated styloid process may occur by either a transpharyngeal (intraoral) or transcervical approach.

In conclusion, Eagle's syndrome should be considered in the differential diagnosis for unilateral odynophagia. Appropriate clinical exam-

ination and radiological investigations should be undertaken when the clinical index of suspicion is high.

References

1. Eagle W. Elongated styloid processes: Report of Two Cases. Arch Otolaryngol (Head and Neck Surgery). 1937;25(5):584–7.

2. Moffat DA, Ramsden RT, Shaw HJ. The styloid process syndrome: Aetiological factors and surgical management. J Laryngal Otol. 1977 Apr;91(4):279–94.

3. Balbuena L, Hayes D, Ramirez S, Johnson R. Eagle's Syndrome (Elongated Styloid Process). South Med J. 1997;90(3):331–4.

4. Eagle W. Symptomatic elongated styloid process Report of Two Cases of Styloid Process-Carotid Artery Syndrome with Operation. Arch Otolaryngol. (Head and Neck Surgery). 1949 May 1;49(5):490–503.

5. Correll RW, Jensen JL, Taylor JB, Rhyne RR. Mineralization of the stylohyoid-stylomandibular ligament complex. Oral Surg Oral Med Oral Pathol. 1979 Oct;48(4):286–91.

6. Lorman JG, Biggs JR. The Eagle syndrome. Am J Roentgenol. 1983;140(5):881–2.

7. Carro LP, Nunez MP. Fracture of the styloid process of the temporal bone: a case report. International Orthopaedics. 1995;19(6):359–60.

8. Camarda AAJ, Deschamps C, Forest D. Stylohyoid chain ossification: A discussion of ethology. I. Oral Surg Oral Med Oral Pathol. 1989;67(5):508–14.

9. Lang J. Clinical anatomy of the head. Berlin: Springer-Verlag; 1983.

10. Bergman RA. Compendium of human anatomic variation. Baltimore: Urban & Schwarzenberg; 1989.

11. Chandler JR. Anatomical variations of the stylohyoid complex and their clinical significance. The Laryngoscope. 1977;87(10):1692–701.

12. Härmä R. Stylalgia: Clinical Experiences of 52 Cases. Acta Otolaryngol. 1967;63(224):149–55.

13. Inaki S, Okamura H, Mori T. A stylohyoid syndrome and its clinical aspect. Nihon Kikan Shokudoka Gakkai Kaiho. 1989;40(3):271–5.

14. Gokce C, Sisman Y, Sipahioglu M. Styloid Process Elongation or Eagle's Syndrome: Is There Any Role for Ectopic Calcification?. Eur J Dent. 2008;2(3):224–8.

15. Gervickas A, Sabalys G, Bojarskas S. The diagnosis and treatment of stylohyoid syndrome (ShS). Int J Oral Maxillofac Surg. 1997;26:119.

16. Unlu Z, Orguc S, Eskiizmir G, Aslan A, Bayindir P. Elongated Styloid Process and Cervical Spondylosis. Clin Med Insignts (Case Reports). 2008;2008(1):57

17. Dolan EA, Mullen JB, Papayoanou J. Styloid-stylohyoid syndrome in the differential diagnosis of a typical facial pain. Surg Neurol. 1984;21(3):291–4.

18. Altun S, Boyacıoğlu Doğru H, Akçiçek G, Avcu N. Vascular Type Eagle Syndrome: A Case of Styloid Process-Carotid Artery Syndrome with Operation. Turkish Journal of Family Medicine and Primary Care. 2019;13(1):107–10.

19. Zuber M, Meder JF, Mas JL. Carotid artery dissection due to elongated styloid process. Neurol. 1999;53(8):1886–7.

20. Har-El G, Weisbord A, Sidi J. Ossified segments of the stylohyoid ligament A case of radiological misdiagnosis. J. Lar. Otol. 1987 May;101(5):516–8.

21. Fini G, Gasparini G, Filippini F, Becelli R, Marcotullio D. The long styloid process syndrome or Eagle's syndrome. J Craniomaxillofac Surg. 2000 Apr;28(2):123–7.

22. Gaillard F. Long styloid process/styloid ligaments. 2010. Image from: https://radiopaedia.org/images/409428?case_id=9350

23. Warrier S, Kc N, Subadra K, Harini DM. Eagle's Syndrome: A Case Report of a Unilateral Elongated Styloid Process. Curēus. 2019 Apr 10;11(4):4430.

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ACADEMIC: REVIEW ARTICLE

Mini-review: Antihypertensive activity of probiotic *Lactobacillus casei* through modulation of the gut microbiota

Muhammad Luthfi Adnan

Abstract

Hypertension is one of the primary risk factors for cardiovascular disease, the leading cause of death worldwide. Traditional pharmacotherapy for hypertension has the potential for adverse side effects. *Lactobacillus casei* (*L. casei*) is a type of bacteria that is widely used as a probiotic in the food and biotechnology industries. This review focuses on exploring the potential of *L. casei* as an antihypertensive therapy. A comprehensive literature search was conducted with the keywords "blood pressure", "cardiovascular disease", "gut microbiota", "hypertension", "probiotic bacteria", and "probiotics". The identified studies reported on the antihypertensive effect of *L. casei* through its modulation of the microbiota in the gut. Although early experimental studies in mice are promising, further research at higher levels of evidence is required to corroborate the antihypertensive mechanism of *L. casei* before the probiotic can be implemented as an alternative or adjunct treatment for hypertension.

Keywords: blood pressure, gut microbiota, hypertension, probiotic bacteria.

Introduction

Hypertension is one of the most common diseases in the world and is a major risk factor for cardiovascular disease.[1] Based on data from the World Health Organization (WHO), hypertension and its complications are the cause of 9.4 million deaths each year, and this mortality rate will increase the number of deaths due to hypertension and its complications from 17% of all deaths in 2008 to 24% by 2030.[2] Risk factors for hypertension include increasing age, obesity, smoking, sedentary lifestyle, and socioeconomic conditions in low- and middle-income countries (LMIC).[3,4]

Treatment of hypertension can include pharmacological therapies, such as angiotensin-converting enzyme inhibitors (ACE-I), angiotensin receptor blockers (ARB), calcium channel blockers (CCB), diuretics, and β-blockers.[5] However, the need for long-term pharmacotherapy can increase the risk of non-compliance.[6] Compliance with treatment is important for reaching the target blood pressure. Non-compliance can lead to a lack of control of blood pressure and its other, and sometimes life-threatening, cardiovascular complications.[7] Thus, blood pressure-lowering agents with less side effects compared to current drugs would be useful to offer patients.[8] Of note, several recent studies have shown benefits in providing probiotics as a dietary supplement to reduce the risk of cardiovascular disease.[9]

Lactobacillus casei (*L. casei*) is one of the bacteria in the *Lactobacillaceae* family, and has a relation with the *L. paracasei* and *L. rhamnosus* species. Much research on *L. casei* has been on its use in the commercial food industry due to its health potential.[10] Several experimental models and clinical trials have shown the health effects of *L. casei* include lowering cholesterol levels, improving immune system function, and preventing obesity and the metabolic syndrome.[11] Several recent studies have shown that the antihypertensive effect of *L. casei* is exerted through the modulation of other intestinal microbiota.[12] This review aims to discuss the relationship between gut microbiota and hypertension, and the antihypertensive effects of *L. casei.*

Methods

A comprehensive literature search was conducted between January–April 2020 using the Google Scholar and PubMed search engines. The literature search used the keywords "blood pressure", "cardiovascular disease", "gut microbiota", "hypertension", "probiotic bacteria", and "probiotics". The inclusion criteria used to select sources for this literature review were studies available in full text, written in English, and that had been published within the last 10 years or that were published more than 10 years ago but support other more recent literature sources.

Results

PATHOPHYSIOLOGY OF HYPERTENSION AND ITS RELATIONSHIPS TO GUT MICROBIOTA

The pathophysiology of hypertension is influenced by impaired regulation of blood pressure through the renin-angiotensin-aldosterone system (RAAS).[13] RAAS affects the activity of the Na^+/K^+-ATPase channel, which plays a role in the reabsorption of water and sodium in the kidney tubules, and regulates blood volume through vasoconstriction of vascular smooth muscle cells.[14] Disorders of RAAS can trigger pathophysiological tubular reabsorption of salt and water through stimulation of the renal sympathetic nervous system. This increases sodium reabsorption, triggering renin activation, which breaks down angiotensinogen to angiotensin I (AT-I), which is further broken down by an enzyme that converts angiotensin to angiotensin II (AT-II). AT-II triggers vasoconstriction of blood vessels[15] and also triggers the release of aldosterone from the adrenal glands which further increases the reabsorption of water and salt.[16]

The RAAS system also affects the resistance of blood vessels by interfering with the function of nitric oxide (NO), which acts as a vasodilator and antagonist to AT-II function.[17] In hypertensive conditions, NO is deficient, resulting in vessel stiffness.[18] This deficiency occurs in hypertensive conditions due to the activation of RAAS, triggering the production of asymmetric dimethylarginine (ADMA), which can inhibit NO synthase activity, resulting in reduced NO.[19] NO deficiency results in loss of nephrons, higher glomerular capillary pressures,

Figure 1. Proposed mechanisms of Lactobacillus casei-mediated antihypertensive effect.

and glomerular hyperfiltration, which, in turn, leads to decreased sodium reabsorption, further increasing RAAS activity and leading to hypertension.[20] Also, the increased production of AT-II results in an increased inflammatory response that results in vascular dysfunction.[21] Furthermore, NO deficiency causes renal ischaemia and subsequent chronic kidney disease, which is another risk factor for cardiovascular disease.[18] Importantly, NO deficiency can be influenced by gut dysbiosis-producing lipopolysaccharide (LPS) and also by oral microbiota, which colonise the intestine, resulting in inflammation and oxidative stress on NO formation.[22,23]

Experimental and clinical studies have demonstrated that there are different gut microbiota in normal and hypertensive subjects.[24,26] These changes in microbiota, mainly an increase in *Firmicutes* and *Bacteroidetes*, were associated with higher blood pressures.[24] An increase in *Firmicutes* and *Bacteroidetes* is a marker of dysbiosis, and results in oxidative stress and impairs NO function.[24] The regulation of gut microbiota is influenced by the activity of olfactory receptors 78 (Olfr78) expressed in the renal juxtaglomerular apparatus, and G protein-coupled receptor 41 (Gpr41) expressed in smooth muscle cells in blood vessels.[25] Further studies are required to explain the causative relationship between dysbiosis and hypertension, and may make modulation of gut microbiota with probiotics a target for the treatment of hypertension.[24,26]

LACTOBACILLUS CASEI PROBIOTIC BACTERIA AS AN ANTIHYPERTENSIVE AGENT

Probiotic bacteria are defined by the Food and Agriculture Organization (FAO) as living microorganisms which, when consumed in sufficient quantities, provide health benefits to the host.[27] *Lactobacillus casei* is one of the probiotic bacteria of the genus Lactobacillus that comes from the family *Lactobacillaceae*. The *Lactobacillaceae* family has been used extensively as a food product and in various fields in pharmacotherapeutics and biotechnology.[28] *L. casei* has been studied extensively because it has the most significant antimicrobial effect on Gram negative and Gram positive bacteria, and a high survival ability in dealing with the environmental stresses of the gastrointestinal tract.[29]

There have been several studies conducted to examine the antihypertensive effects of *L. casei*, in both experimental mouse models and human clinical trials.[30] One such study demonstrated that supplementation with *L. casei* reduced blood pressure and mean arterial pressure after eight weeks of administration in hypertensive rats.[31] The study also demonstrated improved blood vessel dilation function in hypertensive rat subjects, which was followed by increased glutathione and NO activity.[31] The authors propose that inhibition of the formation of the antioxidant glutathione results in oxidative stress in blood vessels, leading to stiffness and, consequently, hypertension. The antioxidant effect of *L. casei* is therefore likely to occur by enhancing glutathione and NO levels, which contribute to the antihypertensive effect.[31,32]

Another study also showed a lower incidence of hypertension in the elderly Japanese population with consumption of fermented milk containing the *L. casei* Shirota strain (LcS) ≥3 times per week, compared to populations with lower consumption levels.[33] However, this study is limited by its retrospective and observational study design, with the control group limited to subjects with consumption ≤ 3 times per week, and the absence of subjects who did not take any probiotics.[33] Also, the risk factors for hypertension are numerous, including salt intake, lifestyle, and genetics; and their confounding roles have not been investigated in these studies.[33,34] In another study, the *L. casei*-mediated antihypertensive effect was associated with beneficial effects on glucose and lipid metabolism.[35] Thus, further studies are needed regarding the antihypertensive activity of *L. casei* in larger and more heterogeneous populations.

ANTIHYPERTENSIVE MECHANISM OF *LACTOBACILLUS CASEI*

Proposed mechanisms are summarised in Figure 1. The antihypertensive activity of *L. casei* is associated with the higher production of short-chain fatty acids (SCFAs) through modulation of gut microbiota.[36,37] SCFAs are widely-studied bacterial metabolites produced by the fermentation of complex polysaccharides, including resistant starches and some of types of fibre, in the colon. SCFAs consist of acetate, propionate, and butyrate, which are widely present in the colonic epithelium.[38] *L. casei*-produced SCFAs are thought to modulate other gut microbiota and exert their antihypertensive effect through Olfr78 and Gpr41 receptors expressed in smooth muscle cells.[25] At Gpr41 receptors, propionate can inhibit the increase in blood pressure through vasodilatory activity in the kidney, and generate a hypotensive response, while the receptor Olfr78 act as support to counter powerful hypotension.[25,39] The interaction of acetate and propionate at the Gpr41 receptor reduces the stimulation of renin secretion in the juxtaglomerular apparatus.[40] Butyrate counteracts some effects of AT-II, which can prevent AT-II-mediated endothelial dysfunction.[41]

Several other studies have demonstrated an association between SCFAs and blood pressure. One study showed that increasing acetate levels through increasing fibre intake can lower blood pressure while reducing left ventricular hypertrophy in a hypertensive mouse model.[42] This study showed that acetate activity from gut microbiota after a high-fibre diet had blood pressure-lowering and cardioprotective effects associated with the inhibitory activity of interleukin-1 (IL-1).[42] Inhibition of IL-1 can reduce fibroblast activity and decrease cardiac fibrosis, which are hallmarks of ventricular hypertrophy and kidney damage and result in hypertension.[43]

Another mouse study has demonstrated the antihypertensive activity of propionate through another anti-inflammatory effect.[44] Propionate-mediated attenuation of the systemic T-cell response to AT-II activity was seen to reduce cardiac hypertrophy and endothelial dysfunction, which leads to the pathophysiological formation of

atherosclerotic lesions and increases the risk of heart failure.[44] Thus, propionate-mediated effects on AT-II activity in hypertension could potentially protect against cardiac and vascular damage and reduce the risk of atherosclerosis and coronary heart disease.[44,45]

The antihypertensive effect of butyrate is mediated through interaction with colonocytes, where butyrate improves the gut epithelial barrier.[46] Butyrate is thought to exert an anti-inflammatory effect through reducing the release of proinflammatory LPS that causes gut dysbiosis.[47] LPS is thought to interfere with NO production and mediate endothelial dysfunction, which play a role in the progression of hypertension.[47] An experimental study has demonstrated an association between butyrate and reduced blood pressure, likely through improving the gut epithelial barrier, preventing LPS from translocating to the circulation, and changing the gut microbiota population, which can influence vascular and cardiac function.[48] However, further research is required to completely explain the antihypertensive mechanism of *L. casei* and the effect of its SCFA metabolites.

Conclusion

Hypertension is a major cause of premature death worldwide and is a major risk factor for serious cardiovascular diseases. At present, there is a relationship between the gastrointestinal microbiota and hypertension. Recent studies have shown that consumption of the *L. casei* has an antihypertensive effect in primarily experimental mouse studies and one human trial. *L. casei* is thought to modulate the gut microbiota through SCFA metabolites, thereby lowering blood pressure via an incompletely understood mechanism. Further research is needed to confirm the promise of *L. casei* as an antihypertensive for clinical use.

References

1. Sarki AM, Nduka CU, Stranges S, Kandala N-B, Uthman OA. Prevalence of hypertension in low- and middle-income countries: A systematic review and meta-analysis. Medicine (Baltimore). 2015 Dec;94(50):1–16. doi:10.1097/MD.0000000000001959

2. World Health Organization. A Global Brief on Hypertension: Silent Killer, Global Public Health Crisis [Internet]. [place unknown]:[publisher unknown]; 2013 Apr. Available from: https://apps.who.int/iris/handle/10665/79059.

3. Basu S, Millett C. Social epidemiology of hypertension in middle-income countries: Determinants of prevalence, diagnosis, treatment, and control in the WHO SAGE study. Hypertension. 2013 Jul;62(1):18–26. doi:10.1161/HYPERTENSIONAHA.113.01374

4. Rahimi K, Emdin CA, MacMahon S. The Epidemiology of Blood Pressure and Its Worldwide Management. Circ Res. 2015 Mar 13;116(6):925–35. doi:10.1161/CIRCRESAHA.116.304723

5. Supraptia B, Nilamsari WP, Hapsari PP, Muzayana HA, Firdausi H. Permasalahan Terkait Obat Antihipertensi pada Pasien Usia Lanjut di Poli Geriatri RSUD Dr.Soetomo Surabaya. J Farm dan Ilmu Kefarmasian Indones. 2014 Dec;1(2):36–41.

6. Tedla YG, Bautista LE. Drug Side Effect Symptoms and Adherence to Antihypertensive Medication. Am J Hypertens. 2016 Jun;29(6):772–9. doi:10.1093/ajh/hpv185

7. Li YT, Wang HHX, Liu KQL, Lee GKY, Chan WM, Griffiths SM, et al. Medication Adherence and Blood Pressure Control among Hypertensive Patients with Coexisting Long-Term Conditions in Primary Care Settings. Med (United States). 2016 May;95(20):1–10. doi:10.1097/MD.0000000000003572

8. Vasquez EC, Pereira TMC, Peotta VA, Baldo MP, Campos-Toimil M. Probiotics as beneficial dietary supplements to prevent and treat cardiovascular diseases: Uncovering their impact on oxidative stress. Oxid Med Cell Longev. 2019 May 7;2019:3086270–11. doi:10.1155/2019/3086270

9. Ettinger G, MacDonald K, Reid G, Burton JP. The influence of the human microbiome and probiotics on cardiovascular health. Gut Microbes. 2015 Nov 2;5(6):719–28. doi:10.4161/19490976.2014.983775

10. Céspedes M, Cárdenas P, Staffolani M, Ciappini MC, Vinderola G. Performance in nondairy drinks of Probiotic *L. casei* strains usually employed in dairy products. J Food Sci. 2013 May;78(5):756–62. doi:10.1111/1750-3841.12092

11. Daliri EBM, Lee BH, Oh DH. Current Perspectives on Antihypertensive Probiotics. Probiotics Antimicrob Proteins. 2017 Jul;9(2):91–101. doi:10.1007/s12602-016-9241-y

12. Upadrasta A, Madempudi RS. Probiotics and blood pressure: Current insights. Integr Blood Press Control. 2016;9:33–42. doi:10.2147/IBPC.S73246

13. Oparil S, Acelajado MC, Bakris GL, et al. Hypertension. Nat Rev Dis Prim. 2018 Jun 7;4(1). doi:10.1038/nrdp.2018.14

14. Feraille E, Dizin E. Coordinated control of ENaC and Na+, K+-ATPase in renal collecting duct. J Am Soc Nephrol. 2016;27(9):2554–63. doi:10.1681/ASN.2016020124

15. Lin S-R, Lin S-Y, Chen C-C, Fu Y-S, Weng C-F. Exploring a New Natural Treating Agent for Primary Hypertension: Recent Findings and Forthcoming Perspectives. J Clin Med. 2019 Nov 16;8(11):2003. doi:10.3390/jcm8112003

16. Saxena T, Ali AO, Saxena M. Pathophysiology of essential hypertension: an update. Expert Rev Cardiovasc Ther. 2018 Dec 2;16(12):879–87. doi:10.1080/14779072.2018.1540301

17. De Mello WC, Frohlich ED. Clinical perspectives and fundamental aspects of local cardiovascular and renal renin-angiotensin systems. Front Endocrinol (Lausanne). 2014 Feb 19;5:1–9. doi:10.3389/fendo.2014.00016

18. Ahmad A, Dempsey SK, Daneva Z, Azam M, Li N, Li P-L, et al. Role of nitric oxide in the cardiovascular and renal systems. Int J Mol Sci. 2018 Sep 3;19(9):2605. doi:10.3390/ijms19092605

19. Sibal L, C Agarwal S, D Home PD, Boger RH. The Role of Asymmetric Dimethylarginine (ADMA) in Endothelial Dysfunction and Cardiovascular Disease. Curr Cardiol Rev. 2010 Mat;6(2):82–90. doi:10.2174/157340310791162659

20. Tain Y-L, Hsu C-N. Targeting on asymmetric Dimethylarginine-Related nitric oxide-reactive oxygen species imbalance to reprogram the development of hypertension. Int J Mol Sci. 2016 Dec 2;17(12):2020. doi:10.3390/ijms17122020

21. Pacurari M, Kafoury R, Tchounwou PB, Ndebele K. The renin-angiotensin-aldosterone system in vascular inflammation and remodeling. Int J Inflam. 2014 Dec 1;2014(2014):689360–13. doi:10.1155/2014/689360

22. Zuo K, Li J, Xu Q, Chaowei H, Yuanfeng G, Mulei C, et al. Dysbiotic gut microbes may contribute to hypertension by limiting vitamin D production. Clin Cardiol. 2019 Aug;42(8):710–19. doi:10.1002/clc.23195

23. Li J, Zhao F, Wang Y, Chen J, Tao J, Tian G, et al. Gut microbiota dysbiosis contributes to the development of hypertension. Microbiome. 2017 Feb 1;5(1):1–19. doi:10.1186/s40168-016-0222-x

24. Jose PA, Raj D. Gut microbiota in hypertension. Curr Opin Nephrol Hypertens. 2015 Sep;24(5):403–9. doi:10.1097/MNH.0000000000000149.

25. Pluznick JL, Protzko RJ, Gevorgyan H, Peterlin Z, Sipos A, Han J, et al. Olfactory receptor responding to gut microbiotaderived signals plays a role in renin secretion and blood pressure regulation. Proc Natl Acad Sci. 2013 Mar 12;110(11):4410–5. doi:10.1073/pnas.1215927110

26. Liu Y, Zhang F-M, Hu W-Z. Hypertension : microbiota-targeting treatment. Chin Med J (Engl). 2020 Jun 5;133(11):1353–4. doi:10.1001/jama.2018.9064.5.

27. Morelli L, Capurso L. FAO/WHO Guidelines on Probiotics. J Clin Gastroenterol. 2012;46:S1-S2. doi:10.1097/mcg.0b013e318269fdd5

28. Huang C-H, Li S-W, Huang L, Watanabe K. Identification and classification for the *Lactobacillus casei* group. Front Microbiol. 2018;9:1–13. doi:10.3389/fmicb.2018.01974

29. Hosseini Nezhad M, Hussain MA, Britz ML. Stress Responses in Probiotic *Lactobacillus casei.* Crit Rev Food Sci Nutr. 2015 May 12;55(6):740–9. doi:10.1080/10408398.2012.675601

30. Khalesi S, Sun J, Buys N, Jayasinghe R. Effect of probiotics on blood pressure: A systematic review and meta-analysis of randomized, controlled trials. Hypertension. 2014 Oct;64(4):897–903. doi:10.1161/HYPERTENSIONAHA.114.03469

31. Yap WB, Ahmad FM, Lim YC, Zainalabidin S. *Lactobacillus casei* strain C1 attenuates vascular changes in spontaneously hypertensive rats. Korean J Physiol Pharmacol. 2016 Nov;20(6):621–8. doi:10.4196/kjpp.2016.20.6.621

32. Steven S, Frenis K, Oelze M, Kalinovic S, Kuntic M, Bayo Jimenez MT, et al. Vascular inflammation and oxidative stress: Major triggers for cardiovascular disease. Oxid Med Cell Longev. 2019 Jun 23;2019:7092151–26. doi:10.1155/2019/7092151

33. Aoyagi Y, Park S, Matsubara S, Honda Y, Amamoto R, Kushiro A, et al. Habitual intake of fermented milk products containing *Lactobacillus casei* strain Shirota and a reduced risk of hypertension in older people. Benef Microbes. 2017 Feb 7;8(1):23–9. doi:10.3920/BM2016.0135

34. Pazoki R, Dehghan A, Evangelou E, Warren H, Gao H, Caulfield M, et al. Genetic predisposition to high blood pressure and lifestyle factors: Associations with midlife blood pressure levels and cardiovascular events. Circulation. 2018 Feb 13;137(7):653–61. doi:10.1161/CIRCULATIONAHA.117.030898

35. Nakajima K, Hata Y, Osono Y, Hamura M, Kobayashi S, Watanuki M. Antihypertensive Effect of Extracts of *Lactobacillus casei* in Patients with Hypertension. J Clin Biochem Nutr. 1995;18(3):181–7. doi:10.3164/jcbn.18.181

36. Rowland I, Gibson G, Heinken A, Scott K, Swann J, Thiele I, et al. Gut microbiota functions: metabolism of nutrients and other food components. Eur J Nutr. 2018 Feb;57(1):1–24. doi:10.1007/s00394-017-1445-8

37. Wang G, Li X, Zhao J, Zhang H, Chen W. *Lactobacillus casei* CCFM419 attenuates type 2 diabetes via a gut microbiota dependent mechanism. Food Funct. 2017 Sep 20;8(9):3155–64. doi:10.1039/c7fo00593h

38. Natarajan N, Pluznick JL. From microbe to man: The role of microbial short chain fatty acid metabolites in host cell biology. Am J Physiol - Cell Physiol. 2014 Dec 1;307(11):C979–85. doi:10.1152/ajpcell.00228.2014

39. Pluznick JL. Microbial Short Chain Fatty Acids and Blood Pressure Regulation. Curr Hypertens Rep. 2017 Apr;19(4):1–5. doi:10.1016/j.physbeh.2017.03.040

40. Natarajan N, Hori D, Flavahan S, Steppan J, Flavahan NA, Berkowitz DE, et al. Microbial short chain fatty acid metabolites lower blood pressure via endothelial G protein-coupled receptor 41. Physiol Genomics. 2016 Nov 1;48(11):826–34. doi:10.1152/physiolgenomics.00089.2016

41. Robles-Vera I, Toral M, de la Visitación N, Aguilera-Sánchez N, Redondo JM, Duarte J. Protective Effects of Short-Chain Fatty Acids on Endothelial Dysfunction Induced by Angiotensin II. Front Physiol. 2020 Apr;11:277. doi:10.3389/fphys.2020.00277

42. Marques FZ, Nelson E, Chu P-Y, Horlock D, Fiedler A, Ziemann M, et al. High-fiber diet and acetate supplementation change the gut microbiota and prevent the development of hypertension and heart failure in hypertensive mice. Circulation. 2017 Mar 7;135(10):964–77. doi:10.1161/CIRCULATIONAHA.116.024545

43. Bageghni SA, Hemmings KE, Yuldasheva NY, Maqbool A, Gamboa-Esteves FO, Humphreys NE, et al. Fibroblast-specific deletion of IL-1 receptor-1 reduces adverse cardiac remodeling following myocardial infarction. JCI Insight. 2019 Sep 5;4(17):1–14. doi:10.1172/jci.insight.125074

44. Bartolomaeus H, Balogh A, Yakoub M, Homann S, Markó L, Höges S, et al. Short-Chain Fatty Acid Propionate Protects from Hypertensive Cardiovascular Damage. Circulation. 2019 Mar 12;139(11):1407–21. doi:10.1161/CIRCULATIONAHA.118.036652

45. Rosenbaugh EG, Savalia KK, Manickam DS, Zimmerman MC. Antioxidant-based therapies for angiotensin II-associated cardiovascular diseases. Am J Physiol - Regul Integr Comp Physiol. 2013 Jun 1;304(11):R917–28. doi:10.1152/ajpregu.00395.2012

46. de la Cuesta-Zuluaga J, Mueller NT, Álvarez-Quintero R, Velásquez-Mejía E, Sierra JA, Corrales-Agudelo V, et al. Higher fecal short-chain fatty acid levels are associated with gut microbiome dysbiosis, obesity, hypertension and cardiometabolic disease risk factors. Nutrients. 2018 Dec 27;11(1):51. doi:10.3390/nu11010051

47. Robles-Vera I, Toral M, de la Visitación N, Sánchez M, Gómez-Guzmán M, Romero M, et al. Probiotics Prevent Dysbiosis and the Rise in Blood Pressure in Genetic Hypertension: Role of Short-Chain Fatty Acids. Mol Nutr Food Res. 2020 Mar;64(6):1–37. doi:10.1002/mnfr.201900616

48. Kim S, Goel R, Kumar A, Qi Y, Lobaton G, Hosaka K, Mohammaed M, et al. Imbalance of gut microbiome and intestinal epithelial barrier dysfunction in patients with high blood pressure. Clin Sci. 2018 Mar 20;132(6):701–18. doi:10.1042/CS20180087.

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ACADEMIC: OBSERVATIONAL STUDY

Eosinophilia as a predictor of response to immune checkpoint inhibition in patients with metastatic melanoma

Tim Bridgman

Abstract

Immune checkpoint inhibitors can prolong survival and lead to cure in metastatic melanoma. Baseline indices have not proven clinically useful as predictors of response. Identifying early treatment response would have clinical and economic benefits.

The Christchurch Hospital Oncology Department maintains a prospective registry of melanoma patients treated with pembrolizumab and nivolumab. Patients were classified as either alive-and-progression-free (responders) or as dead-or-progressive-disease (non-responders).

A total of thirty-six patients were included. Median follow-up was 16 months (range 1–41 months). Twelve patients died and three had progressive disease. Mean eosinophil counts were 0.168×10^9/L in responders and 0.198×10^9/L in non-responders ($p=0.565$). In responders, eosinophil count significantly increased after three treatments to 0.37×10^9/L ($p=0.009$). There was a significant difference in the change in eosinophil count between responders and non-responders ($p=0.02$).

In this small study, response to immune checkpoint inhibitors was associated with increased eosinophils. This finding may help predict subsequent clinical response and may help in assessment of suspected pseudo-progression.

Introduction

Immune checkpoint inhibition of programmed cell-death protein 1 (PD-1) has been shown to be effective for the treatment of metastatic melanoma and to improve survival.[1] Prior to checkpoint inhibition, the prognosis for stage IV melanoma was a 5-year overall survival of 5–19%, and a median survival of five months.[2] Both pembrolizumab and nivolumab have been shown to have response rates of 40–45%, with 5-year survival rates of 41% and 44%, respectively.[3-6] Checkpoint inhibitors are not directly cytotoxic to tumour cells, but by preventing PD-1 from binding to PD-L1, they allow T cell recognition of cancer cells. However, checkpoint inhibition fails to work in 30% of patients at initiation, and 50% of patients overall.

Prior research has identified that patients with certain baseline characteristics have better survival with checkpoint inhibitors compared to controls. High absolute lymphocyte count, high absolute eosinophil count, low absolute neutrophil count, low lactate dehydrogenase, and low pretreatment tumour-infiltrating lymphocytes all correlate with overall survival, but are less helpful in predicting treatment response to immune checkpoint inhibitors.[7–9] Further extensive effort has gone into exploring the use of PD-L1 expression and total mutational burden (TMB) to select patients with tumours most likely to respond.[10] Results have varied, and whilst PD-L1 expression has some potential, it is not currently clinically useful for predicting response.[11]

The checkpoint inhibitors nivolumab and pembrolizumab have been funded in New Zealand for stage III unresectable or stage IV malignant melanoma since 2016. Given their high cost, these drugs are tightly regulated by the New Zealand pharmacy management organisation, PHARMAC. They stipulate that prior to the renewal of prescriptions every 12 weeks, computed tomography (CT) scans are needed to determine an absence of disease progression.[12] However, both financially and clinically, it would be preferable to identify responders earlier, and to administer these drugs only to patients who are benefiting.

Being able to identify a lack of response early might reduce unnecessary drug exposure and reduce costs. As the drugs can have a significant survival benefit, having a marker that indicates the patient is responding may justify persisting with treatment, even in cases where there are side effects. This study examined potential predictors of response to checkpoint inhibition.

Methods

The Oncology Department at Christchurch Hospital has maintained a prospective registry of melanoma patients treated with pembrolizumab and nivolumab since 2016. This trial was approved by the Health and Disability Ethics Commission (HDEC). Following written informed consent, adult patients receiving standard-of-care immune checkpoint inhibitors for stage III and IV metastatic melanoma were entered into the trial database. Five-millilitre samples of whole blood were collected at treatment baseline and then prior to subsequent doses of checkpoint inhibitor. These samples were banked in a −80°C freezer for future analysis.

In addition to the clinical sample collection, clinical, laboratory, and radiographic data were passively collected from electronic medical records. CT scans were reviewed and formally classified as per the Response Evaluation Criteria in Solid Tumours (RECIST) criteria.[13] RECIST is a set of published rules that define when a solid tumour has responded, stabilised, or progressed. RECIST classifies serial scans into four categories: complete response (CR), partial response (PR), stable disease (SD), and progressive disease (PD). In this study, RECIST response and vital status were used to binarise patients into alive-and-progression-free (responders) or as dead-or-progressive-disease (non-responders).

Statistical analysis compared baseline variables between the groups before treatment (week 0) and following the third treatment (week 12), when repeat imaging was mandated as per drug funding criteria. T-tests were used to compare between groups, and paired t-tests were used to compare within groups over time. T-tests are a statistical method of determining the likelihood of the observed difference between two continuous data sets being due to chance. These return a result known as a P-value. P-values close to 1 indicate a high degree of probability that chance has an effect, whereas values closer to 0 indicate that chance is a less likely explanation for the observed difference. A P-value of 0.05 or lower is considered statistically significant. Variables examined in this study include eosinophil count, albumin

level, lymphocyte count, and creatinine level. Analyses were conducted using statistical tools on Microsoft Excel and R.

Results

The study included 36 patients with stage IV malignant melanoma. Thirty-one patients received pembrolizumab and five were treated with nivolumab. The median follow-up was 16 months (range 1–41 months). During this time, 12 patients had died, and amongst the survivors, three had progressive disease. The remaining 21 were alive and free of progression. In the alive-and-progression-free group, 62% were male, compared to 80% in the dead-or-progressive-disease group. There were no significant differences between the two groups at baseline (Table 1).

Table 1. Patient baseline variables.

	Responders n=21	Non-responders n=15	P-value
Age (years)	66.5	68.4	
Hb (g/L)	135.57 ± 3.97	140.67 ± 4.23	0.39
Hct	0.42 ± 0.01	0.43 ± 0.01	0.27
WBC (x10^9/L)	7.56 ± 0.42	8.41 ± 0.81	0.32
Lymphocytes (x10^9/L)	1.72 ± 0.17	1.68 ± 0.19	0.88
Eosinophils (x10^9/L)	0.16 ± 0.02	0.18 ± 0.04	0.69
Creatinine	82.81 ± 3.51	90.07 ± 5.34	0.24
Estimated GFR	77.48 ± 3.68	73.80 ± 4.76	0.54
Albumin	36.75 ± 0.68	34.5 ± 1.30	0.11
GGT	56.36 ± 25.39	108.23 ± 49.98	0.35
AST	24.48 ± 3.46	25.29 ± 3.52	0.88
ALT	25.75 ± 6.48	21.21 ± 3.81	0.59
T4 (free)	13.89 ± 0.5	15.18 ± 1.31	0.29
TSH	1.63 ± 0.20	2.30 ± 0.48	0.14

All data are reported as mean ± standard error (SE). Hb, haemoglobin; Hct, haematocrit; WBC, white blood cells; GFR, glomerular filtration rate; GGT, gamma-glutamyl transferase; AST, aspartate aminotransferase; ALT, alanine aminotransferase; T4, thyroxine; TSH, thyroid-stimulating hormone.

Table 2. Patient variables after three treatments.

	Responders n=18	Non-responders n=14	P-value
Hb (g/L)	138.72 ± 2.90	144.21 ± 3.92	0.91
Hct	0.43 ± 0.01	0.44 ± 0.01	0.93
WBC (x10^9/L)	7.69 ± 0.50	9.44 ± 0.92	0.22
Lymphocytes (x10^9/L)	1.85 ± 0.17	1.44 ± 0.21	0.04
Eosinophils (x10^9/L)	0.37 ± 0.09	0.17 ± 0.03	0.02
Creatinine	85.44 ± 3.76	114.14 ± 22.98	0.33
Estimated GFR	74.56 ± 3.39	68.57 ± 6.52	0.54
Albumin	36.06 ± 0.71	32.64 ± 1.40	0.69
GGT	32.80 ± 5.76	92.21 ± 41.68	0.20
AST	21.71 ± 2.36	80.71 ± 59.22	0.25
ALT	27.47 ± 9.33	41.14 ± 21.78	0.45
T4 (free)	16.31 ± 1.66	13.78 ± 1.15	0.07
TSH	7.43 ± 4.37	5.89 ± 4.58	0.49

All data are reported as mean ± standard error (SE). Hb, haemoglobin; Hct, haematocrit; WBC, white blood cells; GFR, glomerular filtration rate; GGT, gamma-glutamyl transferase; AST, aspartate aminotransferase; ALT, alanine aminotransferase; T4, thyroxine; TSH, thyroid-stimulating hormone.

After three treatments, with the exception of the eosinophil and lymphocyte count, there were no significant differences between the two groups (Table 2). Analysis for this time point excluded four participants due to data after dose three being unavailable at our patient census date. Twelve-week measurements did not reveal any significant difference in the lymphocyte levels from baseline within either group.

Eosinophil change from baseline to after dose three

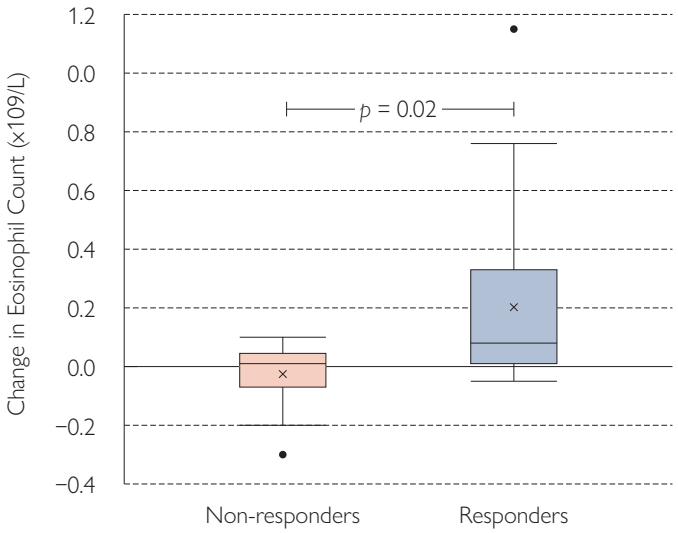

Figure 1. Box plot demonstrating the change in eosinophils calculated as baseline subtracted from post dose three compared between groups. There was a significant diferrence in the change between responders and non-responder (p=0.02).

In the response group group, eosinophils significantly increased from a baseline of 0.16 x10^9/L up to 0.37 x10^9/L (p=0.009). This was an average increase of 126%. In the non-response group, there was no change in the eosinophil count from baseline (p=0.44). The difference in the change between the groups was statistically significant (p=0.02; Figure 1).

Discussion

There were no variables identified at baseline that predicted clinical response. However, clinical response to checkpoint inhibitors was associated with an increase in eosinophils after three treatments. Eosinophilia is a marker of immune-related adverse events to checkpoint inhibitors.[14] An observational case series of 26 patients with an increase in absolute eosinophil count has suggested that eosinophilia potentially correlates with a favourable clinical response.[15] The increase began after a median of three months, and was associated with an overall objective response rate of 69%. Unfortunately, the authors did not report the response rate in the patients who did not have an increase in eosinophil count. In an observational study of 98 patients with advanced melanoma treated with nivolumab, lymphocyte count correlated with clinical response.[8] An increase in absolute lymphocyte count early in treatment correlated with increased overall survival. In our study, the response group showed an increase in lymphocytes greater than that shown by the non-responders. This lends further support to the theory that wider immune activation from checkpoint inhibitors may be beneficial.

There are several implications to clinical care if our work is further validated. Our data suggests that eosinophil count should be explored as an adjunctive predictor of response, and may help with identifying a population not currently likely to benefit from ongoing immunotherapy. In addition, it may also help with identifying a clinically difficult population of "pseudo-progressors". Pseudo-progression is observed post-hoc in patients who have apparent progression by imaging (RECIST PD), but if further followed while on checkpoint inhibitors, appear to have a subsequent stabilisation and response to treatment.[16] Pseudo-progression has been observed in up to 8% of patients enrolled on clinical trials.[17] Mechanistically, this is thought to arise because an immune response triggered against the tumour leads to inflammation, with the inflammatory infiltrate and oedema appearing as an enlarging mass on CT scanning. This, however, is not currently able to be predicted by imaging, and treatment would be stopped, as dictated by funding guidelines, as RECIST shows progressive dis-

ease. Further research is required in cases where pseudo-progression on CT is not correlated to a clinical decline in function. In these cases, pseudo-progression might be suspected, and eosinophils may provide an adjunctive marker.

More work needs to be done in larger cohorts of patients to explore many of these aspects. Specific research into the earliest time when eosinophils become predictive of response is required, as are further studies of the mechanism of action of checkpoint inhibitors. In particular, studies should be done in patients with suspected pseudo-progression, where our finding might have the most clinical relevance.

Conclusion

Response to immune checkpoint inhibitors is associated with an increase in eosinophils after three treatments. This finding may help predict subsequent clinical response, and may help in assessment of suspected pseudo-progression.

References

1. Darvin P, Toor SM, Sasidharan Nair V, Elkord E. Immune checkpoint inhibitors: recent progress and potential biomarkers. Exp Mol Med. 2018 Dec 13;50(12):1-11.

2. Sandru A, Voinea S, Panaitescu E, Blidaru A. Survival rates of patients with metastatic melanoma. J Med Life. 2014 Oct;7(4):572-6.

3. Robert C, Ribas A, Schachter J, Arance A, Grob J-J, Mortier L, et al. Pembrolizumab versus ipilimumab in advanced melanoma (KEYNOTE-006): post-hoc 5-year results from an open-label, multicentre, randomised, controlled, phase 3 study. Lancet Oncol. 2019 Jul 22;20(9):1239-51.

4. Robert C, Long GV, Brady B, Dutriaux C, Maio M, Mortier L, et al. Nivolumab in previously untreated melanoma without BRAF mutation. N Engl J Med. 2015 Jan 22;372(4):320-30.

5. Larkin J, Chiarion-Sileni V, Gonzalez R, Grob J, Rutkowski P, Lao CD, et al. Five-year survival with combined nivolumab and ipilimumab in advanced melanoma. N Engl J Med. 2019 Oct 17;381(16):1535-46.

6. Hamid O, Robert C, Daud A, Hodi FS, Hwu WJ, Kefford R, et al. Five-year survival outcomes for patients with advanced melanoma treated with pembrolizumab in KEYNOTE-001. Ann Oncol. 2019 Apr 1;30(4):582-8.

7. Jessurun CAC, Vos JAM, Limpens J, Luiten RM. Biomarkers for response of melanoma patients to immune checkpoint inhibitors: a systematic review. Front Oncol. 2017 Sep 27;7:233.

8. Nakamura Y, Kitano S, Takahashi A, Tsutsumida A, Namikawa K, Tanese K, et al. Nivolumab for advanced melanoma: pretreatment prognostic factors and early outcome markers during therapy. Oncotarget. 2016 Nov 22;7(47):77404-15.

9. Weide B, Martens A, Hassel JC, Berking C, Postow MA, Bisschop K, et al. Baseline biomarkers for outcome of melanoma patients treated with pembrolizumab. Clin Cancer Res. 2016 Nov 15;22(22):5487-96.

10. Chan TA, Yarchoan M, Jaffee E, Swanton C, Quezada SA, Stenzinger A, et al. Development of tumour mutational burden as an immunotherapy biomarker: utility for the oncology clinic. Ann Oncol. 2019 Jan 1;30(1):44-56.

11. Gandini S, Massi D, Mandalà M. PD-L1 expression in cancer patients receiving anti PD-1/PD-L1 antibodies: a systematic review and meta-analysis. Crit Rev Oncol Hematol. 2016 Apr 1;100:88-98.

12. The Pharmaceutical Management Agency of New Zealand (PHARMAC) [Internet]. [place unknown]: Pharmaceutical Schedule: 2020 [updated 2020 Sep; cited 2020 Aug 30]. Available from: https://www.pharmac.govt.nz/tools-resources/pharmaceutical-scdedule/.

13. Therasse P, Arbuck SG, Eisenhauer EA, Wanders J, Kaplan RS, Rubinstein L, et al. New guidelines to evaluate the response to treatment in solid tumours. J Natl Cancer Inst. 2000 Feb 2;92(3):205-16.

14. Bernard-Tessier A, Jeanville P, Champiat S, Lazarovici J, Voisin A, Mateus C, et al. Immune-related eosinophilia induced by anti-programmed death 1 or death-ligand 1 antibodies. Eur J Cancer. 2017 Aug 1;81:135-7.

15. Moreira A, Leisgang W, Schuler G, Heinzerling L. Eosinophilic count as a biomarker for prognosis of melanoma patients and its importance in the response to immunotherapy. Immunotherapy. 2017 Jan 1;9(2):115-21.

16. Topalian SL, Sznol M, McDermott DF, Kluger HM, Carvajal RD, Sharfman WH, et al. Survival, durable tumor remission, and long-term safety in patients with advanced melanoma receiving nivolumab. J Clin Oncol. 2014 Apr 1;32(10):1020-30.

17. Borcoman E, Nandikolla A, Long G, Goel S, Le Tourneau C. Patterns of response and progression to immunotherapy. Am Soc Clin Oncol Educ Book. 2018 May 23;38:169-78.

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ACADEMIC: REVIEW ARTICLE

A narrative review of the health impact of climate change and food security on Pacific Island countries and territories

Thomas Swinburn, Vili Nosa, Judith McCool

Abstract

INTRODUCTION

Pacific Island countries and territories (PICTs) are experiencing the effects of climate change. A changing climate threatens regional food security. This has implications for the way food is sourced and consumed, and in turn, the health challenges PICTs face. This paper presents a narrative analysis of accessible literature from PICTs on the health impacts of climate change and food security.

METHODS

The MEDLINE and Scopus databases were used to identify relevant literature, with no date restriction. Records were organised using a Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) framework. Ten articles, published between 2010 and 2019, were included in the final synthesis. Included articles were those that explored the convergent themes on the described association between climate change, food security, and health.

RESULTS

Four articles examined the wider Pacific region, four referred to the Micronesia region and/or its constituent countries, and two focused at the country level. Various social, cultural, and economic factors may explain why food security has been worsening over time, coinciding with shifts in dietary patterns, and in turn, health challenges.

DISCUSSION

Climate change is impacting food security through its effects on fisheries, agriculture, and migration. These shifts are documented in various studies based within PICTs, yet there are relatively few studies drawing together climate change and food security with a view to informing public health interventions.

CONCLUSION

Food security remains a major public health issue for PICTs, and further research is needed to support the development of evidence-based public health policy responses to the climate change impacts on health in the region.

Introduction

Climate change presents significant implications for all forms of life.[1] Rising sea levels, changes to the temperature of both the atmosphere and the ocean, and meteorological changes are among the most penetrating impacts. Climate change is having, and will continue to have, an environmental, sociocultural, and economic impact on Pacific Island countries and territories (PICTs), which share an experience of the vulnerabilities that come with being small, developing, island states within a vast oceanic space – and with increasing demands on limited resources. In the immediate future, extreme weather events present disruptions to, and challenges for, everyday living and livelihoods. Should the long-term predictions continue to unfold, island communities will need to adapt and live differently from how they do currently.[1]

Amongst the many impacts of a changing climate is the threat to food security.[2] Food security is the ability to access a safe and nutritious source of food at all times, which is sufficient for maintaining health and wellbeing.[3] In this way, food security is typically assessed according to the following three parameters: firstly, "food availability" is the consistent and sustainable presence of a sufficient quantity of food; secondly, "food accessibility" refers to whether people are able to acquire enough food through a transaction or process; thirdly, "food utilisation" refers to whether the food is stored, cooked, and consumed safely in a way which provides nutrition.[3]

Changing food security environments are anticipated to impact the health challenges PICTs face. For instance, amongst the impacts of climate change, the loss of land and traditional ways of sourcing food may lead to situations of increasing food insecurity. This may require increasing reliance on food imports, further entrenching changes to traditional diets. Diet-related health impacts are well documented, including the global trend towards increased prevalence of obesity, diabetes, cardiovascular disease (CVD), cancers, and other impacts of malnutrition in all its forms.[4] This could in turn adversely impact the health of the population through an increased incidence of diet-related non-communicable diseases (NCDs).[4]

This paper presents a narrative literature review of the health impact of climate change and food security in PICTs.

Methods

The MEDLINE and Scopus databases were interrogated to identify relevant literature. Search terms combined 'Pacific' and a list of PICTs, 'climate change', and 'food security', along with appropriate synonyms. The Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) framework was used to organise the literature search strategy (Figure 1).

From the results, duplicates were removed before screening by title and abstract. Included records were those in the English language which considered all four themes, with no date restriction. In terms of assessing relevance to the Pacific, articles needed to consider either the Pacific region as a whole, a subset of this region (e.g. Melanesia), or a specific PICT. Articles with primarily biological, geo-ecological,

meteorological, or agricultural themes were excluded.

Following screening, 19 full-text articles were assessed for eligibility, with nine subsequently removed. The principal reasons for exclusion were a lack of relevant coverage on food security, and articles which, despite the title, did not focus on the Pacific region. In this way, ten articles were included in the final synthesis (Table 1).

Results

Of the ten articles included in the final synthesis, four considered the entire Pacific region,[5-9] four referred to Micronesia or its constituent countries,[9-12] and two referenced other specific Pacific countries.[13,14] Three articles reviewed the literature to specifically examine the link between climate change, food security and health.[5,6,10] Others generally described trends in food security, the potential impact of climate change, and possible solutions.[7-9,11,14] The remaining articles considered sea level rise[12] and ciguatera.[13] *Figure 2* summarises the key findings.

CHANGING FOOD SECURITY AND HEALTH IMPLICATIONS

Historically, a variety of Indigenous practices maintained food security, including surplus production, famine crops, intra- and inter-community exchange networks, and crop diversity.[6,7,14] It appears to be accepted that food security has typically been worsening over time, coinciding with shifts in dietary patterns.[6-8,11] The literature identifies a plethora of contributing and interacting factors, which include a shift away from traditional agriculture and fishing practices,[7,9,11,13] and cultural changes concerning food perceptions and preferences.[9-11,14] Various economic drivers were identified, such as the establishment of commercial crops, the increasing influence of international markets, and globalisation.[5-10,14] Historical and social phenomena, including colonisation, migration, urbanisation, population growth, and poverty were also explored.[5-7,9,11] Overall food production decline[6,8,9] and health literacy issues[10,11] were also discussed as contributing factors.

There appears to be a consensus that these dietary changes associated with situations of increasing food insecurity can be characterised by reduced dietary diversity[5,9,10] and increasing consumption of low quality, energy dense food of poor nutritional value, typified by that of imports.[5-11,14] Some scholars classify these changes as an example of the "nutrition transition".[5,6,10] There are a number of studies that make a strong association between these changes and the burgeoning incidence of NCD and their risk factors.[5-11,14] These include overweight[5,10] and obesity[5,7,8,11,14]; hypertension[7] and CVD[8,14]; micronutrient deficiencies[8-10,14]; and nutrition problems, including stunting,[6,7,9,11] diabetes,[7,8,11,14] and anaemia[14]. Schubert and Savage note that many communities face the challenge of co-existing, juxtaposed issues of both under- and over-nutrition[5,6]. Ahlgren points out that in the Marshall Islands, a complex syndemic of risk factors are producing diet-related NCD alongside communicable diseases such as tuberculosis.[11] Furthermore, water- and vector-borne infectious diseases were noted as challenges,[5,6,8] with the possibility of secondary malnutrition compromising food security.[6]

CLIMATE CHANGE AND FOOD SECURITY

The acute vulnerability of the Pacific Island region is increasingly recognised.[5,6,10,11] There is recognition that climate change acts both as a direct and indirect risk multiplier, magnifying a background of existing challenges.[5,6,10]

The literature cautiously reports that climate change is likely to exacerbate existing challenges in situations where food security is becoming increasingly precarious as a result of many of the reasons previously described.[5,6,8,11] Explanations of these mechanisms tend to revolve around the impact of climate change on fisheries and agriculture,[5,6,8] livelihoods and migration,[5,6] disaster response,[5,11] and infectious diseases.[5,6,8] Barnett incorporates a slightly broader position, noting that climate change may ultimately impact food production, economic growth, poverty, and health to influence food security, relating wider concepts such as tourism.[8] Overall, the evidence suggests that, much like the contemporary situation, reliance on imported foods will continue, or indeed increase,[5,6,10,11] associated with under- and over-nutrition, and diet-related NCD.[5,6,10] Savage and Cauchi acknowledge that the evidence in the Pacific linking climate change, food security, and health outcomes is not yet robust.[5,10] Difficulties arise due to the array of related, yet distinct, socio-economic factors; for instance, urbanisation. Furthermore, delineating the temporal delay between the onset and tangible manifestation of both climate change and health conditions presents a further methodological challenge.[5,10]

Alongside a general Pacific-wide decline in agricultural production,[8,9,14] the impact of climate change presents distinct challenges to local food production.[5,6,8,9,11,12] Emerging issues for agriculture include the threat posed by extreme weather events in the short term[5]; the emergence of pests and diseases, and threat to livelihoods[5,6]; and the risk to supporting infrastructure.[8]

Fisheries are fundamental for subsistence and income in the Pacific.[5,6,8] To date, the evidence of the effects of climate change is less well-established for fishing than for agriculture. Evidence suggests that increasing extreme weather events, alongside changes in oceanic composition, temperature, and currents, may adversely affect fish availability, contributing to food insecurity.[5,6] Barnett takes a slightly contrary position, suggesting that the effect on small scale fisheries, the lifeblood of many communities, is uncertain.[8] However, increased variability in catches at a commercial level could have economic consequences.[8] One recurrent theme in fisheries was the resurgence of ciguatera fish poisoning, a non-specific illness which occurs when ciguatoxins are transmitted through the food web to humans. It has been speculated that the recent expansion in the geographical incidence of the disease may be associated with rising sea temperatures, which has direct food security and health implications.[5,8,10,13]

Climate change-related migration is real, and has both social and ecological drivers, as discussed.[5,6,9-11] Savage makes an interesting point, suggesting that food insecurity is likely to be both a cause and a consequence of climate migration. Furthermore, Savage questions whether existing relocations observed can be definitively linked to climate change, pointing out that the links with food security and health outcomes remain theoretical.[9] Nonetheless, evidence supports the position that migrants moving from traditional lands to increasingly urbanised areas tend to find themselves in positions of decreased food security, which engenders many of the dietary and lifestyle changes associated with diet-related NCD.[5,6,9,11,14]

There is growing support for the position that the current humanitarian aid response to disasters, whilst ensuring short-term food security, may paradoxically destabilise long-term food security by making traditional coping strategies redundant.[7-9,13] Savage notes that these associations require further research.[7] Furthermore, water- and vector-borne infectious diseases were noted as challenges,[7,8,10] with the possibility of secondary malnutrition compromising food security.[8]

In the face of these interrelated challenges, whilst several papers mentioned policies, principles, and solutions, studies documenting successful adaptation or mitigation interventions remain sparse.[5,10-12] Cauchi cites trust and governance issues as factors hampering progress.[10] In spite of this, principles for combatting these issues point towards multidisciplinary collaboration at all levels,[6,10] placing Indigenous practices at the heart of policies and projects,[5,6,10,14] and taking a broad, integrative, "health in all policies" approach.[5,6]

Discussion

This review accessed peer-reviewed literature on climate change and food security in the Pacific Island region. An important objective of this review was to assess the nature of the current literature, evaluating where our current understanding is sitting in regard to these complex, interrelating topics. It has become clear that the literature is in an early, descriptive, and even cautious stage, with many key authors in the field noting the difficulty in making definitive links between climate change, food security, and health outcomes.

It is important to note the limitations of this review. The selection

of the sample was based on a pre-defined search strategy of a series of databases. This meant that only peer-reviewed literature was included in the analysis. This decision means that technical reports or other commentaries published by governments or non-governmental organisations in the grey literature domain were not accessed. Furthermore, research and commentary on the public health response to climate and food security policies were not identified in our search. This is an area for future consideration, given the importance of public health preparedness in this area. Finally, our results identified that the majority of studies focused on the Micronesian region. This outcome may reflect the greater emphasis on food security, given the unique geography of Melanesia and some parts of Polynesia.

Further research into culturally- and context-appropriate policies, strategies, and solutions is needed, as well as how communities interpret their experiences of climate change on food security and health. Future research will be needed to better understand, and respond effectively to, the vast, interwoven challenges climate change presents and signifies. These include the methodological challenges in the attribution of observed phenomena, such as migration, to climate change, and how these interact with interrelated drivers, such as socio-economic, commercial, and political determinants. Furthermore, distinguishing between anthropogenic-induced climate change and environmental and ecological shifts warrants and receives ongoing investigation. Research also relies on relatively imprecise climate change prediction modelling, as well as temporal variables that influence cause and effect. Perhaps it is for some of these reasons that literature linking all three concepts (climate change, food security, and health) within the context of the Pacific was relatively sparse, and primary data studies were even more scant. Research into adaptation strategies is also in an early stage. Hydroponic gardening and transplanting crops that are typically endemic in hotter climates, such as those of Africa and Asia, may be possible agricultural adaptation strategies for PICTs, and the viability of these novel methods warrants investigation.[15]

Climate migration was raised a number of times in the literature, yet it is among the most poorly understood themes, compared with ones such as agriculture and fisheries. It would be valuable to address the lack of work focusing "closer to home" in Polynesia. Understanding how migration may change in the future in response to climate change could be important in shaping immigration policy, regional security responses, and general preparedness, especially given New Zealand's standing as an influential and affluent, Polynesian country. The contemporary examples of Kiribati's purchase of land in Fiji, and more recently, the landmark United Nations court case in New Zealand of climate refugee Ioane Teitiota, highlight the need for research and discourse, now, and most certainly into the future, as a means to guide decision making. Similarly, issues around humanitarian relief were raised which, with further research, could influence New Zealand's aid agenda.

The PICTs are facing the interrelated challenges of climate change, food security, and health in the here-and-now. As an affluent and influential Pacific Island, New Zealand has an important role to play on several fronts. New Zealand needs to remain a clear and committed ally to our Pacific neighbours – this may be challenging to New Zealand sovereignty when issues of trade are at stake.[16,17] However, a prosperous, secure, and healthy Pacific has collective benefits. Medical students are not only the future health workforce, but they are the future spokespersons for collective action on issues that impact on population health. Access to healthy food is one of the fundamental human rights – and one that needs our collective protection, from advocacy on reducing carbon emissions, to trade agreements that prioritise public health.

Conclusion

Our analyses of published literature on climate change, food security, and health outcomes specific to PICTs identified that climate change acts as an indirect driver to exacerbate existing food security challenges in the region. Food insecurity will remain a major public health issue for the region unless measures are taken to protect and adapt local food systems. Further research is needed to support the development of evidence-based public health policy responses to the climate change impacts on health in the region.

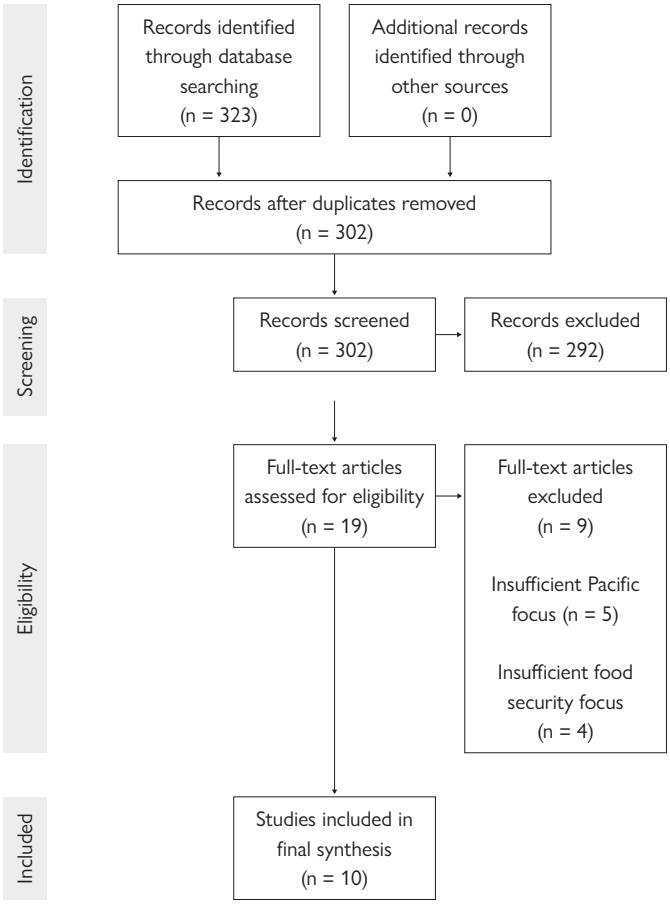

Figure 1: Literature search strategy

Table 1: Climate change and food security in Pacific Island countries and territories

Title	Date	Country/ Region	Author	Type of paper	Aim	Key Findings
Review: the nexus of climate change, food and nutrition security and diet-related NCDs in Pacific Island countries and territories	2019	Pacific region	Amy Savage, Lachlan McIver, Lisa Schubert	Literature review	Investigate the links between climate change, food security and NCDs in support of a 'health in all policies' agenda.	Four key themes were identified: › Climate change events, and particularly extreme weather events in the short term, will have adverse impacts on agriculture, with a potential for a reduction in food availability and dietary quality. › Current pressures on fish and their ecological habitat will be exacerbated by climate change, and food availability in reef fish is unlikely to be adequate to meet requirements. › Climate change migration may serve as both a driver and consequence of food insecurity, while urban migrants typically have reduced food security. › Disaster relief may destabilise long-term food security. The impacts through these four pathways may maintain the reliance on imported foods, which will likely increase the burden of diet-related NCDs.
Small island developing states, climate change and food and nutrition security	2017	Pacific region	Lisa Schubert, Wendy Foley, Amy Savage, Grace Muriuki	Literature Review	Describe the mechanisms linking climate change and food security, the impact, and possible adaptive strategies.	Climate change may impact food security by: › Impinging on livelihoods, affecting food production systems and income, leading to reduced dietary diversity and food security. › Engendering migration, altering lifestyles and diets. › Increasing food dependency for nutrient-poor diets. › Disrupting food markets, resulting in poorer quality food with less availability but increased expense. › Increasing infectious diseases, which risks secondary malnutrition and increases morbidity and mortality in vulnerable populations.

Development, global change and traditional food security in Pacific Island countries	2014	Pacific region	John Richard Campbell	Discussion article	Describe traditional ways of ensuring food security, and discuss how these practices have changed with colonisation and globalisation, and possible ways in which food security might be strengthened.	Traditional practices such as surplus production, agricultural diversity, famine foods, and community networks maintained high levels of food security. In recent times, colonisation, commercialisation of crops, socio-economic changes such as migration, and disaster response have decreased food security, leading to increasing food dependency. Revitalising old ways of ensuring resilience and building strong transnational relationships may be ways to ensure food security in the face of climate change.
Dangerous climate change in the Pacific Islands: food production and food security	2010	Pacific region	Jon Barnett	Discussion article	Discuss the impact climate change will have on food production and security in order to determine whether climate change can be considered a threat.	Climate change is likely to reduce agricultural production through its detrimental effects on crops and infrastructure. Dependency on imports and a drive towards monocultural crops further increases vulnerability to climate change. Fisheries are equally likely to experience increased variability in catches, which has implications for subsistence and income. The combined effects of reduced food availability and ability to purchase food, and health impacts, suggest climate change could be dangerous to food security in the region.
Food security in the island Pacific: Is Micronesia as far away as ever?	2015	Micronesia	John Connell	Discussion article	Describe trends and changes in food security in the Micronesian Pacific, including the impact on health and threat of climate change.	Declines in agriculture, fishing, and local food production as well as wider social, economic, and cultural changes have led to declining food security and an increased reliance on imported food. Resulting changes in nutrition are associated with micronutrient deficiencies and diet-related NCDs. Climate change is likely to continue to impact agriculture, fisheries, and migration, increasing dependence on imported foods.
Climate change, food security and health in Kiribati: a narrative review of the literature	2019	Kiribati	John P Cauchi, Ignacio Correa-Velez, Hilary Bambrick	Narrative Review	Examine the link between climate change and health via the indirect pathway of food security.	Four key themes were identified: › Kiribati is highly vulnerable to climate change owing to social and ecological factors. › Kiribati has been undergoing a nutrition transition, leading to dependence on imports, and subsequently, micronutrient deficiencies and NCDs. › Governance and capacity issues hamper the addressing of climate change and food security challenges. › Traditional knowledge will be important in ensuring a return to food security.

Rising oceans, climate change, food aid, and human rights in the marshall islands	2014	Marshall Islands	Ingrid Ahlgren, Seiji Yamada, Allen Wong	Discussion article	Discuss the rights of Marshallese to good nutrition, whilst considering how this might be impacted by climate change.	Historical events have created a situation of increasing dependency on imported foods and changing cultural preferences, with negative health implications. Food aid may provide short-term food security, but can destabilise long-term food security. It is likely climate change will have an adverse impact on food systems, maintaining dependency on food aid. Combined with migration, this may exacerbate existing syndemics of NCDs and CDs in the Marshall Islands. Policy changes are needed to ensure adequate nutrition for the Marshallese population, including examining the nutritional content of food aid.
Sea-level-rise disaster in Micronesia: sentinel event for climate change	2010	Federated States of Micronesia	Mark E Keim	Original study	Describe the impact of an acute sea level rise on two populations living on atolls.	An acute sea level rise resulted in infrastructure damage, significant food losses, and water and sanitation degradation, with long-standing, devastating effects for food security.
Ciguatera poisoning in French Polynesia: insights into the novel trends of an ancient disease	2019	French Polynesia	M Chinain, C M Gatti, M Roué, H T Darius	Mini review	Describe the clinical manifestations of ciguatera, its causative pathway, and its increasing geographical spread in the Pacific.	Ciguatera is a seafood poisoning which results when humans ingest marine products with a sufficiently high concentration of ciguatoxins, jeopardising reef fish as a subsistence resource and hence threatening food security. Climate change is the likely reason why this disease is expanding geographically, illustrated by the outbreak in a previously unaffected region of French Polynesia.
Neo-traditional approaches for ensuring food security in Fiji Islands	2018	Fiji	Shipra Shah, Asinate Moroca, Jahangeer A. Bhat	Discussion article	Discuss traditional knowledge systems, changes, and the current food security situation, and the possibility of a neo-traditional approach to farming.	Traditional knowledge systems which ensured food security have progressively been eroded by social and economic changes, which has impacted food security, leading to a situation of dependence on imported foods, and in turn, NCDs. Climate change may further expose these vulnerabilities. Combining contemporary knowledge with traditional practices may offer a way to food security.

NCDs: non-communicable diseases
CDs: communicable diseases

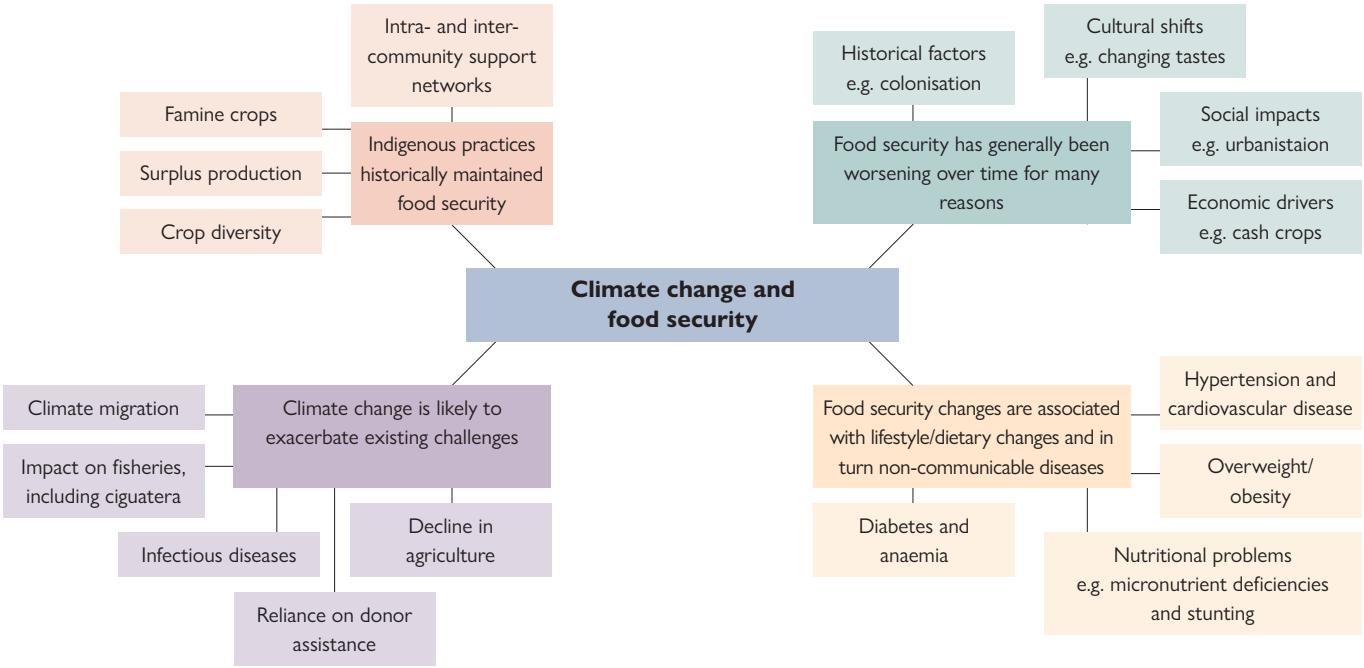

Figure 2: Visual summary of key findings

References

1. Field CB, Barros VR, Dokken DJ, Mach KJ, Mastrandrea MD, Bilir TE, et al. Impacts, adaptation, and vulnerability. Part A: Global and sectoral aspects. Contribution of working group II to the fifth assessment report of the intergovernmental panel on climate change. The United States of America: Cambridge University Press; 2014.

2. Ref IPCC, 2019: Climate Change and Land: an IPCC special report on climate change, desertification, land degradation, sustainable land management, food security, and greenhouse gas fluxes in terrestrial ecosystems. Switzerland: IPCC; 2019.

3. McGuire S. FAO, IFAD, and WFP. The State of Food Insecurity in the World 2015: Meeting the 2015 international hunger targets: taking stock of uneven progress. Adv Nutr. 2015 Sep 5;6(5):623-4.

4. Swinburn BA, Kraak VI, Allender S, Atkins VJ, Baker PI, Bogard JR, et al. The global syndemic of obesity, undernutrition, and climate change: the Lancet Commission report. Lancet. 2019 Feb 23;393(10173):791-846.

5. Savage A, McIver L, Schubert L. The nexus of climate change, food and nutrition security and diet-related non-communicable diseases in Pacific Island Countries and Territories. Clim Dev. 2020 Feb 7;12(2):120-33.

6. Schubert L, Foley W, Savage A, Muriuki G. Small Island Developing States, climate change, and food and nutrition security. Adv Sci Lett. 2017;23(4):3389-92.

7. Campbell JR. Development, global change and traditional food security in Pacific Island countries. Reg Environ Change. 2015 Oct;15(7):1313-24.

8. Barnett J. Dangerous climate change in the Pacific Islands: food production and food security. Reg Environ Change. 2011 Mar;11(1):229-37.

9. Connell J. Food security in the island Pacific: Is Micronesia as far away as ever?. Reg Environ Change. 2015 Oct;15(7):1299-311.

10. Cauchi JP, Correa-Velez I, Bambrick H. Climate change, food security and health in Kiribati: a narrative review of the literature. Glob health action. 2019 Jan 1;12(1):1-8.

11. Ahlgren I, Yamada S, Wong A. Rising oceans, climate change, food aid, and human rights in the Marshall Islands. Health Hum Rights. 2014 Jun 1;16(1):69-80.

12. Keim ME. Sea-level-rise disaster in Micronesia: sentinel event for climate change?. Disaster Medicine and Public Health Preparedness. 2010 Mar;4(1):81-7.

13. Chinain M, Gatti CM, Roué M, Darius HT. Ciguatera poisoning in French Polynesia: insights into the novel trends of an ancient disease. New Microbes New Infect. 2019;31(100565):1-6.

14. Shah S, Moroca A, Bhat JA. Neo-traditional approaches for ensuring food security in Fiji Islands. Environ Dev. 2018 Dec;28(1):83-100.

15. Sharma N, Acharya S, Kumar K, Singh N, Chaurasia OP. Hydroponics as an advanced technique for vegetable production: An overview. J Soil Water Conserv. 2018 Oct;17(4):364-71.

16. Allen MG. Framing food security in the Pacific Islands: empirical evidence from an island in the Western Pacific. Reg Env Change. 2015 Oct;15(7):1341-53.

17. Farrell P, Thow AM, Wate JT, Nonga N, Vatucawaqa P, Brewer T, et ak. COVID-19 and Pacific food system resilience: opportunities to build a robust response. Food Secur. 2020 Aug;12(4):783-91.

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ACADEMIC: REVIEW ARTICLE

A narrative review of noncommunicable diseases in the Pacific region: A case study of the island of Niue

Tahirah Moton, Vili Nosa

Abstract

INTRODUCTION

This literature review takes a strengths-based approach to explore and contextualise noncommunicable diseases in the Pacific region. It compares the noncommunicable disease profile of Niue to that of the Pacific region.

METHODS

The Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) framework was used to search for and screen literature published from 2010 to 2020 pertaining to noncommunicable diseases in the Pacific region. Twenty-five pieces of literature were included in the final data synthesis.

RESULTS

Noncommunicable diseases are a burgeoning issue for the Pacific region. The literature revealed that the risk factors arise from a complex set of socio-political and historical factors, including poverty, colonisation, globalisation, urbanisation, climate change, and poor health system infrastructure. The literature indicated that the noncommunicable disease trends of Niue do not differ greatly from those of the Pacific region. Where Niue does differ is in factors related to its relationship with Aotearoa New Zealand, and issues related to outmigration and the subsequently small population size.

CONCLUSION

This literature review was conducted in a way that endeavoured to avoid victim-blaming, by drawing attention to the broader social, political, and historical contexts in which the Pacific exists. Solutions to the noncommunicable disease crisis must take these contexts into consideration and focus on supporting local capacity and self-determination.

Introduction

The rates of noncommunicable diseases (NCDs) are rising globally. For the Pacific region, NCDs account for around 70% of deaths, with many of these being premature.[1] The risk factors for NCDs must be contextualised within the broader social, political, and historical context of the Pacific. Niue in particular presents a unique case, given the small population size and the nation's close link to Aotearoa New Zealand as a self-governing state in free association. The small population also means that there exists only limited information and research about the specific NCD risk factors affecting Niue.

This scarcity of data in Niue necessitates a consolidation of the current knowledge base in order for gaps in the literature to be identified. This article aims to do so, with the overarching intention being to identify and contextualise NCD risk factors of the Pacific, and to use Niue as a case study.

Methods

The Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) framework was used to gather literature. To capture literature relating to the geographical location we were interested in, the search terms used were "Niue", "Pacific", "Pacific Islands", "PICTs", and "Polynesia". Search terms for NCDs were "noncommunicable disease", "non-communicable disease", "NCD", "chronic illness", and "chronic disease". The search was limited to literature published between 2010 and 2020. Literature pertaining to Pacific peoples residing outside of the Pacific region was not eligible for inclusion. A search of Scopus, MEDLINE, Google Scholar, and the University of Auckland Library website uncovered 193 pieces of literature. These were screened for eligibility, and 25 were used for this literature review. The lead author reviewed each article and identified a set of themes which were then discussed and further developed with the co-author.

Results

A thematic analysis of the literature revealed a set of themes relating to the risk factors of NCDs. How these themes pertain to the Pacific region as a whole will be presented first. This will be followed by a case study which highlights the factors specific to Niue.

THEME 1: SNAP RISK FACTORS

SNAP refers to five common downstream determinants of NCDs: smoking, (poor) nutrition, alcohol, and physical inactivity. Rates of all of these were generally high in the Pacific, with rates being higher for certain groups within the population. For example, men tended to drink more alcohol, women tend to be less active, and rural populations are likely to fare better in all risk factors.[2,3] There is also variance across the Pacific Islands; smoking prevalence for men is over 70% in Kiribati, compared to 25% in Niue.[3] Ultimately, these risk factors all contribute to the high rates of NCDs in the Pacific, and are also the primary reason why the region is facing a double burden of disease, with communicable diseases still prevalent.[4,5]

THEME 2: POVERTY

Many articles emphasised the need to put lifestyle-related risk factors into the context of poverty. NCDs and poverty exist in a vicious cycle, whereby one exacerbates the other.[2] Moore et al stated that for communities who are experiencing socioeconomic deprivation,

affordability always takes precedence over "common-sense" decisions when it comes to making choices that pertain to health.[6] Poverty severely limits not only the choices communities make, but the options that are available in the first place.[7] The relationship also works in the opposite direction, with NCDs exacerbating poverty. The financial costs borne by individuals for treating and managing these conditions is significant, mostly because of the price of medical treatment and the loss of employment opportunities.[2]

THEME 3: COLONISATION, GLOBALISATION, AND URBANISATION

Risk factors also exist within the context of colonisation, urbanisation, and globalisation, which can operate either directly or indirectly on NCD rates. The food and dietary landscape of the Pacific is one example that illustrates the interconnectedness of these three phenomena. Pre-colonial lifestyles in the Pacific were generally healthy, with active lifestyles being supplemented with diets of fish and vegetables.[8,9] However, colonisation has changed this. For example, colonisation saw the destruction of "uninhabited" land, and with it, the destruction of traditional systems of food production, preservation ceremonies, and food-sharing activities.[10] Subsequent globalisation and trade liberalisation resulted in a huge influx of highly-processed, unhealthy foods. As the Pacific entered trade agreements with other countries, the health of Pacific communities was not prioritised.[11] Many articles framed this dietary shift as being devastating to the health of the Pacific.[2,4,7,8,12] Urbanisation, too, has had an impact, with increasingly Western lifestyles in the Pacific being associated with more sedentary lifestyles as the availability of processed foods made growing your own food and other traditional practices less common.[2,7,13]

THEME 4: CLIMATE CHANGE

The risk factors for NCDs also exist in the context of climate change. This can manifest through food insecurity.[8,11,14,15] The erosion of coastlines makes growing healthy vegetables difficult, leading to an even greater dependence on unhealthy, imported foods.[14] Climate change also exacerbates the rate of NCDs as communities move to more urban areas. When coastal areas erode due to rising sea levels, communities are forced to move further inland to larger cities. Consequently, accessing already-overwhelmed health services becomes ever more difficult.[7,16] One study pointed out that the drivers of climate change originate primarily from the greenhouse gas emissions of industrialised countries, yet the effects are felt most acutely in the Pacific.[11] Given this external origin of the problem, such countries should take more responsibility in addressing the resulting NCD crisis in the Pacific region.[11]

THEME 5: HEALTH SYSTEM INFRASTRUCTURE

Poor health infrastructure in the Pacific region is a risk factor and has contributed to an increase in the rates of NCDs. Many Pacific health systems were built to address communicable diseases, and so the rising rates of NCDs mean that many of these mechanisms are no longer fit for purpose.[2] Challenges include limited financial and human resources,[17] poor training and coordination of staff,[18] insufficient NCD surveillance mechanisms,[19] and fragmentation (or altogether absence) of services.[11] Much of the literature also discussed insufficient NCD and cancer surveillance mechanisms as indicators of poor health infrastructure.[2,3,5,16] For example, NCDs may be misdiagnosed or not diagnosed at all.[2] Additionally, deaths in the community may go unreported.[5,20] An implication of this is that the true rates of NCD incidence and mortality are likely to be higher than what the data currently suggests. The absence of good quality data on areas such as risk factors, diagnoses, and mortality rates also makes it difficult to know which areas to prioritise, especially when working with limited resources.

THE CASE STUDY OF NIUE

The literature indicated that these regional themes relating to NCD risk factors also applied to Niue. Like the rest of the Pacific, the rates of NCDs in Niue have been increasing over time. For example, the prevalence of obesity amongst the female population was 32% in 1980, and rose to 46% in 1987.[21] The most recent data, from 2011, places prevalence at 63%.[21] The increasing prevalence amongst the male population in Niue is more dramatic, rising from 8% in 1980 to 59% in 2011. Diabetes amongst men has risen from 5% in 1980, to 12% in 2002, to 42% in 2011. For women it has risen from 9% to 12% to 25%.[21] Other NCDs have followed similar trajectories.

With regard to SNAP risks factors in Niue, there are some differences when compared to the Pacific. Niue has the highest rate of sugar-sweetened beverage consumption for adolescent males, and the second highest adolescent obesity rate out of 15 Pacific Islands surveyed.[22] On the other hand, Niue has lower rates of insufficient physical activity and smoking, with the overall rates for both being around 17%.[3,21] This is relative, as even with these differences, the situation for all risk factors of NCDs is still must be addressed and more research must be done in this area.

Niue's relationship with Aotearoa New Zealand also sets it apart from the rest of the Pacific region. The relationship of free association entitles Niueans to health care in Aotearoa New Zealand, including treatment of NCDs. However, the costs of airfares and accommodation are not guaranteed as part of this.[19] Aotearoa New Zealand also contributes significantly to health expenditure in Niue, accounting for around 30% each year.[23] Additionally, there has been an increase in outmigration of Niueans in recent years.[13] Outmigration is complex, with positives and negatives. Declining social cohesion, fewer skilled workers, and the loss of traditional knowledge being passed down as older people migrate are key concerns. However, migration to Aotearoa New Zealand can mean greater access to health services.[13]

Given the rising rates of NCDs and their risk factors, it is important that Niue's health infrastructure is robust. Increasing rates of outmigration makes sustaining health services difficult.[13,19] Niue's population of less than 2000 means there are very few healthcare services available, even in relation to other Pacific nations. There is no cancer registry, no national health screening programme, and no NCD national plan. Promisingly, there is a Niue Health Strategic Plan, though this must be updated. These health system challenges make responding to the rising rates of NCDs difficult and have a negative impact on the health of the people of Niue.[5,16]

Discussion and recommendations

It was evident from the literature that NCDs in the Pacific must be addressed. The high rates of NCDs have arisen as a result of a complex set of socio-political challenges. The case study of Niue showed that the Pacific Islands each face unique challenges in relation to these rising NCD rates. For Niue, limited health infrastructure and outmigration continue to be challenges, and highlight Niue's complex relationship with Aotearoa New Zealand. The literature revealed that there is nuance to the relationship between the two countries, and it is one that impacts on the NCD profile of Niue in neither wholly positive nor wholly negative ways.

The literature also revealed that solutions are urgently needed to address the NCD crisis. The following recommendations reflect the strong emphasis placed by the literature on strengths-based approaches to interventions.

It is recommended that solutions involve all industries and all levels of the social ecology. For example, NCDs must be addressed in the financial sector such as in relation to taxes on tobacco and unhealthy foods.[24,25] Evidently, solutions must also be strengthened in the health sector. The need to address the entirety of the social ecology—from the individual to the political level—should also be clear, given that we now understand the ways in which individuals are influenced by their socio-political contexts. Focusing too heavily on individual behaviour interventions risks ignoring these contexts at best, or recreating colonial power imbalances at worst.[7,10]

Additionally, solutions should focus on supporting local capacity. This ensures Pacific communities have technical skills, which, when coupled with Indigenous Pacific knowledge and practices, will enable communities to enact self-determination over solutions to the NCD

crisis.[7,24,26] Local capacity is also essential to ensure communities can sustain interventions once external health practitioners leave.[20]

For Niue specifically, it is recommended that a national NCD plan be developed. This will help to set out clear objectives in relation to the NCD crisis and allow for ongoing monitoring. Furthermore, the literature revealed that there is a lack of high-quality and up-to-date data, and cancer in particular was identified as being a significant issue for Niue. It is thus also recommended that a cancer registry database be established to ensure accurate data is available on cancer incidents and survival. Finally, it is recommended that the NCD screening processes in Niue be strengthened. Together, these solutions will enable Niue to respond to the rising rates of NCDs in the short-term, though they must also be considered alongside larger-scale changes that address the environmental drivers of NCDs.

Conclusion

NCDs are a significant issue for the Pacific region. This paper, using Niue as a case study, showed how a strengths-based approach may be used to address the NCD crisis. The case study of Niue demonstrates that while the Pacific Islands share core similarities, each also has its own unique landscape, with the resulting determinants of NCDs also being nuanced. It did so in a way that endeavoured to avoid victim-blaming, by drawing attention to the broader social, political, and historical contexts in which the Pacific exists, and in which health is determined.

References

1. World Bank. Non-communicable Disease (NCD) Roadmap Report [Internet]. Washington DC: [publisher unknown]; 2014. Available from: https://ncdalliance.org/sites/default/files/resource_files/NCD%20Roadmap%20Report.pdf

2. Anderson I. The economic costs of noncommunicable diseases in the Pacific Islands: A rapid stock takes of the situation in Samoa, Tonga and Vanuatu [Internet]. Washington: World Bank; 2012. Available from: https://openknowledge.worldbank.org/handle/10986/17851

3. Kessaram T, McKenzie J, Girin N, Roth A, Vivili P, Williams G, et al. Noncommunicable diseases and risk factors in adult populations of several Pacific Islands: Results from the WHO STEPwise approach to surveillance. Aust N Z J Public Health. 2015 Aug;39(4):336-43.

4. Sievert K, Lawrence M, Naika A, Baker P. Processed foods and nutrition transition in the Pacific: Regional trends, patterns and food system drivers. Nutrients. 2019 Jun 13;11(6):1328.

5. Tervonen H, Foliaki S, Bray F, Roder D. Cancer epidemiology in the small nations of Pacific Islands. Cancer Epidemiol. 2017 Oct;50:184-92.

6. Moore MA, Baumann F, Foliaki S, Goodman MT, Haddock R, Maraka R, et al. Cancer epidemiology in the Pacific Islands - past, present and future. Asian Pac J Cancer Prev. 2010;11(2):99-106.

7. Smith R. Options and choices in relation to adopting healthy lifestyles in the Pacific Islands region. J Dev Soc. 2019 Mar;35(1):62-82.

8. Charlton KE, Russell J, Gorman E, Hanich Q, Delisle A, Campbell B, et al. Fish, food security and health in Pacific Island countries and territories: A systematic literature review. BMC Public Health. 2016 Mar 24;16:285.

9. Taylor M, Kambuou R, Lyons GH, Hunter D, Morgan EH, Quartermain A, et al. Realizing the potential of indigenous vegetables through improved germplasm information and seed systems. Acta Hortic. 2015 Sept;1102:29-42.

10. Wilson M, McLennan A. A comparative ethnography of nutrition interventions: Structural violence and the industrialisation of agrifood systems in the Caribbean and the Pacific. Soc Sci Med. 2019 May;228:172-180.

11. Matheson D, Park K, Soakai TS. Pacific Island health inequities forecast to grow unless profound changes are made to health systems in the region. Aust Health Rev. 2017 Oct;41(5):590-8.

12. 'Ofa SV, Gani A. Trade policy and health implication for Pacific Island countries. Int J Soc Econ. 2017 Jun 12;44(6):816-30.

13. McNamara KE, Lisimoni-Togahai B, Smith R. 'Our kids don't want to eat taro anymore': Unravelling the challenges of contemporary sociocultural change in Niue. J N Z Pac Stud. 2015 Nov 1;3(2):167-82.

14. Kenyon G. Leafy green crops to improve diets on Pacific Islands. Bulletin of the World Health Organization. 2018 Sept 1;96(9):595-6.

15. McIver L, Kim R, Woodward A, Hales S, Spickett J, Katscherian D, et al. Health impacts of climate change in Pacific Island countries: A regional assessment of vulnerabilities and adaptation priorities. Environ Health Perspect. 2016 Nov;124(11):1707-14.

16. Sarfati D, Dyer R, Vivili P, Herman J, Spence D, Sullivan R, et al. Cancer control in small island nations: From local challenges to global action. Lancet Oncol. 2019;20(9):535-48.

17. Ekeroma A, Dyer R, Palafox N, Maoate K, Skeen J, Foliaki S, et al. Cancer management in the Pacific region: A report on innovation and good practice. Lancet Oncol. 2019;20(9):493-5002.

18. Tolley H, Snowdon W, Wate J, Durand AM, Vivili P, McCool J, et al. Monitoring and accountability for the Pacific response to the non-communicable diseases crisis. BMC Public Health. 2016 Sept 10;16(1):958.

19. Sarfati D, Dyer R, Sam FA, Barton M, Bray F, Buadromo E, et al. Cancer control in the Pacific: Big challenges facing small island states. Lancet Oncol. 2019;20(9):475-492.

20. Carter KL, Rao C, Lopez AD, Taylor R. Mortality and cause-of-death reporting and analysis systems in seven Pacific Island countries. BMC Public Health. 2012 Jun 13;12(1):436.

21. World Health Organisation. Niue NCD risk factors STEPS report [Internet]. Western Pacific Region: World Health Organization; 2013. Available from: https://www.who.int/ncds/surveillance/steps/Niue_STEPS_Report_2011.pdf

22. Kessaram T, McKenzie J, Girin N, Merilles OEA, Pullar J, Roth A, et al. Overweight, obesity, physical activity and sugarsweetened beverage consumption in adolescents of Pacific Islands: Results from the global school-based student health survey and the youth risk behavior surveillance system. BMC Obes. 2015 Sept 16;2(1):34.

23. World Health Organisation. Global Health Expenditure Database [Internet]. [place unknown]: [publisher unknown]; 2019 Mar 9. Available from: https://apps.who.int/nha/database

24. Hale M, McCool J, Bullen C, Nosa V. Views from a small Pacific Island: Prospects for tobacco control on Niue. Health Promo Prac. 2012 May 1;13(3):404-11.

25. Magnusson RS, Patterson D. How can we strengthen governance of non-communicable diseases in Pacific Island countries and territories? Asia Pac Policy Stud. 2015 May;2(2):293-309.

26. Kent LM, Reierson P, Morton DP. 'Live more': Study protocol for a community-based lifestyle education program addressing non-communicable diseases in low-literacy areas of the South Pacific. BMC Public Health. 2015 Dec 9;15(1):1221.

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ACADEMIC: CASE REPORT

Streptococcus gallolyticus bacteraemia requiring 12-step desensitisation for penicillin

Oliver Lyons

Abstract
A 65-year-old Tongan man with significant comorbidities and anaphylaxis to penicillin developed infective endocarditis and spinal osteomyelitis as a consequence of recurrent *Streptococcus gallolyticus* bacteraemia. He was commenced on 12-step drug desensitization for penicillin. This case report discusses the process of 12-step drug desensitization and the background of *Streptococcus gallolyticus* (previously known as *Streptococcus bovis*) bacteraemia.

Summary
Mr VF was a 65-year-old Tongan man with significant comorbidities and anaphylaxis to penicillin. He developed infective endocarditis and spinal osteomyelitis secondary to recurrent *Streptococcus gallolyticus* bacteraemia.

Background
This case offers unique insight into the role of antibiotic desensitisation and its potential value in circumstances where patients have an allergy to first-line treatment options, or when alternatives have been unsuccessful.

Case Presentation
Mr VF was a 65-year-old Tongan man who was requested to return to hospital after growing Gram positive cocci on peripheral blood culture (PBC), following a recent admission for fast atrial fibrillation (AF). Apart from a chronic cough and some mild, long-standing back pain, he was generally well, with no febrile or infective symptoms on admission. He had a previous three-week admission in January this year with *Streptococcus gallolyticus* bacteraemia, which was treated with intravenous (IV) vancomycin. A transthoracic echocardiogram from this admission showed moderate left ventricular dilation, reduced left ventricular ejection fraction, and trivial mild mitral regurgitation; however, no valvular vegetation was identified at that time. No source of infection was identified during that admission. He was discharged after having three consecutive negative growths on PBC.

Mr VF had a complex medical background of atrial fibrillation on dabigatran and metoprolol, type 2 diabetes mellitus on metformin, chronic kidney disease, and severe chronic obstructive sleep apnoea secondary to morbid obesity (weighing 156 kg, with a body mass index (BMI) of 45). He also developed cor pulmonale secondary to chronic lung disease, however, this was not significant on echocardiogram. Furthermore, he had myelomalacia, multi-level spinal stenosis, and anaphylaxis to augmentin.

Physical examination was grossly normal, aside from left basal crackles on auscultation, but no wheeze, and a trace of pedal oedema up to his ankles. It was difficult to auscultate heart sounds due to body habitus.

Problem list
1. Recurrent *Streptococcus gallolyticus* bacteraemia
2. *Streptococcus gallolyticus* endocarditis, likely cause of bacteraemia
3. T11/T12 discitis and osteomyelitis

Investigations
Mr VF had a white cell count of 10.79 x10^9/L, a neutrophil count of 8.06 x10^9/L, and a C-reactive protein (CRP) of 66 mg/L. He grew *Streptococcus gallolyticus* on culture on three separate occasions, followed by three subsequent negative results on PBC. Midstream urine, liver function tests, renal function tests, and serum electrolytes were all normal. A transoesophageal echocardiogram revealed a vegetation measuring approximately 10 mm at the anterior mitral leaflet tip, and mild mitral regurgitation. Magnetic resonance imaging (MRI) of the spine showed well-established T11/T12 discitis and new adjacent osteomyelitis with epidural and paravertebral soft tissue inflammation. Due to the strong association between *Streptococcus gallolyticus* and colorectal cancer (CRC), Mr VF underwent a colonoscopy, which demonstrated a single, large, pedunculated rectal polyp, which was then removed. No malignancy was found within the limitations of the study.

Treatment
Due to his penicillin allergy, Mr VF was initially treated with intravenous vancomycin, before being changed to benzylpenicillin after undergoing a successful desensitisation procedure. He was discharged with a peripherally inserted central catheter *in situ*, and treated with a six-week course of IV benzylpenicillin 1.8 g Q4H via the outpatient intravenous antibiotic (OPIVA) service.

Discussion
Infective endocarditis (IE) describes an infection of the endothelial lining of the heart, typically involving one or several cardiac valves.[1] Mr VF's risk factors included his age (>60 years), male sex, and diabetes.[1,2,3] Staphylococcus aureus is the most common pathogenic cause of IE, accounting for 31% of presentations in a large study evaluating a cohort of 2781 patients with IE, whereas Streptoccous bovis was responsible for 7% of cases.[1]
Streptococcus gallolyticus biotype I is a subspecies of the Group D streptococci; *Streptococcus bovis*. Group D streptococci are catalase-negative, Gram positive cocci. *Streptococcus gallolyticus* is the causative organism for the majority of *Streptococcus bovis* IE, and also has a strong association with CRC. In addition, there are documented cases of *Streptococcus gallolyticus* bacteremia causing infections of the bones and joints, as well as the meninges, peritoneum, and urinary tract.[1,4,5] This is likely to have been the cause of Mr VF's new diagnosis of spinal osteomyelitis.

One meta-analysis analysed seven case series, stratifying the number of IE cases among proven cases of *Streptococcus gallolyticus* bacteraemia. Of these, 43%–100% of patients were found to have concurrent or subsequent IE.[4] This indicates a reasonable probability that

Mr VF may have had IE at the time of his initial admission in January 2020. The image quality of his transthoracic echocardiogram was hindered as a result of his BMI. The "trivial" finding of mitral regurgitation during his initial admission is not insignificant. We can only speculate that this may have been the first sign of IE-related sequelae in Mr VF. The specificity of transthoracic echocardiology only reaches 75% for diagnosing IE, thus, it is plausible for a small vegetation to be missed.[6] While fever is by and large the most common symptom of IE (up to 90%), cardiac murmurs are present in 85% of cases,[7] and while this was not documented on admission, adequate auscultation was also appreciably difficult. Nonetheless, the presence of any such valvular defect placed him at a greater risk of developing IE. Interestingly, patients with *Streptococcus gallolyticus* IE are less likely to have the typical risk factors for IE. The presence of chronic liver disease however, or in Mr VF's case, diabetes, does increase one's risk.[1]

Unfortunately, *Streptococcus gallolyticus* bacteraemia is also strongly associated with CRC. One meta-analysis analysed 6 studies and found that patients with *Streptococcus gallolyticus* bacteraemia had a statistically significant higher prevalence of CRC (prevalence range 33%–71%) compared to the normal population (10%–25%).[4] Concomitant IE further elevates this risk.[4] The reason for this association is not fully understood, but explains the importance of regular surveillance with colonoscopy for Mr VF. Due to the strong epidemiologic association, he warrants a further colonoscopy in 4–6 months.[4]

Penicillin allergy is the most widely documented medication allergy in the modern world, yet, for a large proportion, further investigation will reveal that many do not exhibit true allergy, and are able to safely receive the drug.[8] That being said, drug-induced anaphylaxis from penicillin is still a significant cause of morbidity and mortality.[8,9] Caution should be taken before challenging a penicillin allergy. While vancomycin is an effective penicillin alternative in Mr VF's case, the drug's added cost, and associated risks surrounding drug-resistance from overuse, made penicillin desensitisation a worthy option.

Mr VF was unwell with active infection and extensive comorbidities; thus, a decision was made to bypass skin prick testing and to refer him early for desensitisation to minimise treatment delays. While penicillin allergies are commonly misdiagnosed, Mr VF's documented tryptase elevations from prior reactions sufficiently warranted desensitisation.[10, 11]

Desensitisation involves administering a drug in extremely small doses, making gradual increases in a stepwise manner. Provided that it is performed by trained and experienced specialists, the success rate is notably high. Desensitisation can be performed safely on patients of any age. No documented deaths have occurred as a result of the procedure.[10,11] Desensitisation alters a patient's immune response, facilitating a "temporary tolerance," thus allowing patients with hypersensitivity to safely receive an uninterrupted dose of the required medication. The mechanism by which this occurs is not yet fully understood. What is known is that it induces a temporary tolerance of the patient's basophils and mast cells to the drug.[11] Contraindications include any background of reactions relating to drug-related eosinophilia and systemic syndrome, acute generalised exanthematous pustulosis, or skin desquamation such as toxic epidermal necrolysis or Stevens-Johnson syndrome.[10,11] About 20% of patients experience mild breakthrough reactions.[10,11] Provided that the treating clinician is experienced at identifying and managing such symptoms, the risk of these becoming life-threatening is low. Management of symptoms involves temporary cessation of the infusion whilst administering relevant treatment for the symptoms. The infusion is then restarted at the same step as where the symptoms developed.[10,11]

It was important to review the patient's medical background and medications prior to commencing the procedure. Due to its added hypotensive effect, Mr VF's cilazapril was withheld for 24 hours prior to desensitisation, in the event that anaphylaxis was to develop. Ideally, his metoprolol would also have been withheld in case a reaction necessitated adrenaline. However, due to the risk of arrhythmia secondary to his AF, the cessation of metoprolol was deemed to be unwise.[11]

The procedure takes approximately six hours. The protocol commences with an initial intravenous dose that is a 1/10000th dilution of the intended therapeutic dose. This infusion dose is then doubled every 15 minutes (with each increase signifying the next step in the 12-step protocol). This is done until the full therapeutic dose is achieved.[10,11]

Upon completion, Mr VF was able to receive the indicated four-hourly 1.8 g dose of penicillin via a peripherally inserted central catheter for the required 42-day course. It is important to note that maintaining desensitisation relies on the continued presence of the drug. If doses are missed, the desensitisation will dissipate. The speed at which this occurs depends on the drug's half-life, Mr VF's renal function, and various other factors. The desensitisation is also dose-dependent, as any significant dose increase has the potential to trigger allergy.[10]

It was important to inform Mr VF that the desensitisation had not permanently cured him of his allergy, and that once the drug left his system, his sensitivity would return.[10,11]

References

1. Murdoch DR, Corey R, Hoen B, Miró JM, Fowler VG Jr, Bayer AS, et al. Clinical presentation, etiology, and outcome of infective endocarditis in the 21st century: the international collaboration on endocarditis-prospective cohort study. JAMA Intern Med. 2009 Mar 9;169(5):463-73.

2. Hill EE, Herijgers P, Claus P, Vanderschueren S, Herregods MC, Peetermans WE. Infective endocarditis: changing epidemiology and predictors of 6-month mortality: a prospective cohort study. Eur Heart J Case Rep. 2006 Dec 7;28(2):196-203.

3. Castillo FJ, Anguita M, Castillo JC, Ruiz M, Mesa D, Suárez de Lezo J. Changes in clinical profile, epidemiology and prognosis of left-sided native-valve infective endocarditis without predisposing heart conditions. Rev Esp Cardiol (Engl Ed). 2015 May 1;68(5):445-8.

4. Corredoira J, Alonso MP, Coira A, Casariego E, Arias C, Alonso D, et al. Characteristics of Streptococcus bovis endocarditis and its differences with Streptococcus viridans endocarditis. Eur J Clin Microbiol Infect Dis. 2008 Apr;27(4):285-91.

5. García-País MJ, Rabuñal R, Armesto V, López-Reboiro M, García-Garrote F, Coira A, et al. Streptococcus bovis septic arthritis and osteomyelitis: A report of 21 cases and a literature review. Semin Arthritis Rheum. 2016 Jun 1;45(6):738-46.

6. Habib G, Badano L, Tribouilloy C, Vilacosta I, Zamorano JL, Galderisi M, et al. European Association of Cardiovascular Imaging. Recommendations for the practice of echocardiography in infective endocarditis. Eur J Echocardiogr. 2010 Mar 1;11(2):202-19.

7. Cahill TJ, Prendergast BD. Infective endocarditis. Lancet. 2015 Feb 27;387(10021):882-93.

8. Park M, Markus P, Matesic D, Li JTC. Safety and effectiveness of a preoperative allergy clinic in decreasing vancomycin use in patients with a history of penicillin allergy. Ann Allergy Asthma Immunol. 2006 Nov;97(5):681-7.

9. Lee CE, Zembower TR, Fotis MA, Postelnick MJ, Greenberger PA, Peterson LR, et al. The incidence of antimicrobial allergies in hospitalized patients: implications regarding prescribing patterns and emerging bacterial resistance. Arch Intern Med. 2000 Oct 9;160(18):2819-22.

10. Castells M. Rapid desensitization for hypersensitivity reactions to medications. Immunol Allergy Clin North Am. 2009 Aug 1;29(3):585-606.

11. Cernadas JR, Brockow K, Romano A, Aberer W, Torres MJ, Bircher A, et al. European Network of Drug Allergy and the EAACI interest group on drug hypersensitivity. General considerations on rapid desensitization for drug hypersensitivity - a consensus statement. Allergy. 2010 Aug 17;65(11):1357-66.

Patient consent

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ACADEMIC: ESSAY

Fact or fiction: "Skin diseases are the fourth largest cause of disability worldwide"

Jamin Kim

Skin diseases represent a much larger burden of disease than is commonly believed in wider society. The Global Burden of Disease (GBD) project found that skin diseases were the fourth leading cause of disability worldwide in 2010 and 2013.[1] The GBD project remains the main source of global disease burden estimates, and accordingly, the results are used to establish research priorities, set health policies, monitor international health goals, and more. The accuracy of their findings is therefore paramount to achieving equity in global health, especially in terms of appropriate resource allocation. To discuss the veracity of the statement, "Skin diseases are the fourth largest cause of disability worldwide," we will first explore the concept of disability in the context of skin disease, discuss how disability should most accurately be measured, and finally, analyse how the GBD study came to this conclusion in order to explore the validity and implications of such a finding.

Firstly, what is disability? According to WHO, a disability is "Any condition of the body or mind that makes it more difficult for a person to do certain activities and/or interact with the world around them,"[2] i.e., an impairment leading to activity limitation and/or participation restriction. This leads on to the next question; how do skin diseases cause disability? For common skin conditions, the basic answers such as itch, pain, and embarrassment, are of course—obvious—but the multi-dimensional aspect as well as the immense magnitude of impact are perhaps less well appreciated. The myriad effects span across physical, psychological, social, and financial domains of life, all to differing extents, depending on the patient and the disease. In particular, the highly visible nature of the majority of skin diseases contributes significantly to social and emotional difficulties, often in the form of embarrassment, social withdrawal, and fear of rejection based on public misunderstanding. Bearing this in mind, the prevalence of mental illnesses (mainly depression and anxiety) was found to range between 25–43% across dermatologic patients.[3]

But mental illness is only one of many ways in which skin disease contributes to disability, so how should the overall level of disability be measured? There is no perfect methodology, especially in the context of a global study, as will be discussed later, but some methods may confer greater accuracy and representation than others. Disability is a subjective phenomenon, so one way to measure it may be through measuring one's perceived quality of life (QoL), as it is directly influenced by the 3 constituents of disability (impairment, activity limitation, and participation restriction). Although the countless adverse effects of skin conditions on physical and mental health are relatively well known, how these diverse manifestations culminate to truly alter one's overall quality of life is still a matter of great interest. A study in 1999 investigating the health-related QoL in 317 psoriasis patients found that their levels of reduction in physical and mental wellbeing were comparable to that of depression, diabetes, hypertension, heart disease, arthritis, and cancer patients.[4] Moreover, these severely negative effects on QoL are not a phenomenon observed exclusively in adults; a 2006 study found that the health-related QoL impairment caused by chronic skin disease in children was at least equal to that experienced by children with other chronic diseases.[5] This demonstrates that although a large majority of skin diseases may not be as physically harmful as other conditions such as diabetes, they affect QoL just as much—if not more—and are therefore comparably disabling. Another factor which complicates measuring disability for skin diseases is that skin diseases do not always follow a predictable correlation pattern in terms of the observed clinical severity and expected QoL. For example, clinical severity of acne (as rated by dermatologists) was not found to correlate with patients' levels of distress and perceived severity, reflecting the high level of psychosocial distress that conditions such as acne are known to afflict.[6] In contrast, diseases that directly impact physical ability or other easily measurable domains tend to have severity levels which have greater correlation with that of patient perception.[6] This shows that the gathering of mere clinical data is less reliable for determining QoL or the level of true disability for skin diseases.

The veracity of the statement, "Skin diseases are the fourth largest cause of disability worldwide" may now be explored by examining the study that led to this conclusion. The GBD project is funded by the Bill and Melinda Gates Foundation and involves hundreds of scientists worldwide who collaborate to systematically define the epidemiology of a variety of conditions, including diseases, injuries, and risk factors. In the context of skin diseases, data were gathered from over 4000 sources, including systematic literature reviews, hospital data, surveys, and more. A Bayesian meta-regression tool was then used to analyse the extracted data and form estimates around morbidity and mortality. Disability was measured using Disability-Adjusted Life Years (DALYs) and Years Lost to Disability (YLDs) which were calculated using GBD disability weights to represent the disability attributable to each disease and thus determine overall non-fatal disease burden. The study was an extremely comprehensive and valuable measure of global population health; however, the finding that skin diseases are the fourth largest cause of disability worldwide may, in fact, be an underestimation of the global burden of skin disease.

Firstly, underreporting of skin conditions is a major contributing factor to global disease burden underestimation. One example is a 2016 cross-sectional study at Munich Oktoberfest, which randomly screened attending individuals for skin abnormalities and found 64.5% (1662/2701) of participants had at least one skin abnormality, with the top three most common abnormalities being actinic keratoses, rosacea, and eczema.[7] Almost ⅔ of those affected were unaware of their abnormal skin findings. While this study would have been prone to some selection bias, it demonstrates the extraordinary point prevalence of skin disease within a population that has not been referred. Although it is safe to say that all diseases are underreported to some extent, skin conditions are likely to have a comparatively higher rate of underreporting due to a multitude of factors. Many high-risk groups for certain dermatologic conditions (e.g. outdoor workers for actinic

keratoses or melanoma) are less likely to undergo skin examinations.[8] Also, many skin conditions such as acne are often self-treated without patients seeking out medical care, and this means studies relying on secondary data to determine prevalence of skin conditions (such as the GBD study) will underestimate the true burden of disease.

Another contributing factor to underestimation in the GBD study is the fact that the International Classification of Diseases (ICD) system was used to categorise diseases in a mutually exclusive manner. This led to some dermatological conditions being wholly classed under other disease headings, for example, melanoma was classed under "cancer" only. Similarly, the burden of lupus erythematosus was confined to the musculoskeletal disease category, as were the cutaneous manifestations of multiple other systemic diseases.[9] Also, due to the overwhelming number and complex nature of skin diseases, the study (reasonably) focused on the more common conditions, however, this meant that some diseases that were rare but had significant individual disease burden e.g., bullous diseases, were excluded.

Next, it is worth examining how the use of DALYs to represent disease burden/disability contrasts with the earlier discussion involving the ideal methodologies and nuances of measuring such complexity in the context of skin disease. DALYs are calculated using Years Lost to Disability (YLDs) + Years of Life Lost (YLLs). The calculation of YLDs involves using a numerical representation of disability called a "disability weight" which is determined using public opinion through methods such as surveys, thus enabling standardisation and cross-comparison of different disease states. The GBD study determined their disability weights by showing respondents two individuals in two different illness states and asking whom they considered "healthier". The disability weights were intended to estimate mere functional loss of health, with a disclaimer that they were not intended to quantify loss of QoL or well-being. Although this was done intentionally to standardise and simplify the data, it would have led to a greater underestimation of disability attributable to skin disease compared to other diseases because of the disproportionately high psychosocial burden that skin diseases carry.[10] This bias has led some to argue that disability weights should be ascertained in terms of undesirability, or value of the health loss (which may better represent the concept of disability), as opposed to judging the degree of health loss itself.[11] However, one can appreciate that something as broad and subjective as overall wellbeing is very difficult to encompass in a survey that aims for standardisation. Ultimately, the DALY fails to capture the true extent of disability, more so in the context of skin diseases than other diseases, because of these disability weights.

In short, while it is clear the burden of skin disease was underestimated in the GBD study, it is unclear what the cumulative effect these factors have had on the extent of underestimation, and whether a more accurate measurement would allow it to surpass any of the reigning causes of disability. Nonetheless, the fact that skin diseases were still found to be the fourth largest cause of disability worldwide in spite of these factors demonstrates the truly impressive magnitude of their burden. However, they receive comparably little attention in global health; there is a significant need for development of novel treatment and prevention strategies, along with more standardised best-practice guidelines to optimise the ability of health professionals to treat such conditions. In addition, it is important to consider the variation in distribution of different skin disease burdens according to factors such as geographical location and economic status of a country/region. Naturally, the burden was found to be enormous across both high- and low-income countries, but there was significant geographic and age-related variation—more studies should be performed to ascertain the dermatologic needs of different populations/communities to ensure targeted and equitable resource allocation.

So, is it possible to measure global skin disease burden in a way that is more accurate than the GBD project but still feasible? An exciting research initiative arose in 2018, named Global Research on the Impact of Dermatological Diseases (GRIDD), which aims to do just this.[12] In short, GRIDD is developing a new methodology called Global Research of Impact on Patients (GRIP) which proposes a novel way of measuring skin disease burden using questions co-designed with patients internationally. This will address some of the limitations in the GBD study, including the use of DALYs as a flawed measurement for skin disease, and will hopefully capture the true extent of illness burden accurately. The study is still in its early phases, but holds much promise for global future health studies in this area.

The substantial contribution of skin conditions to the overall global burden of disease is continuing to become more recognised within the health sector as well as wider society. The true contribution has yet to be elucidated but the GRIDD is an exciting development that may accelerate this change in how skin conditions are perceived in the context of global health. The GBD study's finding that "Skin diseases are the fourth largest cause of disability worldwide" may be an oversimplified, rough estimate at best, but it has successfully cast the spotlight on skin disease by contextualising its impact with that of other chronic and disabling diseases, demonstrating it to be a significant source of loss of healthy life. The next step is to use this information to propel further public health research and explore innovative ways to reduce this disease burden through prevention, accurate diagnosis, and effective treatment.

References

1. Seth D, Cheldize K, Brown D, Freeman EF. Global Burden of Skin Disease: Inequities and Innovations. Curr Dermatol Rep. 2017;6(3):204-10.

2. World Health Organization. Disability [Internet]. [place unknown]: WHO int; 2020 [cited 2020 Jun 8]. Available from: https://www.who.int/topics/disabilities/en/

3. Hong J, Koo B, Koo J. The psychosocial and occupational impact of chronic skin disease. Dermatol Ther. 2008 Jan;21(1):54-9.

4. Rapp SR, Feldman SR, Exum ML, Fleischer AB, Reboussin DM. Psoriasis causes as much disability as other major medical diseases. J Am Acad Dermatol. 1999;41(3):401-7.

5. Beattie PE, Lewis-Jones MS. A comparative study of impairment of quality of life in children with skin disease and children with other chronic childhood diseases. Br J Dermatol. 2006 Jul;155(1):145-51.

6. Mosam A, Vawda NB, Gordhan AH, Nkwanyana N, Aboobaker J. Quality of life issues for South Africans with acne vulgaris. Clin Exp Dermatol. 2005 Jan;30(1):6-9.

7. Tizek L, Schielein MC, Seifert F, Biedermann T, Böhner A, Zink A. Skin diseases are more common than we think: screening results of an unreferred population at the Munich Oktoberfest. J Eur Acad Dermatol Venereol. 2019 Jul;33(7):1421-8.

8. Zink A, Wurstbauer D, Rotter M, Wildner M, Biedermann T. Do outdoor workers know their risk of NMSC? Perceptions, beliefs and preventive behaviour among farmers, roofers and gardeners. J Eur Acad Dermatol Venereol. 2017 Oct;31(10):1649-54.

9. Hay RJ, Johns NE, Williams HC, Bolliger IW, Dellavalle RP, Margolis DJ, et al. The Global Burden of Skin Disease in 2010: An Analysis of the Prevalence and Impact of Skin Conditions. J Invest Dermatol. 2014 Jun;134(6):1527-34.

10. Ahmed A, Leon A, Butler DC, Reichenberg J. Quality-of-Life Effects of Common Dermatological Diseases. Sem Cutan Med Surg. 2013 Jun;32(2):101-9.

11. Nord E. Uncertainties about disability weights for the Global Burden of Disease study. Lancet Glob Health. 2015 Nov;3(11):e661-2.

12. International Alliance of Dermatology Patient Organizations. Research [Internet]. [place unknown]: Globalskin.org; 2020 [cited 2020 Jun 8]. Available from: https://globalskin.org/about/research

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Conflict of interest

Jamin Kim is a student peer reviewer for the New Zealand Medical Student Journal. This article has gone through a double-blinded peer review process applied to all articles submitted to the NZMSJ, and has been accepted after achieving the standard required for publication. The author has no other conflict of interest to declare.

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ACADEMIC: ESSAY

Disability burden of skin diseases

Christopher Mayo

Introduction

The Global Burden of Diseases, Injury, and Risk Factors Study (GBD) is a study that aims to quantify the worldwide health impacts of a number of diseases and risk factors.[1] An article by Karimkhani et al[2] from the 2013 iteration of the GBD study claimed that skin disease was the "fourth leading cause of nonfatal burden" worldwide; in other words, the fourth largest cause of disability. At 41.0 million disability-adjusted life-years (DALYs), the impact of skin diseases ranked behind iron deficiency anaemia at 43.7 million DALYs, tuberculosis at 49.8 million DALYs, and sense organ diseases at 54.4 million DALYs.[2] This was in agreement with an article by Hay et al[3] from the 2010 iteration of the GBD study, where skin diseases were the fourth largest cause of disability in terms of years lost to disability (YLDs) at 33.7 million YLDs, behind iron-deficiency anaemia at 42.5 million YLDs, major depressive disorder at 63.3 million YLDs, and lower back pain at 80.7 million YLDs.[3] In this essay, I will aim to verify and discuss the accuracy of these assertions that skin diseases are the fourth largest cause of disability worldwide.

Metrics and quantitative analysis

The GBD study uses a number of metrics in order to estimate the health impact of diseases. Disability-adjusted life-years, an innovation of the first 1990 GBD study, is calculated by summing two components: years of life lost (YLLs) and years lived with disability (YLDs). YLLs estimate the impact of mortality caused by a particular disease, with reference to a standard life expectancy. YLDs estimate the impact of disability caused by a disease by weighting the prevalence of disabling sequelae, each receiving a "disability weight" determined by its estimated severity.[4] Disabling sequelae relevant to skin disease include disfigurement (with or without itch or pain) and acute fever.[2] In this essay, I have chosen to use YLDs as the primary measure of disease burden due to disability; it excludes the impact of mortality and weights disabilities by their severity.

The GBD Compare Tool, available online courtesy of the Institute for Health Metrics and Evaluation (IHME), was used to determine where skin diseases ranked in terms of YLDs.[5] Data from the most recent iteration of the GBD study[1] in 2017 was used, with diseases grouped at Level 2 of the GBD cause hierarchy. The result was that skin diseases were the ninth largest cause of disability in terms of YLDs, with a burden of 41.6 million YLDs (95% confidence interval: 27.4 million–61.9 million). This is equivalent to 545 YLDs per 100,000 (95% confidence interval: 358–810). Ahead of skin diseases were nutritional deficiencies (42.4 million), chronic respiratory diseases (44.3 million), diabetes and kidney disease (45.9 million), other non-communicable diseases (53.6 million), sense organ diseases (66.6 million), neurological disorders (73.2 million), mental disorders (122.7 million), and musculoskeletal disorders (135.9 million).

Worldwide, YLD rates for skin diseases have remained relatively constant over time, with a rate of 551 YLDs per 100,000 in the first iteration of the GBD study in 1990 (ranked seventh), although absolute YLDs have been increasing due to worldwide population growth. This ninth place ranking has remained consistent over the years of the GBD study since 2010, including the 2013 iteration. In terms of trends by country, countries with low to middle social development indices (SDI) had a lower rate of skin disease disability burden compared to countries with high SDI. For instance, in 2017, YLDs for skin disease were 852 per 100,000 in the United States and 726 per 100,000 in New Zealand, compared to just 574 in Nigeria and 545 in China.

The skin disease with the highest disability burden in the 2017 GBD study was dermatitis (11.1 million YLDs). This was followed by psoriasis (5.57 million), urticaria (5.01 million), scabies (4.53 million), fungal skin diseases (4.15 million), viral skin diseases (2.60 million), and acne vulgaris (2.55 million).

Discussion

There is evidently a discrepancy between the claim of skin diseases as being the fourth largest cause of disability by Karimkhani et al[2] and Hay et al,[3] when skin diseases have consistently ranked in ninth place in YLDs according to the GBD Compare Tool. It is likely that this difference has occurred due to differences in metrics and disease groupings for calculating disease burden. Firstly, Karimkhani et al[2] and Hay et al[3] compare skin disease against Level 3 groupings on the GBD hierarchy (such as iron deficiency anaemia and tuberculosis), rather than broader Level 2 groupings (such as chronic respiratory diseases and musculoskeletal disorders)[2,3] Level 3 groupings are more specific descriptors than Level 2 groupings; thus, they will naturally have smaller total burdens of disease, making it easier for skin disease to rank higher. It is also important to note that "skin and subcutaneous diseases" is, in itself, a Level 2 grouping, and that the skin disease-relevant Level 3 descriptors are specific skin diseases such as dermatitis and psoriasis.[5] I am therefore of the opinion that it is most appropriate to compare skin diseases against Level 2 groupings.

Furthermore, Karimkhani et al[2] have used DALYs as their primary metric for measuring the impact of skin disease, claiming that skin disease is the eighteenth largest cause of DALYs and fourth largest when considering only "nonfatal burden". It is unclear how nonfatal burden was calculated, but it appears to be measured in DALYs and appears to be distinct to YLDs.[2] I believe that, in the context of ranking causes of disability, it is more simple and appropriate to consider YLDs. Other authors who have ranked causes of disability, such as Hay et al[3] and Steiner et al,[6] have used YLDs as their metric of disability.[3,6]

There are several other issues to consider when attempting to definitively rank the disability burden of skin disease. Metrics such as DALYs and YLDs come with 95% confidence intervals which are often relatively wide[4]; the confidence interval for YLDs due to skin disease in the 2017 GBD ranges from 27.4 million to 61.9 million. This

confidence interval overlaps with the confidence intervals of many other disease classifications. This includes third placed neurological disorders on the high end (50.7 million–100.4 million) and fourteenth placed digestive diseases on the low end (13.9 million–27.9 million). There is therefore a large amount of variability when it comes to estimating the precise ranking of the disability burden of skin diseases; the 95% confidence interval could place it anywhere between third and fourteenth place.

Another issue that exists with the classification system used by the GBD study is the mutually exclusive classification of disease states. For instance, systemic lupus erythematosus (SLE) is solely classified under "other musculoskeletal disease" and is not classified as a skin disease, despite the fact that it often has cutaneous manifestations that will contribute to the overall disability burden of SLE.[3] The result of this is that the GBD study likely underestimates the impact of skin disease. In fact, it is plausible that skin disease has a number of hidden impacts and contributions to other disease classifications.

For instance, mental disorders (ranked as the second highest cause of disability with 122.7 million YLDs)[5] have a strong association with skin disease. According to Dalgard et al,[7] patients with skin diseases are significantly more likely to have depression (adjusted odds ratio (OR): 2.40; 95% CI: 1.67–3.47), anxiety (adjusted OR: 2.18; 95% CI: 1.68–2.82), and suicidal ideation (adjusted OR: 1.24; 95% CI: 0.95–1.62) compared to controls.[7] This suggests a hidden psychological burden of skin diseases that needs to be taken into account when performing a full assessment of the disease burden of skin diseases.

Another significant association of skin disease is the association with diabetes mellitus; "diabetes and kidney disease" was ranked as the sixth highest cause of disability with 45.9 million YLDs.[5] A significant contribution of this is likely to be attributable to the cutaneous sequelae of diabetes, such as foot ulcers and infection (as well as amputation, which may be necessary due to ulcers or skin infection). According to data from the 2016 iteration of the GBD, there were 2.5 million YLDs from diabetic foot ulcers, as well as an additional 1.5 million YLDs due to amputation.[8] This suggests a further burden of disease associated with skin disease that will not be strictly counted as skin disease in the GBD classification. Furthermore, leg ulcers have a particularly strong and well-established association with depression; Dalgard et al[7] found patients with leg ulcers to have the highest odds of depression (adjusted OR: 10.17; 95% CI: 4.07–25.41).[7]

There are also a number of infectious sequelae of skin disease that may lead to further disability. For instance, streptococcal skin diseases such as impetigo can lead to poststreptococcal glomerulonephritis, which creates a significant disease burden in developing countries.[9] In the 2017 iteration of the GBD[1], there were 1.05 million YLDs due to chronic kidney disease caused by glomerulonephritis[5]; it is likely a significant portion of this would have had a poststreptococcal aetiology. Additionally, skin diseases such as atopic dermatitis can predispose people to a number of infections that may spread beyond the skin due to impaired barrier function. For instance, Belden et al[10] found that patients with inflammatory skin diseases such as dermatitis and psoriasis were more likely to develop musculoskeletal infection.[10]

Another issue that may lead to underestimation of the disease burden of skin disease is related to the method used to calculate the weightings of diseases. The disability weighting of diseases in the GBD study is determined via large surveys of members of the public, rather than the experiences of people who have the disease.[11] Many skin diseases (such as psoriasis) are highly stigmatised, and it has been established that the quality of life impact of diseases with high levels of stigma are often underestimated by members of the public,[12] which will lead to an underestimation of the disability weighting of skin diseases such as psoriasis. It is also likely the stigmatisation will also lead to an underestimation of the prevalence of skin diseases due to under-reporting.[13]

Limitations in the geographic coverage of studies may also contribute to a global underestimation of the prevalence of skin diseases. For instance, when estimating the disability burden of skin disease in Sub-Saharan Africa, the GBD study used only 53 studies, compared to the 62 studies used to estimate the disability burden of skin in the United States, which has only a third of the population of Sub-Saharan Africa.[13]

Conclusion

The process of ranking worldwide causes of disability is highly dependent on the metric and disease groupings chosen; it almost becomes an arbitrary task because of this. According to Karimkhani et al[2] and Hay et al,[3] who compared skin diseases collectively against a number of Level 3 disease descriptors, skin diseases were indeed the fourth largest cause of disability worldwide.[2,3] However, according to the 2017 iteration of the GBD[1], based on Level 2 groupings of the GBD hierarchy only, and using YLDs as the primary metric, skin and subcutaneous diseases are in fact the ninth largest cause of disability worldwide, with a 95% confidence interval that could place skin diseases anywhere between third and fourteenth place.

Due to the limitations of the GBD study, it is probable that the disability burden of skin diseases is underestimated, and the true ranking is likely on the higher end of the confidence interval. A number of other disease classifications with high burdens of disease are either strongly influenced by skin diseases (most notably mental disorders),[7] or have skin diseases as a major complication (most notably diabetes),[8] and these are not counted by the GBD study. Furthermore, the prevalence of skin diseases is likely underestimated, particularly in developing countries, and the quality of life impact of skin diseases is also likely to be understated.[12,13] More study needs to be done to accurately quantify the burden of disability of skin disease worldwide, particularly in developing countries, and particularly focusing on lesser-recognised complications of skin disease, such as depression. This will be valuable for developing stronger public health policies internationally.

References

1. Kyu HH, Abate D, Abate KH, Abay SM, Abbafati C, Abbasi N, et al. Global, regional, and national disability-adjusted life-years (DALYs) for 359 diseases and injuries and healthy life expectancy (HALE) for 195 countries and territories, 1990-2017: a systematic analysis for the Global Burden of Disease Study 2017. Lancet. 2018 Nov 10;392(10159):1859-922.

2. Karimkhani C, Dellavalle RP, Coffeng LE, Flohr C, Hay RJ, Langan SM, et al. Global skin disease morbidity and mortality: an update from the global burden of disease study 2013. JAMA dermatol. 2017 Mar 1;153(5):406-12.

3. Hay RJ, Johns NE, Williams HC, Bolliger IW, Dellavalle RP, Margolis DJ, et al. The global burden of skin disease in 2010: an analysis of the prevalence and impact of skin conditions. J Investig Dermatol. 2014 Jun;134(6):1527-34.

4. Murray CJ, Vos T, Lozano R, Naghavi M, Flaxman AD, Michaud C, et al. Disability-adjusted life-years (DALYs) for 291 diseases and injuries in 21 regions, 1990-2010: a systematic analysis for the Global Burden of Disease Study 2010. Lancet. 2012;380(9859):2197-223.

5. Institute for Health Metrics and Evaluation [Internet]. [University of Washington]. GBD Compare; [date unknown][cited 12/10/2020]. Available from: https://vizhub.healthdata.org/gbd-compare/.

6. Steiner TJ, Stovner LJ, Vos T. GBD 2015: migraine is the third cause of disability in under 50s. J Headache Pain. 2016 Dec;17(1):1-4.

7. Dalgard FJ, Gieler U, Tomas-Aragones L, Lien L, Poot F, Jemec GBE, et al. The psychological burden of skin diseases: a cross-sectional multicenter study among dermatological out-patients in 13 European countries. J Investig Dermatol. 2015 Apr;135(4):984-91.

8. Zhang Y, Lazzarini PA, McPhail SM, van Netten JJ, Armstrong DG, Pacella RE. Global Disability Burdens of Diabetes-Related Lower-Extremity Complications in 1990 and 2016. Diabetes Care. 2020 May 1;43(5):964-74.

9. Rodriguez-Iturbe B, Musser JM. The current state of poststreptococcal glomerulonephritis. Clin J Am Soc Nephrol. 2008;19(10):1855-64.

10. Belden KA, Mascarenhas TR, Hendricks T, Merkow D, Chen AF. Skin Disease and Musculoskeletal Infection. Infect Dis Clin Pract (Baltim Md). 2020 Mar;28(2):71-7.

11. Salomon JA, Haagsma JA, Davis A, de Noordhout CM, Polinder S, Havelaar AH, et al. Disability weights for the Global Burden of Disease 2013 study. Lancet Glob Health. 2015;3(11):e712-23.

12. World Health Organisation [Internet]. [Switzerland]:[publisher unknown]; 2016. Global report on psoriasis; 2016. Available from: https://apps.who.int/iris/handle/10665/204417

13. Seth D, Cheldize K, Brown D, Freeman EF. Global burden of skin disease: inequities and innovations. Cur Dermatol Rep. 2017 Sep;6(3):204-10.

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Conflict of Interest

Christopher is a student reviewer for the New Zealand Medical Student Journal. This article has gone through a double-blinded peer review process applied to all articles submitted to the NZMSJ, and has been accepted after achieving the standard required for publication. The author has no other conflict of interest to declare.

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ACADEMIC: ABSTRACTS

The University of Auckland BMedSc(Hons) Abstracts

Reliability of freehand 3D ultrasound for assessment of in vivo triceps surae muscle volume in typically developing infants

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Introduction

Muscle volume is an important architectural parameter linked to the force-generating capacity of a muscle. Infant gastrocnemius and soleus muscle volumes have scarcely been investigated, despite the importance of these muscles in allowing gait and posture maintenance. A key consideration when utilising imaging modalities to assess muscle morphology is reliability. Reliability is vital to ensure that measurements of muscle volume are reproducible and consistent for a given setting. This is especially true given that infant populations possess structurally different muscles from adults. This study aims to assess the intra-acquirer, intra-rater and inter-rater reliability of freehand 3D ultrasound for the assessment of in vivo medial gastrocnemius (MG), lateral gastrocnemius (LG), and soleus (SOL) muscle volume.

Materials and methods

The MG, LG, and SOL volumes of both limbs in eight 3-month-old infants and nine 6-month-old infants were assessed using a freehand 3D ultrasound system. One researcher carried out the scanning, and two researchers independently processed the acquired scans to estimate muscle volume. All reliability measures were assessed using the intraclass correlation coefficient (ICC).

Results

Intra-acquirer, intra-processor, and inter-processor reliability ICCs were higher than 0.7 for both 3-month-old and 6-month-old participants (ICC range: 0.772–0.980).

Conclusions

The freehand 3D ultrasound system demonstrated good to excellent reliability and repeatability in muscle volume measurements in typically-developing infants in vivo. However, future investigations will be required to develop a complete model of typical muscle growth for comparison. Ultimately, 3D ultrasound may be a viable technique for facilitating diagnosis and management of neuromuscular conditions via muscle volume assessment.

Gastric dysrhythmias provoked in healthy subjects correlate with upper gastrointestinal symptoms

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Introduction

Gastric functional disorders are highly prevalent; however, diagnosis and management remain inadequate due to a lack of objective biomarkers. Evaluation of gastric electrophysiology may yield clinically useful biomarkers; however, whether gastric dysrhythmias and symptoms are correlated is yet to be established.

Materials and methods

A combined nicotine/meal stimulus was used to provoke upper gastrointestinal (UGI) symptoms in a group of 10 healthy subjects. Six of these subjects also underwent a non-nicotine control study. Gastric electrophysiology was evaluated using a novel body surface gastric mapping (BSGM) technique, alongside evaluation of UGI symptoms on a 0–10 scale. BSGM data and symptom scores were assessed for correlation.

Results

Nine subjects had symptomatic responses to the stimuli. The most commonly reported symptoms were nausea (median 4/10 severity) and excessive fullness (2/10). After the meal, frequency abnormalities were observed in 7/10 subjects, "uncoupled" (irregular) activity in 7/10, and pattern abnormalities in 5/10. No control arm subjects had symptomatic responses or abnormal gastric electrophysiology. In symptomatic subjects, 7/9 showed a clear correlation between symptom onset and abnormal electrophysiology, encompassing abnormal frequencies, aberrant slow wave propagation direction and uncoupled activity.

Conclusions

A new method of BSGM for measuring gastric electrical abnormalities was validated. The stimulus used was found to induce both symptoms and dysrhythmias, and the results suggest that some UGI symptoms, nausea in particular, have a close relationship with gastric dysrhythmias. In future, this method is likely to find use in the diagnosis of gastric functional disorders.

The pathogenesis of tonsillar hyperplasia in children

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Introduction
The surface area of the human palatine tonsils is extensive, with many folds and crypts. Bacterial microcolonies in tonsillar crypts have been implicated as a target of host inflammatory cells, resulting in chronic inflammation and substantial morbidity in children. Antibiotics are the primary medical treatment for both recurrent tonsillitis (RT) and sleep-disordered breathing (SDB), even though tonsillar microbiology is not well understood. The role of atopy in tonsillar hyperplasia is also largely unknown. We aimed to determine the underlying immunological and microbiological factors that may influence tonsillar hyperplasia in children.

Materials and methods
Paired tonsils were collected from 25 children undergoing tonsillectomy in the Auckland region. Immunohistochemistry and immunofluorescence techniques were used to identify local inflammatory cells and immunoglobulin isotypes. Fluorescence in situ hybridisation techniques were also used to determine the spatial distribution of specific bacterial species within tonsillar microcolonies.

Results
Strong immunoglobulin E (IgE) staining was observed in the tonsillar follicles and was associated with B lymphocytes. *Bacteroides* spp., *Fusobacterium* spp., *Streptococcus* spp., *Haemophilus influenzae*, and *Pseudomonas* spp. were all present in tonsillar microcolonies in decreasing quantities. *Bacteroides* spp., *Fusobacterium* spp., and *Streptococcus* spp. were most commonly located around the periphery of the microcolonies, while *H. influenzae* and *Pseudomonas* spp. were found nearer the centre.

Conclusions
This is the first study to determine and analyse the spatial arrangement of specific bacterial species within tonsillar microcolonies. These results advance our understanding of the microbiology and immune response of tonsillar hyperplasia and may provide promising avenues for developing effective treatments.

Using a novel adeno-associated virus screening method in primary mouse and human cells to optimise gene therapy for neurological disease

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Introduction
Gene therapy is an exciting treatment option for neurological disease. Adeno-associated virus vectors (AAVs) have emerged as the best vehicle for delivering therapeutic genes. Clinical translation requires specific, efficient vectors for human use and regulation of gene expression. Multiple AAV serotypes and promoters exist, but few have been comprehensively compared. A screening method was developed to identify the optimal AAV for delivering a novel gene regulation system.

Materials and methods
Primary mouse neurons were treated on day *in vitro* 8 (DIV8) with a panel of different AAVs expressing a green fluorescent protein (GFP) transgene. Cells were fixed, and immunofluorescence labelling and imaging was performed on DIV15. Primary human glioblastoma cells were cultured from brain biopsy tissue. AAVs were applied on DIV0 or DIV3 and cells were fixed for immunofluorescence detection and imaged on DIV7.

Results
AAVs containing GFP under control of the human synapsin promoter mediated strong GFP expression in mouse neurons. Purified AAVs caused toxicity at high concentrations, but mediated stronger GFP expression and less toxicity than crude preparations. Of 15 AAVs compared, AAVs 1 and 1/2 transduced the most neurons, 80% and 90%, respectively. GFP intensity was highest with AAV 1/2. AAV 1/2 was also the strongest serotype when part of the gene regulation system was inserted. AAVs 2 and 6.2 were the strongest transducers in primary human cultures.

Conclusions
These experiments have identified the optimum AAV serotype for insertion of a gene regulation system into mouse neurons. Human data suggests that AAV tropism is different between models.

Feasibility and development of a novel diagnostic tool: body surface colonic mapping

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Introduction
Current routine investigations of colonic motility and functional disorders are invasive or require ionising radiation, provide inadequate data on specific motility patterns, and fail to identify symptom-producing abnormalities. Recently, body surface electrical recordings have identified rhythmic colonic activity stimulated by food intake. This has led to a new clinical test called 'Body Surface Colonic Mapping' (BSCM). BSCM measures contraction frequency and spatial patterns, allowing high-resolution identification of complex contraction patterns.

Materials and methods
A literature review was completed to evaluate current investigations of colonic motility and functional disorders and their suitability as tools in the clinical environment. A physiological validation study following colonoscopy was undertaken with concurrent, time synchronised High-Resolution Colonic Manometry (HRCM) and non-invasive BSCM tests plus meal challenge. ITK-Snap was used to segment the colon between the upper rectum and splenic flexure in 41 de-identified computed tomography (CT) scans. Segmentations were transcribed to three-dimensional matrices to determine sigmoid colon position.

Results
Time synchronised HRCM and BSCM were conducted in three participants and stand-alone BSCM in one participant. A moderate correlation was identified between the manometry and BSCM methods (Pearson's correlation $r=0.43$; $P<0.0001$). This correlation indicates that the BSCM was reliably detecting the colonic activity, showing proof of concept for BSCM. Significant correlations were found between the positioning of anatomical surface markers and the maximal extent of Left and Right areas of interest.

Conclusions
BSCM is a clinically feasible diagnostic and research tool. It has potential to refine our understanding of, and the diagnostic criteria for, functional colonic disorders; provide patients with an explanation for their symptoms; and support biomarker-driven development of innovative therapies. Now that sigmoid colon position has been defined, and a colon-specific electrode array is in development, validation against gold standard HRCM is the next step toward clinical practice.

Myometrial and fetal hepatic oxygen delivery with maternal position: an MRI study

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Introduction
Maternal supine sleep position is an independent risk factor for stillbirth. Alongside reduced placental perfusion, oxygen delivery to the fetus is significantly reduced with the maternal supine position. Fetal adaptation to hypoxia involves increased shunt through the ductus venosus away from the fetal liver, therefore increasing cerebral perfusion and oxygenation. The delivery of oxygen from the maternal myometrium and fetal adaptation to changes in oxygen delivery have not been directly assessed.

Materials and methods
Twenty women 34–38 weeks' gestation with normal singleton pregnancy were recruited and underwent MRI using phase contrast and DECIDE MRI sequences in a 1.5T scanner. Segmentation of the myometrium, placenta, and fetal liver was performed with the patient in supine and left lateral decubitus positions.

Results
In the myometrium, perfusion decreased, but not significantly; however, the small effect was enough to decrease oxygen saturation in the supine position by 3% (p=0.03). This is consistent with aortocaval compression reducing both blood flow and oxygen delivery to the uterus and downstream, and with previous data showing a decrease in placental oxygen saturations in the maternal supine position in the same patients. Neither perfusion nor diffusivity of the fetal liver changed significantly, nor did oxygen saturation, which may point to the operation of hypoxic compensatory mechanisms.

Conclusions
Our results are the first to quantify the myometrial and fetal effects of position change, and are consistent with the concept of the oxygen margin of safety of the healthy fetus so that it may tolerate hypoxic stresses.

Exploring the role of dexamethasone on glioblastoma invasion

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Introduction
Glioblastoma (GBM) is an extremely malignant brain tumour with a median survival of 14.6 months. This is attributed to the increased invasiveness of a subpopulation of cells known as the glioblastoma cancer stem cells (gCSCs). Recently, dexamethasone (Dex), has been shown to reduce migration and further invasion of GBM. The interactions Dex has on these cells is unknown.

Materials and methods
The Cell Invasion and Migration (CIM) and sphere migration assay were used to measure the effects of Dex on NZB11 gCSC invasion. Flow cytometry and cytometric bead arrays were used to quantify the associated changes in invasion-related integrin, chemokine, and chemokine receptor expression.

Results
Dex treatment reduced invasion of NZB11 gCSCs by 77% (p=0.0627), 65% (p=0.0012), and 37% (p=0.0213) at 24hrs, 48hrs, and 72hrs respectively. Furthermore, Dex-treated gCSC spheres had a 41% reduction of migration (p=0.002) over laminin, when compared to the control, over the first 24hrs. Dex-treatment resulted in no changes to chemokine receptor expression, but increased integrin α3 expression by 23% (p=0.0392) and decreased integrin αv and β8 expression by 41% (p=0.0015) and 66% (p=0.0002) respectively.

Conclusion
These findings demonstrate that Dex treatment leads to reduced migration and invasion of gCSCs, with associated modulation of the integrins α3 and αvβ8.

Improving the lives of hydrocephalus patients – a novel brain implant

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Introduction
Hydrocephalus is a life-threatening neurosurgical condition. It involves an excessive accumulation of cerebrospinal fluid (CSF) within the cranial vault, and consequently, an increase in intracranial pressure (ICP). The gold standard management involves CSF drainage via a ventriculoperitoneal shunt (VPS). Within the first two years, 50% of VPS fail, and the signs and symptoms that follow are mimicked by common benign illnesses such as gastroenteritis or simple headaches. Thus, 70% of patients presenting with suspected VPS failure are false positives. To improve the accuracy of diagnosing shunt failure, a novel pressure sensor that will be fully implantable within the brain is being developed. The objectives of this project were to: i) carry out a preliminary risk analysis on the current design of the implant; and ii) in light of the device's non-tethered feature, assess the risk of the intraparenchymal implant displacing over time.

Materials and methods
An internationally-recognised standard for medical device risk management (ISO 14971) was implemented to guide the risk analysis. To assess the risk of implant migration, ten sheep underwent neurosurgery to insert two non-working implants, one in each cerebral hemisphere; and two small screws to the skull, one near each implant (20 implants). X-ray scans were taken postoperatively and three months later, and the screws were used as reference points to measure implant displacement.

Results
The non-tethering element of the implant design was identified as a potential critical risk and accordingly warranted further investigation. Following the in-vivo sheep study, the average absolute displacements of the 20 implants were 1.2 mm +/- 0.2 mm (horizontal) and 1.6 mm +/- 0.3 mm (vertical), relative to the two reference screws.

Conclusion
The findings indicate minimal displacement of the implants three months post-insertion. This suggests that the risk of inserting the implant without an anchor attachment to another anatomical structure is low. However, the study is ongoing, and a six-month follow-up scan, along with histological analysis of the brain tissue, will provide critical information on the long-term risk of the implant migrating. Before clinical translation, further studies to validate the safety of the implant will be required.

Management of severe or recurrent neonatal hypoglycaemia

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Introduction
Neonatal hypoglycaemia is a common and preventable cause of brain injury in infants. New, physiologically-targeted approaches are needed in newborns resistant to first-line management for hypoglycaemia to improve glucose stability, decrease interventions, and promote breastfeeding. Diazoxide is one such potential adjunctive therapy. The primary objective of this thesis was to determine the efficacy and safety of oral diazoxide for the treatment of neonates with severe or recurrent transitional hypoglycaemia in the first week after birth. A secondary objective was to determine the predictive value of continuous glucose monitoring (CGM) trend alarms for detection of blood glucose concentrations (BGC) outside the target range.

Materials and methods
Preliminary evidence for the use of diazoxide in transitional neonatal hypoglycaemia was obtained from a systematic review of the literature and a case series. These data informed the development and implementation of a phase IIB, placebo-controlled, randomised, two-arm, parallel trial of early oral diazoxide for treatment of severe or recurrent neonatal hypoglycaemia, the NeoGluCO Study (I). This included validation of the placebo and physicochemical testing of the active intervention. A real-time Guardian 3 CGM sensor (Medtronic) was inserted on the lateral thigh at enrolment.

Results
Evidence of low certainty, from one randomised controlled trial, suggests that early use of diazoxide therapy in late preterm and term infants admitted with transitional neonatal hypoglycaemia may reduce the duration of intravenous fluid therapy and time to full enteral feeding by two days. In transitional hypoglycaemia, use of lower doses of diazoxide appears to be effective in achieving euglycemia while avoiding hyperglycaemia. Suspension of diazoxide capsules in Ora Blend SF (10 mg/mL) provides a physicochemically stable intervention for at least 35 days. Ora Blend SF combined with a small amount of cornstarch is an effective placebo, with similar sensory characteristics to the active intervention.

Conclusion
The NeoGluCO Study (I) will determine if early use of oral diazoxide for severe or recurrent transitional hypoglycaemia promotes successful metabolic transition by decreasing the time to establish enteral bolus feeding and normal BGC without intravenous fluids.

An analysis of case fatality and community management among people suffering an acute stroke in Aotearoa New Zealand, 2014 – 2016

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Introduction
It is unknown what portion of decreasing stroke mortality trends in New Zealand are a result of decreasing trends in incidence or improvements in management and case fatality. This study aims to describe the 28-day and one-year case fatality in New Zealanders hospitalised with acute stroke, to describe medical management post-discharge, and to identify features associated with disparities in these outcomes.

Materials and methods
Using individual patient linkage across national datasets, New Zealand residents aged 25 or older hospitalised with stroke (excluding subarachnoid haemorrhage) between 2014 to 2016 were included. Deaths from any cause within 28 days and between 29 to 365 days following admission to hospital were used to calculate 28-day and one-year case fatality, respectively. Dispensing of antithrombotic medications, statins, and antihypertensive medications at 3 months, 6 months and 12 months post-stroke were used to calculate the proportions of patients with stroke appropriately treated in the community. Analyses were completed in age-stratified groups by prior history of stroke, sex, socioeconomic deprivation, and ethnicity. Multivariable logistic regression models adjusting for demographic features and comorbidities were used to determine the effect of these factors on case fatality at 28 days and one year post-stroke.

Results
A total of 22,547 people were included. After adjustment for demographic features and comorbidities, older age, female sex, intracerebral haemorrhage (OR 5.8, 95% CI: 5.2 to 6.5), unspecified stroke (OR 1.6, 95% CI: 1.3 to 1.8) and recurrent stroke (OR 1.3, 95% CI: 1.1 to 1.4) were associated with increased 28-day case fatality. Only older age was associated with increased one-year case fatality. Compared to people aged ≥75 years old, fewer people aged 25 to 64 years old were dispensed antithrombotic and antihypertensive medications, while fewer women and people aged ≥85 years old were dispensed statins compared to people aged 25 to 64 years old. Indians aged 25 to 64 years old were less likely than Europeans of the same age to be dispensed any of the three medication classes. Māori aged 25 to 74 years old were dispensed more antihypertensives and statins than Europeans of the same age.

Conclusion
This study found substantial differences by various demographic features in 28-day case fatality, one-year case fatality, and medical management. Further research to understand the cause of these disparities is required.

A novel technique for the non-invasive measurement of the cerebral metabolic rate of oxygen ($CMRO_2$) in a preclinical model

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Introduction
The brain is almost entirely dependent on oxidative metabolism. Changes in cerebral metabolic rate of oxygen ($CMRO_2$) occur in many neurological diseases, but often require invasive procedures to measure accurately. The aim of this study was to develop and validate a novel method to assess whole brain $CMRO_2$ in a rat model.

Materials and methods
$CMRO_2$ was assessed in anaesthetised Wistar rats (n=19, 270–396g) during randomised changes in inspired oxygen (21, 30, 40, 70 and 100% O_2). A perivascular probe was used to measure internal carotid flow. Non-invasive measures of oxygen saturation (SO_2) in the superior sagittal sinus (venous) and arterial circulation (pulse oximeter) were validated against direct measures of SO_2 in blood samples taken from the abdominal aorta and just distal to the retroglenoid vein, which drains the cerebral sinuses.

Results
There was no significant difference between venous SO_2 from photoacoustic imaging versus direct blood samples (mean absolute difference 8.60 ± 8.33% Hb, p=0.10). $CMRO_2$ (2.13 ± 0.70 $\mu mol \cdot g^{-1} \cdot min^{-1}$ by blood test results versus 2.79 ± 1.28 $\mu mol \cdot g^{-1} \cdot min^{-1}$ by novel method, p=0.02) was preserved across profound changes in arterial (43–100%) and venous (31–96%) SO_2. Bland-Altman analyses revealed a high degree of agreement between invasive and non-invasive measures of SO_2 and $CMRO_2$.

Conclusion
Our results confirm that our photoacoustic measure of venous SO_2 is comparable to the 'gold-standard' method using direct blood sampling. Thus, our non-invasive approach to measuring $CRMO_2$ appears to be viable.

Topical tranexamic acid in endoscopic sinus surgery

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Introduction
Bleeding after Endoscopic sinus surgery (ESS) is unpleasant for patients and generates significant costs. Tranexamic acid (TXA) is an inexpensive and widely used medication for the reduction of bleeding. Currently, the practice of the senior author is to use both topical and intravenous (IV) TXA during ESS to minimise bleeding. However, little is known about the safety and efficacy of this policy.

Materials and methods
To investigate this, three studies were conducted. First, a scoping review was used to investigate the effect of TXA on respiratory mucosa. A retrospective single-surgeon study was used to assess all comprehensive ESS cases at Waikato Hospital from January 2017–December 2019 for the safety and efficacy of combined IV and topical TXA. A randomised controlled trial (RCT) is being conducted to evaluate the immediate post-operative use of topical TXA with regards to bleeding and healing.

Results
Evidence from the scoping review suggests that TXA has no detrimental morphological or cytological effects on respiratory mucosa and may have a positive effect on healing. The retrospective study suggests that using both topical and IV TXA in ESS is safe and effective at minimising post-operative bleeding and scar formation. The randomised controlled trial is still ongoing, and to date, we have randomised 30 patients.

Conclusions
In this thesis we explore the use of topical TXA in ESS. There is evidence that topical TXA may be an ideal and low-risk wound dressing. We anticipate that the RCT will provide more evidence to support its use.

The effect of maternal consumption of oxidised fish oils on offspring skeletal development

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Introduction
Fish oils are rich in omega-3 polyunsaturated fatty acids (n-3 PUFAs) and are commonly consumed during pregnancy. N-3 PUFAs readily degrade into oxidised lipids, and exposure to oxidised lipids results in oxidative stress and potential growth retardation. This study examined the effect of maternal consumption of varying doses of oxidised lipids on femur length and growth plate development in male offspring at postnatal day 21. We hypothesised that maternal consumption of oxidised fish oil would lead to shorter femur length, abnormal growth plate organisation, and reduced hypertrophic chondrocyte cell area in the offspring.

Materials and methods
Five groups of Sprague-Dawley dams (n=42) were fed gels containing oxidised fish oils at known doses: a control group which received no fish oil, three groups fed 0.05mL of oxidised fish oil with peroxide values of 5, 10, and 40, and one group fed 1mL of oxidised fish oil of peroxide value 40. At postnatal day 21, offspring were weighed and culled, the femora and tibiae were removed and fixed. Femur length was measured using digital callipers, and proximal tibiae were processed for histology. Growth plate zone heights were measured from toluidine-stained sections of each tibia (n=5 per treatment group), and the cell area of hypertrophic chondrocytes was measured using haematoxylin and eosin Y-stained sections (n=4 per treatment group), and values were expressed as a mean and standard error of the mean (SEM).

Results
At post-natal day 2 there was significantly high mortality within PV40 and PV40^ offspring. At day 0, nose-to-anus length was shorter in PV40^ offspring compared to control offspring. At post-natal day 21, femur length was longer in PV40 and PV40^ male offspring compared to control offspring. Growth plate zone heights and ratios remained constant across treatment groups, and cell area of hypertrophic chondrocytes was constant as well.

Conclusions
The finding that femur length was longer in the highly oxidised fish oil treatment groups was contrary to the hypothesis of the study. As the growth plate zone heights, ratios, and cell area remained constant, differences in the organisation of the growth plate were not the cause of greater femur length. The longer femur length implies a period of more rapid skeletal growth, but this was not measured. Potential mechanisms for greater femur length include: 1) a survivorship bias, if in the groups with high mortality, death was non-random and animals that would have had smaller femurs were more likely to die; and 2) a biomimetic growth-accelerating effect of oxidation products such as isoprostanoids, which are suspected to have been present at high concentration in the oxidised fish oil. Despite the apparent growth-enhancing effect of oxidised fish oil, its use should not be encouraged during pregnancy, as it increased newborn mortality, and the effects on the adult offspring were not determined. Further research should include female offspring, and analysis at different time points such as GD20, PN2, and PN100.

The predictors of compassion in medical students: a systematic review and preliminary study of the origins of care in our future doctors

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Introduction
Despite being a mandated, foundational value in healthcare, compassion remains poorly researched. Existing work has contributed little towards the understanding of the origins of compassion, or identifying potential targets and avenues for compassion-enhancing interventions. In contributing to this area of work, the current thesis builds on studies in empathy – a related, but distinct construct with a stronger empirical base – to investigate a) the factors associated with compassion in medical students, and b) whether the factors that influence compassion vary across the course of medical training.

Materials and methods
Two studies, both based within the Transactional Model of Physician Compassion ("Transactional Model"), were conducted. In this view, compassion arises (or does not arise) from the interactions between student-related, patient-related, clinical, and environmental factors. In the first study, a systematic review identified studies assessing factors associated with compassion among medical students. Studies were synthesised within the four-domain framework of the Transactional Model. In the second study, data from an existing dataset on the barriers to compassion were analysed. Three-hundred and fifty-one New Zealand medical students in their clinical years (Years 4–6) completed measures of student-related, patient-related, clinical, and environmental barriers to compassion, and potential confounders. Analyses of variance and regressions were used to examine the effect of year level on each type of barrier.

Results
The review found that among the limited empirical work to date, the majority of studies have focused on the student-related factors associated with compassion. This focus has not only neglected three key areas of influence on compassion, but has also limited the study of factors to those that are generally "fixed" and therefore not amenable to intervention. In the second study, analyses indicated that Year 6 students reported higher student-related, patient-related, and environmental (but not clinical) barriers to compassion than Year 4 students; the degree of difference was comparable across the three barriers. Hierarchical regression confirmed that year level predicted barriers to compassion and showed that greater self-compassion consistently predicted lower barriers.

Conclusions
The combination of review and empirical work in this thesis suggests that current research on compassion in medical students remains limited in quantity, quality, and scope. A more multifactorial approach is needed in future studies to provide a fuller understanding of the influences on compassion in medical students and identify targets better suited to intervention. Given that the barriers to compassion vary in a way that suggests students find it harder to care for patients as they progress through training, the opportunity for intervention is clear. Directions for future research are discussed.

The reliability and measurement of muscle volume of the knee extensor muscle using magnetic resonance imaging in infants

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Introduction
Muscle growth through childhood is believed to impact further growth and development of an individual across the lifespan; however, very little is currently known about early muscle development through infancy—the most rapid period of growth. The aims of this study were to: i) establish reliability for the measurement of infant thigh muscle volume (MV) using magnetic resonance imaging (MRI) and ii) establish normative values for knee extensor MV in infants under the age of 6 months.

Materials and methods
A total of 24 typically-developing infants aged 0–6 months were recruited. Axial spin-echo T1-weighted proton density sequence MRI scanning took place in a 3T whole-body MR. Post-imaging analysis was conducted in 3D Slicer Medical Imaging software by two independent raters to assess and compare knee extensor MV by slice-by-slice manual segmentation. Scans were repeated by raters to establish levels of inter-rater and intra-rater reliability.

Results
Inter-rater reliability for all knee extensor muscles was excellent (Intraclass correlation coefficient (ICC))=0.914-0.954, n=15 limbs). Intra-rater reliability was excellent (ICC= 0.901-0.972) for the four knee extensors muscles (n=10 limbs), with vastus intermedius having the lowest reliability (ICC=0.901). Of 24 infants (median age 76 days (38.6 days), range 6–174 days), the MV for each part of the knee extensor muscles were as follows (mean ± SD): rectus femoris 6.2 ± 1.7 cm^3, vastus medialis 9.6 ± 2.5cm^3, vastus lateralis 20.7 ± 4.6cm^3, vastus intermedius 4.8 ± 1.1cm^3.

Conclusions
Quantification of knee extensor MV in 0–6 month old infants by manual segmentation is a reliable method of assessing infant muscle growth. Care needs to be taken with defining volumes of the vasti, as the indistinct borders and variable morphology make manual segmentation difficult to conduct, introducing variability in measurement. Inter-individual variability as large as 24.5cm^3 in the MV of one limb is evident from as young as 3 months of age.

INVITED FEATURE: MAORI HEALTH REVIEW SERIES

The assertion of Tino Rangatiratanga in tertiary education and by Iwi: The Tū Kahika foundation year health sciences scholarship at the University of Otago and the Te Rarawa Response to COVID-19

Nadine Houia-Ashwell

Introduction

Welcome to the fourth New Zealand Medical Student Journal (NZMSJ) Māori Health Review. This review was prepared in January 2021, after an unprecedented year that challenged Māori assertion of *tino rangatiratanga* (self-determination) by *iwi* (tribes), and also within the tertiary education sector. Over 50 *iwi* had developed pandemic response plans by April 2020,[1] with a number including checkpoints to protect those within their tribal boundaries.[2] Māori professors called for a nationwide review of universities, highlighting the Crown's failure to protect Māori staff and students,[3] following serious allegations of systemic and casual racism at the University of Waikato.[4]

In the context of Te Tiriti o Waitangi (Treaty of Waitangi), *tino rangatiratanga* guarantees the right of Māori to self-determination, that is, the advancement of Māori, as Māori. This includes the right to make decisions to advance their *whenua* (land), communities, cultural identity, and health and wellbeing.[5,6] However, differences in the translations of Te Tiriti o Waitangi have resulted in ongoing efforts to restore equality, honour Te Tiriti, and consequently, affirm Māori *tino rangatiratanga*.[7] Despite Aotearoa New Zealand's fluctuating political climate, the endeavour for Māori *tino rangatiratanga* remains constant and enduring.

In light of the recent Waitangi Day, the author encourages NZMSJ readers to consider how they can contribute to Māori aspirations for *tino rangatiratanga*, through reflecting on different expressions within the tertiary sector and by *iwi*, including the University of Otago's Tū Kahika Foundation Year Health Sciences scholarship and the Te Rarawa response to the coronavirus disease 2019 (COVID-19).

The Tū Kahika Foundation Year scholarship at the University of Otago

An important part of realising *tino rangatiratanga* for Māori health and wellbeing is to ensure a representative and culturally safe health workforce. There is currently a major and enduring under-representation of Māori in the health and disability workforce.[8-12] Increasing and upskilling the Māori health workforce has long been identified in New Zealand Government policy and strategy as an important priority for improving Māori health outcomes and reducing health inequities.[10,13-18] Over time, there have been some Māori health gains, including an increase in life expectancy, lower childhood mortality, and the wider adoption of healthier lifestyles.[13] While these developments in Māori health should be celebrated, significant and persistent inequalities remain. At present, health inequities for Māori are evident across many indicators, from before birth, through to old age.[13,14] Effort to eliminate these inequities is ongoing. Increasing the Māori health workforce is recognised as an important part of this *mahi* (work).[8,10,12,13,15-22]

A common approach for addressing inequities in the socio-demographic composition of health professions involves a "pipeline" framework, extending from the secondary school sector, to Tertiary Education Institutions (TEIs), through to health workforce employers (Figure 1).[12,23] This pipeline highlights a number of key areas for targeted recruitment and retention interventions, including early exposure activities for secondary school students and foundation programmes (such as Tū Kahika). These intervention points facilitate entry into tertiary courses by enhancing access to financial, pastoral, and academic support, as well as assisting with ongoing postgraduate and professional training.[23,24] The Tū Kahika Foundation Year Health Sciences scholarship fits into the pipeline schematic (Figure 1) as a recruitment intervention during the transitioning phase between secondary school and tertiary study.

Tū Kahika was first established in 2010 as a culturally responsive transition programme, providing holistic, wraparound support that prepares students for both their study in Health Sciences (particularly Health Sciences First Year (HSFY)), and a future career in Māori health.[25-27] Tū Kahika assists Māori secondary school leavers who may be socio-economically and/or educationally disadvantaged to enter into, and progress through, the Foundation Year Health Sciences Course at the University of Otago Language Centre and Foundation Year (UOLCFY).[25] Tū Kahika has seen a range of successes to date, including a retention rate of 98%, with many recipients (from 2010–2019) progressing into tertiary study at the University of Otago following the Foundation Year Health Sciences Course.[28] In addition, 60% of Tū Kahika scholarship recipients have completed or are currently completing health professional programme study, 25% have completed or are currently completing tertiary degree-level study at the University of Otago, and 15% have completed or are currently completing tertiary qualifications at other TEIs.[28] A further indication

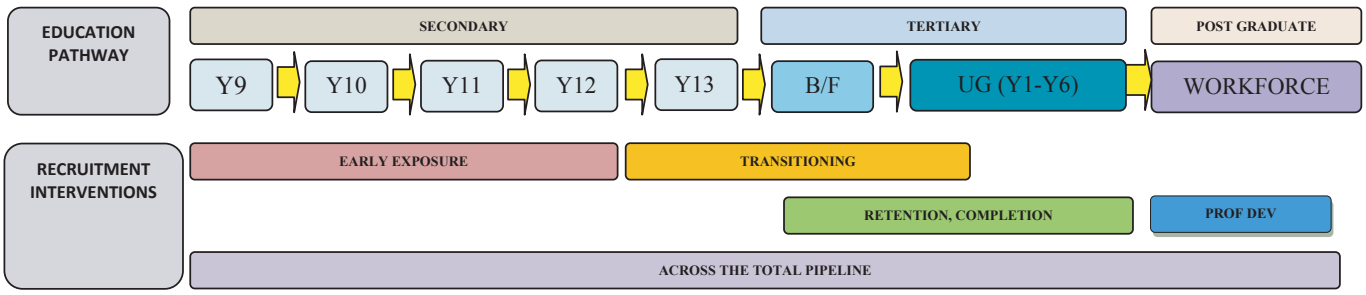

Figure 1. Schemata of the recruitment pipeline in the New Zealand context.[23]
Y=year; UG=undergraduate; prof dev=professional development.

of the programme's success includes an increase in the number of Māori students gaining entry into health professional programmes at the University of Otago.[26,29] Based on its successes to date, the Tū Kahika Foundation Year Scholarship is making a positive contribution towards the Māori health workforce.

A recently completed BMedSc(Hons) project sought to evaluate Tū Kahika via a Kaupapa Māori,[30] two-phase, mixed-methods quantitative and qualitative study. Results from this project identified a number of critical success factors for Tū Kahika, including *whakawhanaungatanga*, *mana motuhake*, *manaakitanga*, and *tino rangatiratanga* (Table 1).[31] These critical success factors may be applied in other educational settings where there is a genuine commitment to increasing Māori student participation in TEIs.

***Table 1: Critical success factors of the Tū Kahika Foundation Year Health Sciences scholarship*[31]**

Themes	Sub-themes
Whakawhanaungatanga	Becoming part of the Tū Kahika *whānau*
	Providing a sense of belonging at university
	Being surrounded by like-minded people
	Specific opportunities to *whakawhanaungatanga* (establish relationships)
	Tuākana-Tēina (older sibling-younger sibling relationship)
Mana motuhake	Learning efficient and effective ways to study at University
	Developing confidence to succeed at University
	Content preparation (the FYHS course)
Manaakitanga	Pastoral, academic, and financial support provided as part of Tū Kahika
Tino rangatiratanga	Providing a safe space for Māori
	Affirmation of Māori identity
	Shared aspirations of making positive contributions to Māori health

FYHS=Foundation Year Health Sciences

Whakawhanaungatanga is commonly referred to as the establishing of relationships.[32,33] However, in the context of Tū Kahika, *whakawhanaungatanga* is interpreted as fostering a sense of *whānau* (family) and community amongst Māori students, through working together to achieve goals and providing a wider peer-support network. The sub-theme *tuākana-tēina* is commonly known as the relationship shared between a *tuakana* (older sibling) and *teina* (younger sibling).[34,35] However, in the context of Tū Kahika, *tuākana-tēina* refers to when a more experienced or older Tū Kahika scholarship recipient helps and guides a new Tū Kahika scholarship recipient. In a learning environment that acknowledges *ako* (reciprocity), the *tuākana-tēina* roles may be reversed at any time, recognising the strength that both the *teina* and *tuakana* bring to the relationship. *Mana motuhake* is commonly translated to autonomy.[36] However, in this context, it refers to empowering students to have a positive university experience. Similarly, *manaakitanga* is often defined as being hospitable to others.[37,38] In this context, it is interpreted as the provision of holistic, wraparound support, which includes pastoral, academic, and financial support. The last critical success factor, *tino rangatiratanga*, is the prioritising of Māori student success at university. [31] This includes sub-themes such as providing a safe space for Māori at university, affirmation of Māori identity, and shared aspirations of making positive contributions to Māori health.[31]

Over recent months, Māori academics and students have fought relentlessly to assert and maintain Māori *tino rangatiratanga* within TEIs across Aotearoa.[3,4] The Tū Kahika Foundation Year scholarship is a modern-day application of Māori *tino rangatiratanga* within the tertiary education sector, and reflects the aspirations that Māori communities have towards making positive contributions to the health and wellbeing of our own people. The critical success factors described above may be transferrable to other educational settings where there is a genuine commitment to increasing Māori student numbers through the implementation of Māori-targeted recruitment interventions.

Te Rarawa response to COVID-19

While the *uri* (descendants) of Te Rarawa can be located across Aotearoa, and indeed across the world, Te Rarawa is one of the well-known autonomous, self-governing, and independent *iwi* located in Te Hiku o Te Ika a Māui (the Tail of the Fish of Māui). The boundaries of Te Rarawa are characterised by the fluid relationships shared with their neighbours, and can be found in the history of deep and complex tribal narratives as opposed to the prescriptive notion of land blocks. Taking this fluidity into consideration, Te Rarawa exercises *tino rangatiratanga* generally in the areas from Hokianga, east to Mangataipa, north along the Raetea and Takahue ranges, down the Pamapuria *awa* (river) to Maimaru, across towards Awanui, and west to Hukatere on Te Oneroa a Tōhē (Ninety-Mile Beach), then back down to Ahipara, south to Tauroa, Ōwhata, and Whāngāpe, and down the coastline to Mitimiti and back to Hokianga.[39]

When COVID-19 reached the tribal boundaries of Te Rarawa, the *iwi* not only had to respond to the realities and impacts of the COVID-19 lockdown, but also the most severe drought recorded to date. *Whānau* experienced extreme water shortages, and drastic water restrictions were imposed in order to preserve water.[40] The rural and isolated location of Te Rarawa created an added layer of complexity to the response. Despite these complicated circumstances, Te Rūnanga o Te Rarawa gained an essential service status under the COVID-19 alert level system, enabling the Rūnanga team to move safely around the *rohe* (territory) to serve and provide support to *whānau*.[40] Te Rūnanga o Te Rarawa is the Post-Settlement Governance Entity (PSGE) for Te Rarawa, and it has two arms: one for managing its commercial base, the rūnanga central office; and the other being its service delivery arm, Te Rarawa Anga Mua.

The author spoke to George Riley (Te Rarawa), the General Manager of Te Rarawa Anga Mua, in regards to the Te Rarawa response to COVID-19 (Zoom interview, 2020 May 14). He explained that at the start of COVID-19, the *iwi* was very aware of the limited resources they had to support *whānau*, so they carried out an information-gathering exercise to try and assess the need for, and therefore distribute, their limited resources to those who needed them most.

They obtained approximately 600 surveys from Te Rarawa *whānau*. The author also spoke with Reretai Hauiti (Te Rarawa), who works in Operational Communications for Te Rarawa Anga Mua, and was involved in the distribution of care and *kai* (food) packages to *whānau* (Zoom interview, 2020 May 14). Hauiti highlighted that Te Rarawa not only supported its own *iwi* members, but also the wider *whānau* of Te Hiku—"we distributed not only to the 23 Te Rarawa marae, but we also gave a lot to the other four *iwi* up here as well." The 2020 Annual *Iwi* Report revealed that Te Rarawa reached 796 *whānau*, delivering 1162 *kai* packs/vouchers and 1289 hygiene packs.[40] In addition, 189 *whānau* were referred to other services for support or supplies, and two health and education programmes were launched online, enabling *whānau* to engage from home. [40] An 0800-crisis line was also established to provide immediate support.

Makere Ngaropo-Haati (Te Rarawa) worked at a *hapu* (sub-tribe) level to support *whānau* during this time (Zoom interview, 2020 May 20). She reported that the stance the *hapu*, Ngāti Manawa, took to supporting their community could be explained through the motto coined by Mina Pomare-Peita (Te Rarawa), "*hapu* business is our business." Ngaropo-Haati reported that the *hapu* led a roadblock at Whakarapa, and initiated a *kaumātua-kuia* (elders) roll-out structure where *rohe kaitiaki* (regional caregivers) were assigned areas, similar to a neighbourhood watch or street wardens. Ngaropo-Haati explained that "they would check in with kaumātua-kuia to see if they needed *tautoko* (support) in some way or (if) they needed someone to pick up their kai or someone to pick their medication up." In addition, they were able to fast-track the opening of the local shop, so *whānau* wouldn't have to travel out of the area for essential grocery shopping. They also opened their own *pātaka kai* (community food pantry) to provide for *whānau* in need. This was particularly important for those *whānau* whose primary source of income was from forestry, as many forestry workers had recently been let go due to COVID-19.

The extreme circumstances of COVID-19, combined with the severe drought, called for extraordinary action to support those located in Te Hiku o Te Ika. Te Rarawa as an *iwi*, as well as *hapu* and *whānau*, mobilised quickly with local agencies and businesses to protect and support the community. The Te Rarawa response to COVID-19 is an example of *tino rangatiratanga* in action, and highlights that when resourced appropriately, our people are more than capable of taking an evidence-based approach to looking after and supporting our own people.

Conclusion

Māori assertion of *tino rangatiratanga*, within the tertiary education sector and by *iwi*, has, and continues to be, constantly challenged. The Tū Kahika Foundation Year scholarship at the University of Otago, as well as the Te Rarawa response to COVID-19, are modern-day applications of *tino rangatiratanga* that are inherently linked to the health and wellbeing of those Māori communities. Both Tū Kahika and the Te Rarawa response to COVID-19 not only reflect the aspirations of these communities, but are successful examples of Māori *tino rangatiratanga* in action today. The author encourages NZMSJ readers to reflect on other expressions of *tino rangatiratanga* that surround them, and how they might contribute to fulfilling the aspirations of Māori.

References

1. Watts K. Young Leaders' vision and wero. Paper presented at: Post-COVID19 reset: Transformational opportunities for a healthier, fairer, more sustainable Aotearoa; 2021 Feb 1-2; University of Otago, Wellington.

2. Biddle D-L. Coronavirus: Iwi band together for Covid-19 response, checkpoints to continue. Stuff [Internet]. 2020 Aug 15 [cited 2021 Jan 28]. Available from: https://www.stuff.co.nz/pou-tiaki/300082899/coronavirus-iwi-band-together-for-covid19-response-checkpoints-to-continue

3. Naepi S, McAllister T, Kidman J, Theodore R. Correcting the Course. E-tangata [Internet]. 2020 Sep 14 [cited 2021 Feb 14]. Available from: https://e-tangata.co.nz/comment-and-analysis/correcting-the-course/

4. Gabel J. Professors call out racism as a 'major issue' at universities. NZ Herald [Internet]. 2020 Sep 24 [cited 2021 Feb 14]: Education. Available from: https://www.nzherald.co.nz/nz/professors-call-out-racism-as-a-major-issue-at-universities/ZSQ2UDFJAMK2XHZEWDGTYLMXEA/

5. Durie M. Te Mana, Te Kāwanatanga: the politics of Māori self-determination: Auckland: Oxford University Press; 1998.

6. Wilson MA. The reconfiguration of New Zealand's constitutional institutions: the transformation of Tino Rangatiratanga into political reality. Waikato L Rev. 1997;5: 17-34.

7. Orange C. The Treaty of Waitangi. Wellington: Bridget Williams Books; 2015.

8. Health and Disability System Review. Health and Disability System Review - Final Report - Pūrongo Whakamutunga. Wellington: Health and Disability System Review; 2020.

9. Medical Council of New Zealand. The New Zealand Medical Workforce in 2018. Wellington: Medical Council of New Zealand; 2019.

10. Ministry of Health. He Pa Harakeke: Māori Health Workforce Profile: Selected Regulated health occupations 2007. Wellington: Ministry of Health; 2007.

11. Ministry of Health. Health of the Health Workforce 2015. Wellington: Ministry of Health; 2015.

12. Ratima M, Brown R, Garrett N, Wikaire E, Ngawati R, Aspin C, et al. Rauringa Raupa: Recruitment and retention of Māori in the health and disability workforce. Auckland: Taupua Waiora, Division of Public Health and Psychosicial Studies, Faculty of Health and Environmental Sciences, AUT University; 2008.

13. Ministry of Health. Whakamaua Māori Health Action Plan 2020-2025. Wellington: Ministry of Health; 2020.

14. Health Quality & Safety Commission. A window on the quality of Aoteroa New Zealand's health care 2019 - a view on Māori health equity. Wellington: Health Quality & Safety Commission; 2019.

15. Cram F. Improving Māori access to health care: Research report. Wellington: Ministry of Health; 2014.

16. Ministry of Health. He Rito Harakeke: Retention of Māori in the Health and Disability Workforce. Wellington: Ministry of Health; 2008.

17. Ministry of Health. He Tipu Harakeke: Recruitment of Māori in the Health & Disability Workforce. Wellington: Ministry of Health; 2008.

18. Ministry of Health. He Korowai Oranga: Māori Health Strategy. Wellington: Ministry of Health; 2002.

19. Ministry of Health. Whakatātaka Tuarua: Māori Health Action Plan 2006-2011. Wellington: Ministry of Health; 2006.

20. Ministry of Health. The Guide to He Korowai Oranga - Māori Health Strategy. Wellington: Ministry of Health; 2014.

21. Ministry of Health. Achieving Equity in Health Outcomes: Summary of a discovery process. Wellington: Ministry of Health; 2019.

22. Waitangi Tribunal. Hauora: Report On Stage One Of The Health Services And Outcomes Kaupapa Inquiry. Wellington: Waitangi Tribunal; 2019.

23. Curtis E, Wikaire E, Stokes K, Reid P. Addressing indigenous health workforce inequities: A literature review exploring 'best' practice for recruitment into tertiary health programmes. International journal for equity in health. 2012 Mar 15;11(1): 1-15.

24. Cram F. Shifting Māori Health Needs - Māori Population Trends, health service needs and medical workforce requirements - issues arising. Wellington: Ministry of Health, 2010.

25. Maxwell-Crawford K. The Otago University Māori Health Workforce Development Project. Wellington: Reanga New Zealand Consultancy Ltd; 2012.

26. Universities Academic Quality Agency for New Zealand. Report of the 2016 Academic Audit of the University of Otago - Te Whare Wānanga o Otāgo: Cycle 5 academic audit undertaken by the Academic Quality Agency for New Zealand Universities. Wellington: Universities Academic Quality Agency for New Zealand ;2016.

27. University of Otago. Tū Kahika: A Health Sciences scholarship programme for Māori. University of Otago [Internet]: University of Otago; 2021 [cited 2021 Jan 14]. Available from: https://www.otago.ac.nz/mhwdu/tukahika/

28. Feeney S. Tū Kahika: A Culturally Responsive Foundation Year Programme. Paper presented at: LIME Connection VIII - Pouhine Poutama: Embedding Indigenous Health Education; 2019 Nov 5-8; University of Otago, Christchurch.

29. Crampton P, Weaver N, Howard A. Holding a mirror to society? Progression towards achieving better sociodemographic representation among the University of Otago's health professional students. NZMJ. 2018; 131(1476):59-69.

30. Katoa Ltd. Kaupapa Māori Research [Internet]. [place unknown]: [publisher unknown]; 2021 [cited 2021 Mar 8]. Available from: https://www.katoa.net.nz/kaupapa-maori

31. Houia-Ashwell N. E Tū Kahikatea: An Evaluation of the Tū Kahika Foundation Year Scholarship at the University of Otago [Honours]. Wellington: University of Otago; 2020.

32. Bishop R, Ladwig J, Berryman M. The centrality of relationships for pedagogy: The whanaungatanga thesis. Am J Educ Res. 2014 Feb 1;51(1):184-214.

33. McNatty W, Roa T. Whanaungatanga: An illustration of the importance of cultural context. He Puna Korero: Journal of Māori and Pacific Development. 2002 Feb;3(1):88.

34. Ministry of Education. Te Aho Arataki Marau mō te Ako i Te Reo Māori - Kura Auraki: Curriculum Guidelines for Teaching and Learning Te Reo Māori in English-medium Schools: Years 1-13 [Internet]. [place unknown]: Learning Media Limited; 2009 [cited 2021 Feb 18]. Available from: https://tereomaori.tki.org.nz/Curriculum-guidelines

35. Ministry of Education. Teaching Methods [Internet]. 2020 [cited 2021 Jan 12]. Available from: https://tereomaori.tki.org.nz/Curriculum-guidelines/Teaching-and-learning-te-reo-Maori/Aspects-of-planning/The-concept-of-a-tuakana-teina-relationship

36. Hawksley C, Howson R. Tino rangatiratanga and mana motuhake: Nation, state and self-determination in Aotearoa New Zealand. AlterNative: An International Journal of Indigenous Peoples. 2011;7(3):246-57.

37. Duncan S, Rewi P. Tikanga: How Not to Get Told Off! In: Reilly M, Duncan S, Leoni G, Paterson L, Tai Ratima M, editors. Te Kōparapara: An Introduction to the Māori World. Auckland: Auckland University Press; 2018. p. 30-47.

38. Ka'ai T, Higgins R. Te Ao Māori - The Māori Worldview. In: Tania Ka'ai T, Reilly M, Mosley S, editors. Ki Te Whaiao: An Introduction to Māori Culture and Society. Auckland: Pearson Education New Zealand; 2004. p. 13-25.

39. Te Rūnanga o Te Rarawa. History: Tāhuhu Kōrero: Te Rarawa Iwi Narrative [Internet]. [place unknown]: [publisher unknown]; 2021 [cited 2021 Jan 18]. Available from: https://www.terarawa.iwi.nz/history/history-of-iwi

40. Te Rarawa. Te Rūnanga o Te Rarawa: Annual Report - Pūrongo-ā-Tau: For the year ended 30 June 2020 [Internet]. Kaitaia: Te Rūnanga o Te Rarawa, 2020. Available from: https://www.terarawa.iwi.nz/files/about/2016-te-rarawa-annual-report-2016-(id-15797)-web.pdf

About the author

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Conflicts of Interest

Nadine Houia-Ashwell (Te Rarawa, Ngāpuhi, Ngāti Porou, Kāi Tahu) is a previous Tū Kahika Foundation Year Health Sciences Scholarship recipient (2013) and completed the BMedSc(Hons) project, "E Tū Kahikatea: An Evaluation of the Tū Kahika Foundation Year Scholarship at the University of Otago" in 2020. Nadine has *whakapapa* (ancestry) to Te Rarawa and is a registered *iwi* member. Nadine received a scholarship from Te Rarawa in 2019 for her medical studies. This invited article has gone through a double-blinded peer review process applied to all articles submitted to the NZMSJ, and has been accepted after achieving the standards required for publication. The author has no other conflict of interest to declare.

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INVITED FEATURE: STATISTICS PRIMER

Sample size in health research

Ari Samaranayaka, Claire Cameron, Robin M. Turner

What is sample size and why does it matter?

How big should my sample be? Will I have enough statistical power? How much precision will my estimates have? These are important questions asked by researchers while designing a study. When the study is over, the researcher may ask: why was my result significant or why was it not significant? Could it be related to the sample size achieved in the study? This leads to the critical questions; why is sample size important, and when should it be considered in the research process?

Loosely speaking, an a-priori sample size estimate is the optimum number of items (usually individuals) that should be included in the study in order to answer the research question.

Sample size determination is an integral part of the research process

There are two types of analyses where the sample size estimate is pivotal in the design of the study:

1. A study where you wish to estimate a quantity with a certain level of precision. Prevalence studies are a common example of this where you may want to estimate the proportion of people in the population with a particular disease.
2. A study where you are testing a hypothesis, i.e. when you will be using a P value (see our Statistics Primer in issue 31[1]). One of the most common examples of this would be when comparing two groups to see if they have different effect estimates (e.g. means or proportions). We often call this difference the "effect size".

The process of deciding on the statistical analysis plan requires the best guess at which differences/variabilities are expected in the outcome measure. This often leads to refinement of the research question (see Figure 1) as the outcome measure and study design have to be precisely defined: they directly influence the analysis plan and the sample size calculations. In practice, the initial calculations can produce a sample size that cannot be achieved within practical limitations. In such cases, changes need to be made (in consultation with content experts) to the analysis plan, and even to the research aims, so that an achievable sample size estimate can be obtained. This iterative process is the norm in the development of most studies. The determination of sample size cannot be seen in isolation; it is an integral part of the overall study design process.

The approach taken for a particular study depends entirely on whether the research question, and subsequent analysis plan, are about an estimation (Approach 1) or testing a hypothesis (Approach 2). Therefore, sample size determination cannot be separated from the other components of the design process.

These two approaches are illustrated below, using simple study designs as examples. Unlike other disciplines where the experimental environment can be tightly controlled, health-related studies often have

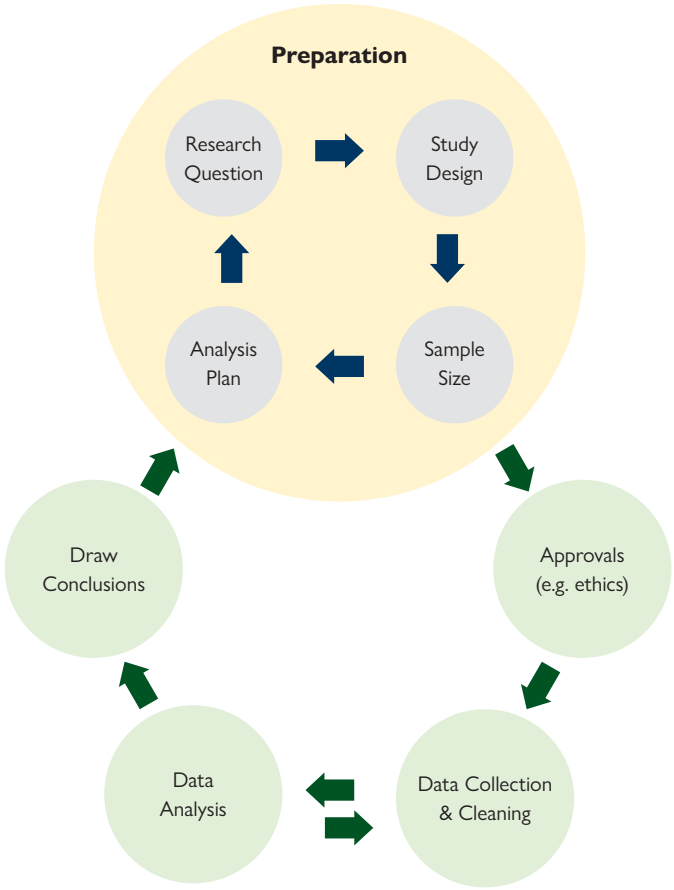

Figure 1: Place of sample size calculation within the research process

to use observational study designs. This means that we may need to account for potential confounders in the analysis. Other complexities can sometimes arise, such as needing repeated measurements from each individual, meaning that the measurements are no longer independent (which is one of the assumptions underpinning many standard statistical methods). The analysis plan will need to be tailored correspondingly to account for situations like these. In some instances, these adaptations can lead to complex analyses, which require customised approaches to sample size determination. These customised approaches may require simulations or other complex methods. We have chosen simple study designs below to illustrate the application of these two approaches.

Approach 1

To illustrate the precision-based approach, consider a survey aiming to estimate the prevalence of a chronic health condition, such as di-

abetes. For simplicity, assume that we have a simple random sample, meaning that every person in the population has an equal chance of being selected for the survey. Suppose that, based on our knowledge of the literature, we expect the prevalence of this disease to be approximately 0.2 (20%). We want the 95% confidence interval around our estimated prevalence to be no wider than 0.16 to 0.24, i.e. no wider than 0.20 ± 0.04. We call this '0.04' the half width of the 95% confidence interval. This is also known as the "margin of error". Under this study design, the confidence interval can be estimated as

$$P \pm Z\sqrt{\frac{P(1-P)}{N}}$$

In this equation, P is the prevalence estimate (0.20 in this case), Z is the value from the standard normal distribution corresponding to 95% (which is 1.96), and N is the study sample size. The precision of our estimate is determined by the half-width of the 95% confidence interval (the quantity on the right-hand side of ± sign). We need to find a sample size N that makes this quantity = 0.04 or lower. Putting this information together gives the following expression:

$$0.04 \geq Z\sqrt{\frac{P(1-P)}{N}}$$

This can be rearranged to determine the sample size:

$$N \geq Z\left(\frac{Z}{0.04}\right)^2 P(1-P)$$

This becomes N≥385 for our example where Z=1.96 and P=0.20. Note that we always round up to the next integer when estimating sample size (for both approaches). This is because if we round down, our sample size will be slightly too small, and our confidence interval will be slightly wider than required.

The estimation of the confidence interval is not only dependent on the sample size, but also on our initial guess of the prevalence (P). However, given the aim of this study was to estimate the prevalence (P) in the first place, we might not know what value of P to use in order to include it in the sample size estimation. What can we do if we don't have an approximate value? Prevalence must lie between zero (no one has the disease) and one (everyone has the disease). It is helpful to know that the quantity P(1−P) in our equation takes on a maximum value when P=0.5, and a minimum when P=0 or P=1 (pull out your calculator and check this for varying values of P). Therefore, the sample size corresponding to P=0.5 is the largest and the most conservative sample size (i.e. our sample will always be large enough regardless of the prevalence value). However, if the required precision changes (i.e. the half-width is bigger or smaller), then the sample size will also change.

Approach 2

This approach can be more challenging, due to the fact that the sample size estimates are particular to the hypothesis test that you have decided will answer your research question. There are a number of commonly used simple hypothesis tests, including the independent samples t-test and the paired t-test for investigating the difference between two means, and the binomial test for investigating the difference between two proportions.

Statistical power is a concept that arises out of hypothesis testing. With a hypothesis test, we are trying to make an inference about the population while looking at the results of a study. There are two errors that can be made when using hypothesis tests. You could, for example, incorrectly conclude that there is a difference between the means of two groups when there really is no difference in the population. Alternatively, you could incorrectly state that there is no difference in those means when, in fact, there is a real difference in the population. This second type of error is related to "statistical power". The power of a hypothesis test is the probability of finding an effect (i.e. the difference between two groups), if this really exists. When you are running a study, you want this probability to be high, to ensure that you do not miss a real effect, if it exists. The size of your sample, along with the variability in the measures you are using, directly impacts the amount of statistical power that your study will have.

Formulae used in every statistical hypothesis test can be rearranged to estimate sample size, based on the assumptions about the power, variability, and the difference you are trying to detect. In order to estimate the sample size, you need to have a good understanding of the difference that you are trying to detect. This difference should be the minimum clinically important difference (also known as the "effect size"). This is one of the more difficult parts to guess at when initially designing the study, and has a critical impact on the estimated sample size. Guessing an appropriate value for this is not a biostatistics question. For example, a study could be designed to detect a 1 mmHg difference in systolic blood pressure between two groups. Is this 1 mmHg difference an important difference clinically? What about a 5 mmHg difference? If the study was powered to detect a 15 mmHg difference but missed a 10 mmHg difference, is that a problem? These are the questions to be considered by content experts when looking at the minimum clinically important difference. Other critical information needed when estimating sample size is the expected variability of the measure. If an approximate value for this cannot be found from the literature, then pilot studies can be useful not only to test out all aspects of the design, but to inform future sample size estimates for the main study.

There are formulae available to calculate the sample size for many commonly used hypothesis tests.[2,3,4] Alternatively, there are some good online calculators that exist, although we suggest that you check which assumptions they make, and that they reference the particular formulae they are using. Using a calculator is a good way to understand how the minimum clinically important difference (or other measures of interest, such as variability or the desired level of power) may impact on sample size for an assumed significance level. The significance level (usually set at 5%) is the level below which a P value will be considered "significant", although we do not advise significance be based on a P value alone[1].

If you change the following values one at a time, you will notice that the required sample size is large:

1. When the effect size of interest is small
2. If the variability is large
3. If higher statistical power is needed
4. If the selected significance level is smaller

The estimated sample size (from both approaches) then needs to be scaled up to account for things like participation rates and loss to follow-up, otherwise the final analysis will not have sufficient participants to meet the sample size requirements, and the study will be considered under-powered.

Sample size calculations are not applicable for some studies. Pilot or feasibility studies, proof of concept studies, and clinical audits do not aim to estimate a quantity with a given precision, or to test something with specific power, therefore, a formal determination of sample size is not applicable. Even though formal sample size calculations may not be required, it is still important to consider whether the sample size is big enough for the desired purpose; is the pilot study large enough to be able to pilot all features of the trial and obtain reasonable information to inform the full trial in future?

Sometimes researchers decide that it is not possible, for practical reasons, to use the sample size appropriate to answer their research question. We sometimes see statements like, "Our non-significant results could be due to our small sample size." The problems with this statement are (1) it assumes that they would have obtained a significant result if they had had a larger sample when there is no evidence to support that claim, and (2) it attempts to justify running an underpowered study. In order to support such statements, some researchers calculate the statistical power of the already conducted study to show the insufficiency of the power (this is called a *post hoc*

power calculation). No *post hoc* power calculation is acceptable, nor can it be used as a substitute for a sample size calculation in the initial stages of designing and planning a study.

In summary, sample size estimation is an educated guess to ensure that the effect of interest is likely to be detected if it really exists, or that the precision will be of a certain magnitude. The sample size calculation is therefore an integral aspect of the research study design process, which cannot be viewed in isolation. The process of estimating sample size helps clarify the research question and the analysis plan. It requires input from content experts, and cannot be done purely by a biostatistician without a deep understanding of the design, analysis plan, and outcome measures. In reality, sample size estimates can be complicated by many factors, such as contamination of interventions, non-independence of participants, longitudinal outcome measures, design effects, and covariate adjustments, to name but a few. Obtaining professional input in the initial stages of the design process is highly recommended in these complicated situations, preferably by including a biostatistician as a member of your research team.

References

1. Cameron C, Samaranayaka A, Turner RM. P values: What are their significance? NZMSJ (31):48-49.

2. Machin D, Campbell MJ, Tan SB, Tan SH. Sample size tables for clinical studies. 3rd ed. Wiley-Blackwell; 2009.

3. Armitage P, Berry G, Matthews JNS. Statistical methods in medical research. 4th ed. Oxford: Blackwell Science; 2002.

4. Chow SC, Shao J, Wang H, Lokhnygina Y. Sample size calculation in clinical research. 3rd ed. New York: Chapman & Hall; 2018.

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FEATURE ARTICLE

Undergraduates' medical education in the time of COVID-19: Lessons learned & strategies formulated from and for low and middle income countries.

Shibu Sasidharan, Harpreet Dhillon

Introduction

The coronavirus disease 2019 (COVID-19) pandemic has led to unprecedented disruptions to medical training. During the COVID-19 dilemma, all human effort is being harnessed to meet this unprecedented challenge. While many natural disasters, attacks, and epidemics have challenged the delivery of education in the past, nothing compares to the level wreaked by this potentially fatal pandemic. Widespread interruptions to medical education are seen throughout history.[1,2] At times of major conflicts, the quality of training suffers as a result. For example, during the blitz[2], students and newly qualified interns were distributed to areas of need. Also during World War II, certain American medical schools shortened their postgraduate degree programme from four years to three years to address doctor shortages.[3] Despite the disruptions, there are always silver linings. After the two world wars, there have been radical reforms in the medical education system, leading to improvement of the curricula and intake, including an increase in women admissions to medical schools.

While the need for medically trained doctors has never been so important globally, preparing doctors couldn't be more challenging. Worldwide, virtual classrooms (with flipped and blended learning approaches) are now the norm, the bedside has changed to the "Webside of Telemedicine", and Competency Based Medical Education (CBME)[1] is being taught to a large extent using Simulation Based Medical Education. In India, for instance, CBME was embarked upon in 2019 for undergraduate (UG) batches throughout India, to produce competent Indian medical graduates with training skills in Empathy, Ethics, Attitude, and Communication[2] (the AETCOM Module), with early preclinical exposure.

Distance e-learning is defined as using computer technology to deliver training, including technology-supported learning either online, offline, or both. It is aimed at the effective construction of knowledge regarding individual experience, practice, and knowledge of the learners and students. Internet-based learning, computer-based learning, virtual classrooms, and digital collaboration all represent different types of e-learning.

There are two modes of e-learning: distance learning and computer-assisted interaction (CAI). Moore et al. defined distance e-learning as providing access to learning for those who are geographically remote from the instructor, while CAI is an interactive technique whereby instructional material is presented by and a computer, and a students' progress is monitored and evaluated during this process.

In this article, using the model of Democratic Republic of the Congo (DRC), authors like to discuss how in many other low- and middle-income countries (LMIC) like the DRC, the practical and logistical trials are immense, and things are far from the "norm" of other developing countries.

Unique health implementation problems in the DRC

Before suggesting recommendations for medical education in low-income countries like the DRC, it is important to fully appreciate the complexities and challenges for each of the considered countries. In this lies the key to achieving a better quality of education. The DRC's current situation with respect to health is described below:

1. POOREST COUNTRY IN THE WORLD

While its poverty rate has fallen to some extent over the past 20 years, particularly in rural areas, the DRC nevertheless remains one of the poorest countries in the world.[3] The DRC is one of the countries with the highest maternal and child mortality ratios in the world.[3] Women have an average of 6.6 children; and 42% of women in the 15–19 year old age group are either mothers, or pregnant with their first child. For every 1,000 children born, 58 die before the age of one, and 104 die within the first five years of life. Chronic malnutrition affects 43% of children under the age of five.[4]

2.MARKEDLY LOW EDUCATION

The DRC ranks 135/157 in terms of human capital. It has a human capital index score of 0.37%, which is below the average in Sub-Saharan Africa (0.40%).[3] This means that a child born today will be 37% less productive than another child receiving complete education and healthcare in other parts of the world. Congolese children, on average, spend only 9.2 years in school, and more than 43% of children are malnourished.[3] There are eight medical schools in the DRC.[5]

3. HIGH DEMAND FOR HEALTHCARE

Long before COVID-19, infectious diseases have swept throughout this country. Hepatitis A, Ebola, measles, malaria, lower respiratory tract infections, tuberculosis, diarrheal diseases, and human immunodeficiency virus/acquired immunodeficiency syndrome (HIV/AIDS) are some of the major causes of death. Neonatal disorders, ischemic heart disease, stroke, congenital defects, and road traffic injuries are the major remaining contributors.[6] Mental health and the consequences of violence are major public health challenges. With significant cases under each category, along with malnutrition and other diseases, the demand for healthcare is immense.

4. INSUFFICIENT RESOURCES

Health financing in the DRC is almost totally dependent on external

aid, which is essentially based on humanitarian assistance. COVID-19 has frozen many external supplies of funds, due to allocation of those funds into the respective countries' own health systems. With no public funding, and fragmented national leadership, the regulation of the health sector is essentially broken. Developing a strategy for medical education with such scarce funds is unthinkable.[7]

5. DYSFUNCTIONAL HEALTHCARE SYSTEM

The lack of a strategy for developing organised human resources for health, combined with stopping recruitment in the public health service for more than 20 years, has led to the dwindling of healthcare worker (HCW) densities in the DRC. With 0.28 physicians and 1.91 nurses and midwives per 10,000 people, the DRC has one of the lowest numbers of skilled health professionals and medical educators in the world.[4] The existing health sector workforce is also aging, and the quality of work has been considerably compromised.[7]

Above all, chronic political instability, social unrest, and armed conflict have made it difficult for the DRC to increase domestic spending on health care and education. Now, COVID-19 has spelled out uncertain and uncharted territories, and we are all grappling to find alternatives for the new norm.

Challenges to education

1. No face-to-face teaching is a challenge. Medical students in face-to-face classes have a consistent schedule that is easy to follow, guided by regular physical classes where they can be taught the "science and art" of the practice of medicine. Online classes make it the students' responsibility to ensure they stay organised and follow the class.[8]
2. Educators need to cope with clinical responsibilities. While the whole world, and especially DRC, is struggling with the magnitude of patients, an already considerable deficiency of doctors makes coping with the clinical load and online classes especially demanding.
3. A top-down process from educators to students, with no, or hardly any, input from students, is an established hindrance to learning, irrespective of the domain.[1]
4. In the traditional teaching format, there are long hours of classes, but with online classes, there is a need to re-invent teaching styles, time frames, and methodologies.
5. Other factors affecting teaching/classes worldwide are:
   a. Lack of COVID-19 testing facilities
   b. Decreased attendance of patients in outpatient departments (OPDs)
   c. Cancellation of elective surgical cases
   d. Lack of personal protective equipment (PPE)
6. Assessments are a vital component of competency-based education.[9] In addition to making pass/fail decisions, an essential role of assessments is to provide feedback to the learner and help him/her to improve their learning. Assessments occur in the practical laboratory, skills laboratory, and skills station using mannequins, paper cases, simulated or real patients, as the context demands. These cannot be evaluated in an online scenario.

Recommendations

In the face of the current situation, coping can be planned by identifying the problem and approaching it using the following mechanisms:

1. Adjust your camera to the eye level and find a quiet area
2. Encourage learners to connect to both audio and video
3. To minimize background noise, mute participant's and encourage them to unmute as needed[10]
4. If hosting a video conferencing session, start the session a few minutes early. Enable the "waiting room" as needed and admit participants once the speaker is ready
5. Orient learners to all different options to interact (eg, chat, nonverbal feedback, unmute)
6. Schedule faculty development or orientation sessions for educators to review use of software before teaching sessions[11]
7. Place the chat window in a visible location on the screen while teaching, or designate a chat moderator to consolidate and verbalize questions
8. Set up an "ice breaker" poll and introduce participants to software features
9. Consider the use of standardized patients via video conferencing platforms
10. If internet connectivity is poor, consider assigning a cohost to ensure that the meeting remains active[12]
11. In a setting like "Grand Rounds," consider unmuting all participants at the end of a session to allow for applause
12. Consider sharing meeting links privately to minimize intrusion by unwanted participants. If shared more publicly, adjust security settings (eg, limit chat, unmuting) to avoid disruptions[13]
13. For recurring sessions with the same group, consider using one meeting link[14]

Conclusion

With advances in technologies and social media, distance learning is a new and rapidly growing approach for undergraduate, postgraduate, and health care providers. Regardless of reported benefits, medical students preferred the blended approach in teaching as distance learning represented a major challenge to acquire adequate clinical medical skills. Satisfaction in distance learning is strongly linked to students' prior experience in distance learning as well as instructors' experiences and interactions.[15] Technical and infrastructural resources reported as a major challenge for implementing distance learning, so understanding technological, financial, institutional, educators, and student barriers are essential for the successful implementation of distance learning in medical education. While the integration of technology is a critical and required part of medical education, it should not cause overreliance, or decrease our human skills like compassion and empathy, which form the core cultural value of DRC. Therefore, as we cultivate plans to reintroduce elements of face-to-face teaching, we need to ensure that these nuances are also integrated with medical education.[16] There is also a need for leveraging funds from donors and finding innovative financing models to improve medical infrastructure and education. The need of the hour is to think outside the box and set objective standards for the online format of classes. We need forward thinking and scholarly approaches in order to review the curriculum for future doctors and find solutions to having a near-authentic patient experience.[17] When used optimally and despite their inherent limitations, virtual tools can be used by both learners and educators to achieve a shared goal of providing effective and efficient medical education to train our next generation of physicians. At the same time, in LMICs like the DRC, what we need to prioritise is that education does not stop. While this is a time for both students and medical educators to help contribute to the advancement of medical education, and to formulate skills for the times ahead, this could also be the defining time in history when the new code of medical education is written.

References

1. Harris P, Snell L, Talbot M, Harden RM. Competency-based medical education: implications for undergraduate programs. Med Teach [Internet]. 2010 Aug [cited 2020 Jul 16];32(8):646–50. Available from: https://www.tandfonline.com/doi/abs/10.3109/0142159X.2010.500703

2. Supe A. Graduate Medical Education Regulations 2019: Competency-driven contextual curriculum. The National Medical Journal of India. 2019 Sep 1;32(5):257-61.

3. The World Bank. Democratic Republic of Congo Overview [Internet]. [updated 2020 May 4; cited 2020 Jul 14]. Available from: https://www.worldbank.org/en/country/drc/overview

4. Ministère du Plan et Suivi de la Mise en oeuvre de la Révolution de la Modernité (MPSMRM) Ministère de la Santé Publique (MSP) et ICF International. Demographic and

Health Survey (DRC-DHS II 2013–2014): supplemental vaccine-preventable diseases report: a serosurvey of population immunity to measles, rubella, and tetanus among children 6–59 months.

5. Geneva Foundation for Medical Education and Research. Medical schools, governments, ministries, medical associations: Democratic Republic of Congo [Internet]. [updated 2020 June 12; cited 2020 Jul 14]. Available from: https://www.gfmer.ch/Medical_search/Countries/Congo_Democratic.htm

6. Sasidharan S, Dhillon HS. Ebola, COVID-19 and Africa: What we expected and what we got. Developing world bioethics. 2020 Sep 20; 00: 1-4.

7. World Health Organization. Improving health system efficiency: Democratic Republic of the Congo: improving aid coordination in the health sector [Internet]. World Health Organization: Geneva; 2015. Available from: https://apps.who.int/iris/bitstream/handle/10665/186673/WHO_HIS_HGF_CaseStudy_15.4_eng.pdf?sequence=1&isAllowed=y

8. Sasidharan, S., H. S. Dhillon, and S. Singh. "Medical Pedagogy in the time of COVID-19." Kathmandu University Medical Journal 18.2 (2020): 105-106.

9. Holmboe ES, Sherbino J, Long DM, Swing SR, Frank JR. The role of assessment in competency-based medical education. Med Teach [Internet]. 2010 Aug [cited 2020 Jul 16];32(8):676–82. Available from: https://www.tandfonline.com/doi/abs/10.3109/0142159X.2010.500704

10. Thomas CJ. Coronavirus and challenging times for education in developing countries [Internet]. Washington, DC: Brookings Institution; 2020 Apr 13 [cited 2020 Jul 16]. Available from: https://www.brookings.edu/blog/education-plus-development/2020/04/13/coronavirus-and-challenging-times-for-education-in-developing-countries/

11. World Health Organization. Collaborating centres [Internet]. [place unknown]: [publisher unknown]; [cited 2020 Jul 16]. Available from: https://www.who.int/about/partnerships/collaborating-centres

12. Crisp N, Gawanas B, Sharp I. Training the health workforce: scaling up, saving lives. Lancet [Internet]. 2008 [cited 2020 Jul 16];371(9613):689-91. Available from: https://pubmed.ncbi.nlm.nih.gov/18295028/

13. Sasidharan, Shibu, Harpreet Singh Dhillon, and Shalendra Singh. "Medical edification curated for COVID-19." International Archives of Health Sciences 7.3 (2020): 156-157.

14. Cecilio-Fernandes D, Parisi MCR, Santos TM, Sandars J. The COVID-19 pandemic and the challenge of using technology for medical education in low and middle income countries. MedEdPublish [Internet]. 2020 Apr 23 [cited 2020 Jul 16];9(1)74. Available from: https://doi.org/10.15694/mep.2020.000074.1

15. Lepp A, Barkley JE, Karpinski AC, Singh S. College Students' Multitasking Behavior in Online Versus Face-to-Face Courses. SAGE Open [Internet]. 2019 Jan 13 [cited 2020 Jul 15];9(1):215824401882450. Available from: http://journals.sagepub.com/doi/10.1177/2158244018824505

16. Gagné RM, Wager WW, Golas KC, Keller JM, Russell JD. Principles of instructional design, 5th edition. Perform Improv [Internet]. 2005 Feb 1 [cited 2020 Jul 16];44(2):44-6. Available from: http://doi.wiley.com/10.1002/pfi.4140440211

17. Sasidharan S, Harpreet Singh D, Vijay S, Manalikuzhiyil B. COVID-19: Pan(info)demic. Turk J Anaesthesiol Reanim. October 7, 2020;48(6)438-42. 10.5152/TJAR.2020.1008.

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CREATIVE ARTS: POEM

Love letter to child

Emi Frost

We watch my belly grow and our hearts are filled with joy
We can't wait to meet you, our precious girl or boy

We go to sleep and think of all the things you'll want to know
We'll teach you about the world and help your mind to grow.

We lie in bed and think of you until we dim the light
We touch my belly and whisper that we 'love you' every night.

We don't have much to give you except our never ending love
We promise you a better life, we've asked the angels up above.

We welcomed you to the world today, your life has just begun
It feels different now you're here, I miss when we were one.

Your daddy caught me crying, I told him nothing's wrong
I force myself to smile and soon the tears are gone.

I sense your daddy's judging eyes as I lay you down to sleep
I feel nothing for you as I kiss you on the cheek.

I know you crave my touch but I stand inside your door
It's not meant to be this way, I'm meant to love you more.

Your grandmother has come round, she strokes you tenderly
Why can't I do the same? What is wrong with me?

Your daddy called the midwife, he thinks I'm feeling blue
He thinks I can't take care of you, he's not sure what to do.

I told her that I'm broken, I dread the rise of each new day
She told me they would get me help, everything would be okay.

For the first time since I had you, I don't feel so alone
Lots of mums go through this, if only I had known.

It's starting to get better now, today we shared a smile
We laugh at the silly noise you made, we haven't done that in a while.

We count your tiny fingers and play little piggy on your toes
We blow raspberries on your belly and kiss your button nose.

We think you've got my smile, and every day it brings us joy

We love you to the moon and back, our gorgeous little boy.

About the author

› Emi is a Trainee Intern at Auckland City Hospital with a special interest in women's health. In her spare time, she enjoys exploring our own backyard and spending time with friends and whānau.

Acknowledgements

This piece was inspired by a dear friend's journey with postnatal depression. It is dedicated to parents and whānau affected by postnatal depression, and to the healthcare professionals that support them.

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CREATIVE ARTS: POEM

Let the grief wash off you

Ria George

When the news comes, in splutters and waves, let it swallow you
And when you're alone, let the tap open and the tub fill with your tears
Peel back your dead skin and wade into the tub
Slowly at first, a foot at a time
Immerse yourself in the warmth, in its embrace
Let yourself wallow in the brine
Let the water fall between your fingers and seep through your hair
Let the grief wash off you.

Sit there until you start to raisin.

When you feel ready, peel back the oceans and dry yourself off
Let the light in the room fall warm upon your skin
And when you're done, rub lotion on the parts of you that still need healing
Run your fingers through your hair and slip into silk
Perfume your collarbones and your wrists
Let the fragrance waft around you like a new breath
Let these things happen in this very order
Let the grief wash off you.

About the author

› Ria is a fifth-year medical student at The University of Auckland, currently based in the Waikato/Lakes District Health Board regions.

Conflicts of Interest

Ria is a student reviewer for the New Zealand Medical Student Journal (NZMSJ). This creative arts competition entry underwent the double-blinded peer review process applied to all entries submitted to the NZMSJ, and was judged to be one of the two winners of the competition.

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CREATIVE ARTS: ARTWORK

Physically isolated, but socially connected

In honour of Mr Hunia Dean

Hannah SY Kim

About the author

› Hannah is a Trainee Intern at Auckland City Hospital. She painted this piece during the 2020 nationwide lockdown, as it was her first opportunity to paint since leaving high school. This painting was inspired by the 2020 nationwide lockdown, as well as the memory of her old art teacher, Mr Dean, whom she sadly lost to suicide two years ago. This painting symbolises our need for social connection in times when physical distancing may be required, to keep Aotearoa not only physically, but mentally healthy.

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Information for authors

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- Health informatics.

CLINICAL TOPICS

Clinical research is also encouraged by STONZ and can also be funded to an upper limit of $1,000.

These clinical projects will prioritised below the above topics as are less likely to have a direct influence on RMO working and training environments as a whole.

Please note that application for STONZ research funding is not limited to STONZ members nor is it limited to RMOs or medical students.

UNION **FOR JUNIOR DOCTORS**
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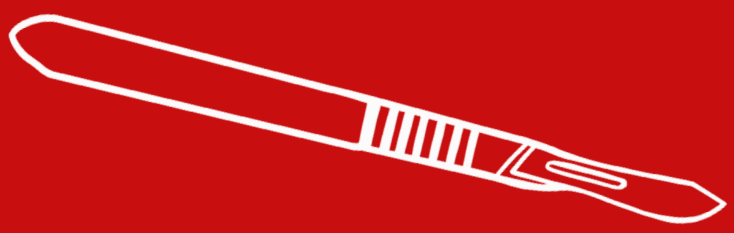
For more information and how to apply, please visit:
stonz.co.nz/research



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