TRUST IN MEDICAL RESEARCH

What Scientists Must Do to Enhance It

PROFESSOR WARWICK PETER ANDERSON AO

TRUST IN MEDICAL RESEARCH

What scientists must do to enhance it

PROFESSOR WARWICK PETER ANDERSON AO

MONASH
UNIVERSITY
PUBLISHING

Published by Monash University Publishing
Matheson Library Annexe
40 Exhibition Walk
Monash University
Clayton, Victoria 3800, Australia
publishing.monash.edu

Monash University Publishing: the discussion starts here

Trust In Medical Research: What Scientists Must Do to Enhance It
ISBN: 9781922979292 (PDF)
ISBN: 9781922979315 (ePub)

Cover design by Les Thomas
Typesetting by Jo Mullins

Contents

The book is dedicated to Deborah, Flora and Matilda,
with everlasting love, and apologies for the many times
that I was absent or (all too often) distracted.

It is also dedicated to my parents,
for the values of respect and service that they instilled.

Preface

Medical research is one of humankind's most successful endeavours. Now, many cancers can be successfully treated, Australia's heart disease death rates have plummeted, AIDS is no longer a death sentence and vaccines prevent diseases that previously killed millions of people or left them damaged for life. Through science, researchers have progressively destroyed oppressive myths that disease and ill health are caused by bad luck, malign spirits or sorcery.

Why have I written this book if medical research is so successful? One reason is that no one else who has led a large national medical research funding body seems to have written about the topic. I have had more than two decades in research funding leadership: six then nine years at the National Health and Medical Research Council of Australia (NHMRC) and six years at the International Human Frontier Science Program (HFSP).

Another reason is to give the citizens and taxpayers of Australia, the people who provide the money, a look into the system. After all, without their money, no research would be done. I expect that few people outside scientific research circles know who decides what to fund and how they go about it. I try to explain how scientists make these decisions and why politicians should never do so.

The main reason, though, is because I want to enlist the help of medical researchers in tackling the threats that I see facing medical research. Not all is well in our world. Many threats to the success and

integrity of medical research come from forces and pressures outside medical science. But they come, too, from our use of legacy practices that are no longer fully fit for purpose, or have been distorted and sometimes misused. My concerns include unwise and unproductive setting of priorities, government interference, lack of reward for peer review, misuse of publishing statistics, unreliable and fake publications, insecurity of employment for emerging researchers, and lost opportunities over the use of data.

The world is becoming more hostile to science. Fake news, disinformation, social media, celebrity culture: all these are far from the values of the Enlightenment from which modern sciences developed. All have been on vivid display during the COVID-19 pandemic. Even though science has produced evidence-based public health measures and effective vaccines against and treatments for COVID-19, many people have fallen victim to false information, with terrible consequences. More generally, trust in experts is being eroded, including trust in medical research. It's a trend that we must oppose.

I have written about the problems in contemporary medical research with trepidation. I understand why heads of funding bodies have rarely written about their experiences. We fear that governments may seize upon any criticism to reduce funding or intervene in the funding process, attempting to direct funds themselves, and we worry that anti-science forces will leap on the opportunities to attack our work.

However, I have put my trepidation aside and proposed in these pages some ideas for change that will, I hope, help the medical research community to better push back against these pressures and forces. After all, scientific training and practices teach us to critique, assess, evaluate and review, and to change our research plans and methods when we need to. This is how we approach our own day-to-day research

work, how we spot errors and problems, how we find better methods and techniques, and how we conduct peer review. We should apply the same methods of science to improve our system.

What is the best metaphor for describing the job of a head of a funding agency – juggler, circus master, air-traffic controller, school principal, riot-control commander? A job description might read: secure the funding; establish a system that directs it to the best research; make funding decisions that balance building for the future (funding new postdocs) against the immediate (funding the best research now by the best researchers); worry continually about getting quality peer reviews; fret over the information technology; ensure that the subjects of research are treated ethically according to codes and guidelines; deal with explosions (such as a well-known researcher accused of research fraud); deal with disappointed applicants (the vast majority); look for opportunities for international funding collaboration; navigate Australian Public Service protocols and rituals; elicit the best from your public servants; communicate the triumphs of the research (within the strict government communication guidelines); and, in my case, face the task and inevitable criticism of revising NHMRC guidelines on water quality, alcohol and the Australian diet, and worry about responsibly discharging the *Research Involving Human Embryos Act 2002*, with various associated Acts and amendments.

So, it is interesting and sometimes fun. You need a thick skin because it is inevitable that there will be dissatisfied people. Thousands of researchers each year are disappointed with the outcomes of their applications for funding – given the many hours of work needed to submit an application and (sometimes) the technical difficulties of grant system software. Whole research fields become antsy about how little funding they received. Politicians may be vocal about the

amount of funding won by researchers in their state, frustrated that they can't control what gets funded. Heads of funding bodies have never a dull moment.

I worked as a medical researcher for three decades, starting with postdoc and research-fellow positions at Harvard Medical School, the University of Sydney and the Baker Medical Research Institute, and then moving to academic jobs at Monash University. As a postdoc, a research group head and a university department head, I experienced the many highs of medical research (projects completed, exciting new ideas generated, papers accepted, grants awarded, the fellowship of other scientists and the delight of new PhD students) and lows (rejections aplenty, great ideas that turned out not to be, seemingly endless bureaucracy). My research passion was to understand the causes of hypertension – high blood pressure. It is the silent disease that underlies cardiovascular disease, strokes and heart attacks, the most common causes of death worldwide. According to the World Health Organization figures, more than 1.2 billion adults have hypertension, two-thirds of them in low- and middle-income countries. The causes of most hypertension still elude medical researchers, despite the condition's ubiquity and even though it can be diagnosed with simple and cheap technology. My group worked on understanding how the kidney is sometimes (perhaps even mostly) the culprit.

In the latter years of my career, it was a great privilege to have been at the NHMRC during a period of rapid growth in funding from the government. The Howard government decided to double NHMRC funding in the late 1990s (thanks, Michael Wooldridge), and then double it again in their 2006 budget, a commitment that the Rudd and Gillard Labor governments kept. All up, I oversaw more than seven billion dollars of Australian taxpayers' money at the NHMRC.

As HFSP Secretary-General between 2015 and 2021, I oversaw the combined funding from fourteen different countries and the European Union: more than US$50,000,000 each year. I am humbled that I was entrusted with such responsibility. I took it utterly seriously and I am immensely grateful for the trust that was put in me. I hope I was worthy of it, as a share-farmer's son from a small country high school.

I have written this book with an Australian audience in mind. Yet science is international. Most of the issues that I discuss are not unique to Australia, and so researchers from outside the country might also find interest in its pages.

Lastly, I have used the term 'medical research' for convenience, but the fuller 'health and medical research' is a better description and is always implied.

Chapter 1

Trust and Honesty

Why we must drive change

The success of medical research is built on honesty and trust.

We need to trust that other researchers are working accurately and publishing truthfully, so others can reliably base work on theirs.

We need to trust that peer reviewers conduct their work honestly and without bias.

We need to trust that funding bodies operate transparently, without hidden traps, biases or exclusions.

We need accountable publishers so we can have confidence in what they publish.

We need governments to trust that medical research benefits community health and to continue to fund it adequately.

The outcomes of medical research affect more than just medical researchers. Health practitioners need to trust the published results that shape their practice. Patient and advocacy groups need to trust what they read in medical publications. Individual patients need to trust that doctors and patient advocacy groups have access to reliable information.

Trust is a fragile thing. Once lost, it is hard to regain. In this third decade of the twenty-first century, some of this trust has been eroded.

Parts of the medical research system are creaking and buckling under pressure. They are becoming less fully fit for purpose, less suited to the contemporary demands of science and less receptive to the hopes of new generations of scientists. Changes are needed.

Many researchers will disagree. They point to the ongoing spectacular achievements of medical research, and they are right to do so. These successes are everywhere to be seen. Many more conditions can now be treated, and even better methods of prolonging healthy life keep being invented. Vaccines have eradicated some diseases (for example, smallpox), almost eradicated others (polio) and vastly reduced the death rate of even more (measles, mumps, chickenpox, typhoid, yellow fever, shingles, flu and COVID-19). Scientific advances in disease prevention, and medical and surgical treatments, have dramatically reduced the age-standardised death rate from coronary heart disease in Australia – by around 80 per cent since 1980.[1] AIDS is now treatable and not a death sentence. Reproductive choices abound, bringing joy to many who were not previously able to become parents.

Australian researchers have played an admirable role in medical research's successes. Few readers may have heard of Dr Ruth Bishop, but her research has had a vast impact on the lives of children around the world. She showed that many cases of deadly diarrhoea in children were due to rotaviruses, a discovery that led to a successful vaccine that has saved countless lives. Ian Fraser's name is more widely known in Australia and, like Ruth, his research has benefited people worldwide. Ian and colleagues Jian Zhou and Xiao-Yi Sun conducted the science behind the vaccine that protects people from the human papilloma virus. Another modest researcher, Dr Graeme Clark, brought hearing to the deaf through the cochlear implant, or 'bionic ear'.

Tens of thousands of other Australian medical researchers have made the discoveries that are beams of light into biological and pathological darkness, conducted the trials that showed what worked and what is needed, and changed the delivery of care by applying the rules of science. Spend a few minutes reading what medical researchers are doing on their university home pages: it will inspire you and remind you of the goodness that is in the world.

Science has brought us these improvements in the prevention and treatment of disease. But science alone is not enough to ensure that everyone benefits from medical research. Inequalities in access to the means of preventing and treating disease entail that the benefits of research are not shared as they should be, and billions of people miss out.

Accounting for human nature

To state the obvious, medical researchers are human. We are not saints. We are members of society and each of us is affected by fashions, trends, societal changes and personal relationships. We have the same admirable and sometimes not-so-admirable characteristics and personalities, loyalties and aspirations as anyone else. We are not devoid of the emotions of envy, resentment and jealousy, love and hate, boredom and excitement, fear of the future and nostalgia for an imagined past. We are not devoid of prejudices, ambition and, sometimes, hubris. (That said, I contend that the average quantity of honesty, compassion, intelligence, cooperative spirit and generosity are far above average among our ranks.)

What makes the difference, despite all these human foibles, is that we use science, with its values, systems and ethics. Understanding our human nature, scientists have developed a system for exploring

the world that counters some of our baser tendencies. We have peer review to aid in determining funding fairly, conflict-of-interest rules to prevent personal views from influencing funding decisions, and ethics reviews of our plans to guard the welfare of human and animal participants in our research.

However, the systems of medical research must keep evolving to cope with changes that occur in society, and within science itself. Honesty, personal integrity and generosity – all necessary in science – are under attack in the wider society. Fake news, deep fakes, lies and dissembling in politics and product advertising have a corrosive influence. When public figures can lie openly and get away with it, the contrast with the need for complete honesty in medical research could not be starker.

Because medical research is competitive, with financial and reputational rewards, some researchers behave poorly, finding ways to game the system, take shortcuts, be dishonest. Trust is eroded by research misconduct scandals, fake journals, lack of reproducibility of published results and the interference of politicians in scientific decision-making. We must face up to problems and come up with solutions, just as we do in our own research. It is up to us to look after our systems to ensure that cores values of science remain central.

Scientists must lead the change

Scientists have provided the leadership for change in the past. Australian guidelines for human participants in medical research in Australia were developed by the NHMRC through the Medical Research Ethics Committee, established in 1982. The committee was chaired by a leading medical researcher, R.H. (Dick) Lovell, Professor of Medicine

at the University of Melbourne. The NHMRC also made sure though that it had respected non-scientists on the committee too, such as the Reverend Dr Davis McCaughey (later the Governor of Victoria) and Mrs Elizabeth Grant AM, a leading community health advocate.

The first guidelines for the use of animals were developed in the 1970s by a group of medical researchers led by the Melbourne-based internationally renowned neuroscientist Ian Darian-Smith.[2] I was a lab scientist at the Baker Medical Research Institute (as it was called in those days) in Melbourne when I chaired a NHMRC committee of scientists, animal welfarists and community members to develop these guidelines into a code of practice for the care and use of animals for scientific purposes, published in 1990. Similarly, a small working team of medical researchers led by Ian Darian-Smith developed the first guidelines on research misconduct in the 1990s. These were then developed into the Australian Code for the Responsible Conduct of Research in 2007 by a committee that I chaired.

All of these guidelines have been progressively updated and developed by NHMRC-nominated groups led by medical researchers, showing that we can reform our systems to ensure their integrity and maintain the trust of the public and our colleagues.

Internationally, scientists have led discussions of the reforms needed in peer review, such as scientists at the American Society for Cell Biology who developed the Declaration on Research Assessment (DORA), and the Research on Research Institute, a group based primarily in the United Kingdom and the Netherlands.[3]

Scientists are also leading the way in how we deal with research data. The biologists of the Human Genome Project in the 1990s set an ethos that research data should be open to everyone. In the last thirty years, scientists have generously developed countless data resources for

the use of other researchers worldwide. In recent years, far-sighted scientists have introduced open access systems to make all results of publicly funded research available to everyone, quickly. In clinical trials, researchers have developed ways to improve their field with databases to minimise unnecessary replication of trials and maximise transparency.

If scientists do not take responsibility for the design and operation of medical research systems, others may force changes upon us. These will be less likely in our interests, or in the interests of medical research itself and of the health of the broader community. History shows political intervention in medical research can be heavy-handed, block much-needed research and usher ideology into decision-making. We have seen this with laws on reproductive research and stem cells. In Australia, the Howard government passed unworkable legislation that blocked ethical research and soon had to be revised, an effort led by the courageous Senator Kay Paterson. In the United States, the George W. Bush government illogically banned public but not private funds being used for stem-cell research.

* * *

Scientists must lead, but we must also involve the wider community if we are to maintain its trust. We already know how valuable members of the public are on human and animal ethics committees, on all NHMRC working groups and committees, and on governing boards of institutes and centres. We should extend this approach to research that risks public safety, such as research on changes in viruses with a potential to become infectious. The purpose of medical research is to improve people's health, so the public must be partners in our work.

Australian medical research has long attracted smart, altruistic and capable people. Until the late twentieth century, the biological sciences were regarded as 'soft science' by many traditionalists. Physics and chemistry were seen as more rigorous and intellectually challenging than biology and biomedicine. This despite the life-changing work of individuals such as Charles Darwin, Ignaz Semmelweis, Marie Curie, Louis Pasteur and many others in the nineteenth century. This attitude has changed now, thankfully, and Bachelor of Biomedical Science courses at Australian universities attract many of the brightest high-school graduates year after year.

Medical research's success is not due to researchers alone; it relies on participation by the broad community. Hundreds of thousands of people have consented to be in clinical research and clinical trials and research on the delivery of health services over decades. It has been of immense benefit to researchers that many patient groups and individuals living with specific diseases are well organised and are actively involved in medical research. In my time at the NHMRC, I greatly admired the leadership and the work of the Consumers Health Forum of Australia, for instance. They offered strong and wise advocacy, standing their ground when needed, and were resolutely pro-science.

But this engagement only occurs when the community trusts that medical research can benefit them and the results are reliable. As a society, we must preserve the core scientific values that have made medical research one of the most successful human enterprises ever. Of these core values, first in importance is honesty in all matters – in our research work, in our applications for funding, in our interactions with collaborators and colleagues, and in reporting the results.

Chapter 2

Public Funding Success

A century of medical research funding in Australia and beyond

Medical research has long had strong financial support from national governments, reflecting their citizens' hopes for better health. It is our responsibility to repay this trust by using this money in the best ways we can.

Early in the twentieth century, governments began to understand the potential of medical research to improve their citizens' health. In Australia, the NHMRC held its first meeting in February 1937, at which it awarded grants for research totalling £30,000. The US National Institutes of Health (NIH) began to emerge in its current form with the *Ransdell Act* in 1930, establishing the new name of the National Institute of Health (previously the Hygienic Laboratory) and authorising fellowships for research into basic biological and medical problems. In the United Kingdom, the Medical Research Committee and Advisory Council was set up in 1913 with funds for research. By the 1950s, most developed countries had established medical research funding bodies. The Chinese Academy of Science was founded in 1949, originating from the Academia Sinica, founded in 1928.

The National Natural Science Foundation of China was established in 1986.[1] Now, governments in most countries, from the poorest to the richest, support medical research in one way or another.[2]

Leadership and influence in healthcare research

The US government is the largest supporter of medical research worldwide – something of a paradox in a country often antagonistic to government expenditure. Politicians have consistently supported major funding for the NIH and the National Science Foundation (NSF), as well as research at the departments of Defense, Energy and Agriculture. And they have grown these funds in a mostly bipartisan way. Even when President Donald Trump planned to cut NIH and NSF budgets, a Republican-led Congress voted to increase them.[3]

Philanthropists also support medical research in a big way in the United States. For example, the Howard Hughes Medical Institute has an annual budget similar to the NHMRC's, and the Bill and Melinda Gates Foundation is ten times larger. The private foundations have often been innovative too, such as Howard Hughes' integrated research facility, Janelia Farm, and the Bill and Melinda Gates Foundation's new thinking on research priorities in low-resource communities.[4] In contrast, the Australian super-rich have seemed less interested in science and medical research. There are exceptions, such as Andrew 'Twiggy' and Nicola Forrest's Minderoo Foundation, which funds cancer research through its Collaborate Against Cancer Initiative, among other philanthropic endeavours. Interest does seem to be growing recently, with organisations such as Research Australia actively connecting donors and researchers, but it is nowhere near the level of the United States.[5]

Since World War II, the cultural and economic influence of the United States has affected how medical research has developed around the world. This has overwhelmingly been for the good, though the system does reflect American values and mores in ways that we don't often think about. It is important to advertise, to speak, be seen and network at conferences where one's peer reviewers and potential employers will be. A researcher's 'brand' needs to be nurtured. A lab's webpages need to be engaging and emphasise the research group's successes and competencies. Control of the outputs of medical research – publications – is primarily in the hands of private corporations that seek profits to publish. Medical research even has some characteristics of the gig economy for many young medical researchers, whose employment is precarious.

How researchers get the funds for their research also mirrors an open competitive marketplace. I point this out as a fact, not as a criticism. Taxpayers' money should go to the worthiest ideas and to those who can best contribute to new knowledge, new treatments, new preventive strategies and better policy, as well as to those new and emerging researchers who show the most promise. There must be competition for the available funding. But the system is tough on individual researchers, who may have large financial commitments, mortgages and dependents. The first few years of a medical research career are the toughest. Few of the many who begin a career survive for a lifetime. Success depends not only on continuing creativity and achievement, but also on luck, good fortune, timing and privilege.

Other countries have also brought new ideas to the funding of medical research. In the United Kingdom, the National Institute for Health and Care Research (NIHR) developed innovative research and implementation programs linking research and practice on the

ground in hospitals and healthcare networks. Conceived of and driven by Professor Dame Sally Davies, a leading figure in global health, the approach has been influential internationally – including in Australia, through the NHMRC's Partnership Projects, which 'create partnerships among decision makers, policymakers, managers, clinicians and researchers', and the NHMRC's development of Research Translation Centres, which promote implementation of research evidence into practice and policy through universities, healthcare organisations and state health department collaboration. Similarly, the EU's research frameworks are a novel and largely successful approach to building large, cooperative multinational networks of goal-focused researchers. The current program, Europe Horizon, is set to run to 2027 and has a budget of €95.5 billion. It focuses on topics such as health throughout the life course, infectious diseases and environmental and social determinants of health.[6]

In a transformative turn of events in Alice Springs in 1986, Indigenous leaders stood up to the NHMRC, convincing it that consent and full involvement in research involving First Peoples and their communities must be obtained and maintained.[7] This in turn led to a broader shift in thinking about the ethics of research involving groups of peoples and their ownership of the research and its findings. New approaches to address health among First Nations populations were developed by the Canadian Institutes of Health Research and by New Zealand's Health Research Council, funding community-focused research in consultation with their indigenous peoples. British-Canadian researcher Jonathan Lomas led a transformation in thinking about health services research at the (then) Canadian Health Services Research Foundation (CHSRF).

Australia has benefitted from these examples.

When it comes to commercial development of medical research findings, the United States has been by far the most successful country over the last century. The products developed there tend to benefit the whole world, even though the pharmaceutical firms can often be 'the ugly face of capitalism'.[8] Israel also excels in translating scientific discoveries to commercial products, as any visitor to the Weizman Institute of Science or the leading Israeli universities will quickly discover.

Australian medical research support

Medical research is funded more generously by government than other sciences in Australia. The NHMRC spent around AU$850 million in 2020–2021 (it is by some estimates the eighth largest medical research funder in the world) and the Medical Research Future Fund provided almost AU$600 million.[9] To these, add money from charities such as the Juvenile Diabetes Research Foundation, the Cancer Council and the National Heart Foundation of Australia, and the total for medical research is probably three or four times that distributed by the government's Australian Research Council (ARC). This disparity is even starker when we consider that the ARC is responsible for a much wider brief: 'all fields of science, social sciences and the humanities'.[10] The greater relative support for medical research, even taking into account the Cooperative Research Centres Program (which provides funding for medium- to long-term industry-led research collaborations) and the CSIRO, reflects both the public's interest in their own personal health and the successes of Australian medical research.[11] This differential in funding between medical and other types of research is mirrored in the United States, where the

NIH annual budget of over US$40 billion dwarfs the approximately US$8 billion of the National Science Foundation.[12]

The growth of medical research funding in Australia began with the first Howard government. The new Health minister, Michael Wooldridge, had a strong personal commitment to scientific medical research, sparked by a summer studentship working in the lab with John Funder, one of Australia's most eminent medical researchers and mentors. Using his political nous, Dr Wooldridge commissioned an excellent blueprint for the future (the Wills Report, 1999, led by business figure Peter Wills AC) and used it to gain Prime Minister John Howard's support for a progressive doubling of NHMRC funding over five years. The conceptual framework that Wooldridge built around the Wills Report was critical, too, in a second doubling of NHMRC funding announced in the Howard government's 2006 Federal Budget – a commitment then honoured by the Rudd and Gillard governments. Since 2014, NHMRC funding has been flat, maintained at around AU$800–850 million.[13]

Medical research is not a cure-all, but it is important

Good science alone does not guarantee longer and healthier lives. Social and economic conditions are the major determinants of health, so improved health outcomes rely on political, economic and social circumstances and policies. The fruits of medical research are not available to all. The COVID-19 pandemic showed both the absolute necessity of medical research and the inequities in its benefits. The triumphs of science in the development of vaccines have been outweighed by the health and economic inequities in low-income countries. By March 2023, almost 90 per cent of Australians had

received a first dose, but to our immediate north, just 4.2 per cent of Papua New Guineans had received a first dose.[14]

The United States demonstrates that good science does not correlate with national health outcomes. It spends more than any country on medical research but ranks just thirty-eighth when it comes to the population's life expectancy.[15] The excellence of US medical science brought forth novel and effective COVID-19 vaccines in record time but, despite this, the nation's death rate per 100,000 in mid-2022 was higher (around 310) than poorer countries such as Mexico (around 255), Namibia (160) or Vietnam (45), according to John Hopkins' Coronavirus Resource Center statistics.[16] The benefits of having first access to the new vaccines in the United States were cancelled out by problems with Donald Trump's leadership, public policy, public health readiness, social inequalities in access to care and the underlying health status of citizens. We should be glad that Australia was not captive to some of those factors to the same extent, and we must ensure that our political leadership continues to understand the value of medical research, and to support it adequately.

Chapter 3

Deciding What to Fund

Peer review, ideas to improve it and what not to do

Peer review – the process of having research evaluated by peers – is a major part of the everyday work of researchers and the central activity for funders. Trust in medical research depends on how well peer reviewing works. Researchers are sent applications for research funding by the NHMRC, the ARC and many of the charitable sector foundations for expert review. Reviewers may be 'external' experts, researchers who are asked to write reviews on application, or be appointed to a peer review committee. Reading and assessing each application takes at least a couple of hours and usually much longer. Publishers also ask researchers to peer review manuscripts of completed research, but here we concentrate on peer review for funders of research.

An essential but under-rewarded task

The usual criticisms of peer review are that it is imprecise, subjective and time-consuming. Yes, this is true. But, like Winston Churchill's comment about democracy, peer review is the worst possible way of making decisions on research funding, except for all the alternatives.

Imprecise? Yes, of course, but this imprecision can be lessened if the funder establishes clearer parameters, as we will explore in this chapter.

Subjective? Certainly, but the subject of careful thinking and consideration by experts.

Time-consuming? Absolutely, but we think about it this way mainly because it is undervalued, seen as something outside what researchers are paid for and irrelevant to our career progression.

Peer review does not guarantee that the 'right' decisions will be made. It is conducted by human beings, judging other human beings and their ideas, in a system designed by human beings, with all our strengths and foibles. In essence, peer review is simply an informed opinion. Though that is obviously better than an uninformed one.

Almost all scientists complain about the time taken up by peer reviewing, but who else should judge a researcher other than their peers? A few big egos have claimed to me over the years that they have no true peers, no one equal to the task of judging them – so I guess they expected funding by divine right.

Scientists know that it is our responsibility to participate in peer review, but the workload can be heavy. It seems perverse, then, that we get no formal recognition or reward for it. Peer reviewing is not taken into account when one seeks appointment or promotion at a university, or when applying for a research grant or fellowship. No one asks about the time spent in the last year reviewing applications for funding or articles for journals. Almost no one assesses the quality of your reviews (though NHMRC does for some schemes). All of this is surprising because the quality and effectiveness of medical research relies fundamentally on the quality and thoroughness of other scientists' reviews when we apply for funding or try to publish our results. We hope that they will take care to do a good job, that they read and

analyse our application or submitted manuscript thoroughly, and that they do so fairly.

Peer review is typically an activity that gets squeezed into spare hours in evenings and weekends, stolen from family life, social life and sleep.[1] Asked to serve on a peer review panel for research funding, it can be tempting to just say no because your inbox is already cluttered with requests. But less peer review would mean poorer science and poorer spending of taxpayers' funds. Peer review is so central to the funding of medical research, so vital as a scholarly exercise relying on hard-gained knowledge and expertise, and so crucial to the work and livelihood of others that it deserves much more serious consideration in careers than it has currently. Employers and funders should explicitly value the quality and quantity of peer reviews. I have a few thoughts in the final chapter on how to do this. But for now let's look at ways to improve the system.

What researchers should expect of funding organisations

Researchers should expect the best possible peer review of their applications because their work and careers depend on it. It is essential that applicants know what they will be assessed on.

Funders should be clear on what they want to fund and align reviewing with that. For example, is the funding scheme aimed at supporting the important next steps in highly productive lines of research, or is it seeking to fund blue-sky innovation? Are the applicants expected to have already demonstrated that the project plan is feasible, or is it okay to have a significant element of risk in the research plans? What is being looked for in the applicants' track records? Is there an aim of developing early career applicants or increasing the research

workforce diversity? If it is an early career fellowship, what are the applicants expected to have already achieved? Is multidisciplinary and interdisciplinary research encouraged? Is it a scheme aimed at improving research translation into clinical care? Or into commercial development? And, of course, the criteria should encompass the DORA principles.

However, the aims for a scheme can often be vague and generic, or selection criteria may not be adequately aligned with the scheme's aims; they can be imprecise, with no information provided on the relative importance of each.

Applicants should be able to write to each aim, and reviewers to assess against each. Both should know the relative importance of each aim and weight scores accordingly. Simple scoring systems will not do. When I was first on a NHMRC peer review panel in the 1990s, we were expected to score on a 100-point scale of 0 to 10 to one decimal point. It took me half my first committee meeting to begin to understand it all. What, for example, did a 7/10 mean, in what ways was an 8/10 better, and what exactly was the difference in applications between a score of 8.3/10 and 8.5/10?

To make it easier for everyone, funders should ask applicants only for information that is relevant to the aims of the scheme, the aligned assessment criteria and to assess eligibility. (They might, however, also need to ask questions for data to inform their own policies, such as whether women and other minorities are applying and succeeding in their applications, and information required by governments.)

A detailed budget and a highly detailed research plan are hardly ever necessary or desirable. Scientific research is by definition an exploration of the unknown, so most projects will change as biology gives its usual unexpected surprises. It is unrealistic to ask applicants to detail the costs they will incur up to five years in advance. Costs change, as

do personnel, and new and better methods may arise. Furthermore, most research groups have several projects underway, and the people, methods and resources may be spread across them.

Instead, it is better to provide financial support in sizeable chunks, say in multiples of AU$10,000, $20,000, $50,000 or $100,000 per year, and ask applicants to justify their bid for one or more of these amounts. Good peer review panels can judge whether a request is justifiable or not and add to or reduce the amount if needed. This approach to funding builds in the flexibility that scientific research requires.

Funders should also resist the temptation to 'vegemite' – to spread funding thinly so that more grants can be funded, but all of them inadequately. Scientific talent is not equally distributed. Trying to make the available money go further, while it may seem noble, only results in research projects that are smaller in ambition – 'safe science' rather than bold science.

Good peer review committees

Peer reviewing of a funding application is different to reviewing a manuscript for publication. For the former, the review is to help predict the future. For the latter, it is to assess the past, in the form of an individual's completed research. Reviewing alone at a desk is an important part of peer review for both research funding and publication, but it must not be the only step, or the final step for research funding, where public money and careers are at stake.

Peer reviewing decisions for research funding are best made as a group, by a diverse committee, independently chaired and well briefed on the funder's aims and the committee's rules. In a committee, the opinions of any member are open to immediate questioning by the

other scientists in the meeting. Most scientists want to perform well in front of their peers, and views that seem poorly founded can be contested and challenged. This form of accountability cannot be achieved if the final review step is only individual reviewers working alone. In turn, though, committees can do their best work when they have written reviews from other experts, to provide additional, field-specific input.

Some question whether these external written reviews should continue to be anonymous, as is the established convention, and argue that the identity of the reviewer should be disclosed to the applicants. There are sound arguments for this approach, including that reviewers might be more thorough and balanced if their names were known. On balance, I think they should be anonymous. Would identified reviewers always be fully frank? Would they not tend to hold back on their critiques if they knew that the applicants would learn who wrote them? Would they not worry that some desire for revenge may be harboured in the hearts of those who read a less-than-glowing review report of their own application and who are not saints? Would reviewers not tend to be less critical of the powerful and influential researchers in their field than of younger scientists whom they do not know?

I make these comments in relation to grant funding rather than publication, though it could also be time for some experimentation. One of the world's leading science journals, *Nature*, is trialling a system in which authors can have anonymous peer review reports, and their own responses to these reports, published alongside their article. Reviewers can also choose to be named.[2]

In terms of medical research funding, it is encouraging to see more thought being given to openness in grant applications themselves, and in the researchers' aims in applying for funding. The Dutch funder

NWO has begun to publish successful applications to its Open Science Fund where they have the consent of the applying researchers, and Wellcome in London has introduced the Open Research Fund, which includes grants for researchers who 'want to develop and test incentives for making health research more open, accessible and reusable'. All successful proposals to the fund are published online.[3]

For peer review committees, pre-meeting briefings are crucial, especially for newcomers, even though some experienced members roll their eyes at the prospect. Funders should not take it for granted that everyone on the committee understands what is expected of them. Everyone benefits if funders explain at the outset the application-by-application review process, the criteria that will be used to make the assessments, their relationship to the scoring, and the policies on conflicts of interest, confidentiality, equity and diversity. Members should also be reminded that they must not raise issues that are irrelevant to the assessment of an application or make personal remarks about applicants. Though not a guarantee, thoughtful briefings can ameliorate unconscious biases.

At the Human Frontier Science Program, our pre-meeting briefing concentrates on helping the committee to understand that we really do want highly innovative, frontier-extending ideas. We remind them that we do not want applicants to have demonstrated feasibility beforehand. It is not frontier science if the applicants already know that it works. HFSP needs to emphasise this because many other research funding bodies do expect that applicants have already performed some of the research to show that their research plans are feasible, and so this can be ingrained thinking for some reviewers.

Committees in all walks of life benefit from good chairing. I introduced the concept of independent chairs at the NHMRC and

the HFSP, appointing highly regarded researchers with a personal reputation for fairness and integrity. Independent chairs do not vote or present or discuss the applications. Instead, they concentrate on the chairing itself, making sure that all applications are treated equally and fairly, and that all review committee members keep to the rules of the organisation, address the criteria, do not make gratuitous remarks about the applicant and treat other committee members respectfully. A good chair can help the committee avoid getting bogged down on minor issues and 'red herrings', and they can remind everyone of the funder's polices for the scheme when that's needed. As they are not voting or introducing any applications, the other committee members can trust them to be impartial.

I began the policy of independent chairs after the Australian National Audit Office reviewed the NHMRC's grant procedures. It was critical of the practice of the chair being one of the assessing and voting committee members. The ANAO commented with disapproval that 'of the 42 Grant Review Panel Chairs, 17 had applications that were being reviewed by that GRP'. Despite a policy that the chair stepped outside when their applications were being considered, the ANAO commented in their 2009 report that the NHMRC should make changes to 'conserve the probity of the peer review/GRP model and protect the NHMRC's reputation': that is, to preserve trust.[4]

Review committees with diverse membership and a wide range of expertise work best. We all have cognitive biases, so diversity helps 'average out' these across the committee. Narrow, discipline-based committees can fall easily into groupthink. Funders should include not only well-known, established scientists but also active, engaged mid-career and even early career scientists, and aim to have around half women and half men (unless there is a good reason not to – for example,

to review a special call for research into women's experiences of breast cancer).

Some of the finer details matter, too. Review committees should devote about the same amount of time to discussing each application. A protracted discussion usually simply drags the score down. As scientists, we are trained to dissect, analyse and critique, and so as time goes on in a peer review discussion we tend to find more and more things to worry about. On the other hand, a strong personality can try to close a discussion prematurely before all aspects are discussed, in which case the chair needs to intervene. Once a committee has considered and voted on an application, it should never go back later and re-open it for further discussion. To re-open a discussion risks deliberate but hidden tactics being used to push undisclosed biases or prejudices, subverting the group decisions made after the previous, considered discussion.

Be wary of undisclosed strategic and biased voting. It is of course perfectly acceptable for a review panel member to have a different scientific view to other members and vote accordingly. But scientists on panels are still humans. They may hold unconscious or conscious biases against, for example, female scientists, or older scientists, or even against a type of research (public health research, qualitative research, *in silico* research). So, to counter this at the time of voting on each application, committee members should be required to state whether they will be scoring significantly differently to the score suggested by the spokespersons, and if so to give an explanation. This way, any biases of the reviewer can be exposed, or any deeper insights of that reviewer can be shared. This also guards against strategic voting, to boost the number of grants to, say, Victoria or to basic neuroscience, to choose two examples at random.

I found that having an independent observer silently observe proceedings during the review committee meetings was also a big plus. These observers reported directly to me and senior NHMRC staff at the end of each day on the committees' proceedings and let us know whether we needed to alert the chair to some gaps in their chairing, or to adjust our briefings to the committees. They also produced an independent report for the Council of NHMRC afterwards. A side benefit was that these observers from the general community were able to inform critics and health advocacy groups about the rigour and fairness of the processes.

There are some, though very few, researchers who are best avoided for review committee membership because they have been found to be unreliable, erratic or prejudiced. These types are usually grandly self-regarding older scientists who say, 'I don't bother with all your criteria – I know a good grant when I see it.' They are likely to be notorious for their arrogance and to be completely unaware of their biases. They are also, pleasingly, a disappearing breed.

It aids transparency if funders acknowledge publicly those who have participated in their review processes – but only after the decision-making has concluded, to avoid unscrupulous applicants seeking to influence reviewers.

Giving feedback on applications

Should funders give applicants an explanation of why they have not been funded? At first impression, it seems only fair that they do. But care is needed because feedback can also be misleading. The reason an application is not funded is very often not a scientific one but a financial one. That is, while the application was fine scientifically and worth funding, there is not enough money available to do so. Adding scientific

commentary to that bleak fact risks suggesting to applicants that if they fixed a few scientific details next time, the grant would be funded. But the application, though fine, might have had a mid-range score and so be hundreds, perhaps thousands, away from the funding cut-off. Therefore, tinkering with details will not help much next time.

I am a fan of structured and quantitative feedback, giving the applications their scores against each of the criteria and their overall percentile outcome. This latter can be something like, 'Your application ranked in the 30–40 percentile of a total of 2536 applications. However, there were sufficient funds for only 12 per cent of the applications,' or 'Your application ranked in the lower 50 per cent of a total of 2536 applications. There were sufficient funds for only 12 per cent of the applications.'

Good data aids good policymaking. It is great when funders publish their statistics on the demographics of applicants and success rates, outcomes for research institutions and the number of applications that could have been funded as worthy research if there had been more money available. This is good accountability practice, and these statistics are also valuable for scholars of science, other funding agencies and health and educational policymakers.

Finally, funders should review their peer review systems frequently. A good system is a well-reviewed one.

Avoiding conflicts of interest and biases

As humans, we all have beliefs, conscious and unconscious biases and prejudices. Much as we try to avoid it, these affect our reviews, even if subtly. Every one of us cannot help but be influenced, if only a little, by who we are, by what beliefs we hold about other human beings and by self-interest.

Guarding against bias and self-interest is one of the things that makes science so successful. We have developed rules around conflicts of interest to be able to support the best science, regardless of self-interest.

Some conflicts of interest are obvious to all, such as when a reviewer has a personal or professional relationship with an applicant, a partner or a supervisor. Others are more contested, such as whether to allow a reviewer from the same institution as the applicant. My view has always been that this is a conflict of interest, because in the eyes of a neutral observer, there is both a perception of conflict of interest and an actual conflict of interest. The institution can benefit from the outcome of the peer review, in prestige (Australian research institutions boast about their grant successes) and financially, through formula-driven Research Block Grants for universities and state infrastructure support for institutes. I heard many times, 'No, I don't have a conflict of interest because this applicant works in a different department at my university and I have never met them.' This misses the point. An impartial observer can perceive that a reviewer from that university may be more kindly predisposed toward applications from there, through loyalty to the institution or awareness that it adds to the institution's prestige and income. It could also be the opposite – a negative bias – given the rivalries that exist within academia between departments and faculties.

Medical research is more interdisciplinary than ever before

Health and medical research has long involved multidisciplinary collaborations with biomedical, clinical, public health and health service researchers. Now, research often involves interdisciplinary collaborations

too, with researchers from engineering, physics, informatics, mathematics, economics, policy analysis and many other fields.[5]

This presents challenges for peer review because the breadth of expertise needed to properly review applications is greater. Consider by way of example an application for a brain-cancer research project that could include molecular genetics, neurology and population epidemiology, advanced bioinformatics analytical methods, mathematical modelling and perhaps materials engineering.

To review multi- and especially interdisciplinary applications, review committees may need to be larger than normal to encompass all the expertise needed. The number of external reviews might also need to be greater than usual to help the review committee members in their judgements. At the Human Frontier Science Program, all research applications must be interdisciplinary (and must involve international collaboration). We have found that large committees, twenty or more, are needed to cover the range of expertise needed, supported by six written reviews from experts.[6]

Interpreting authorship is another complication in reviewing interdisciplinary applications. It can be a challenge for some biomedical scientists to understand the often quite different publication paradigms in the non-biomedical disciplines. Reviewers also need to be counselled on the interpretation of citations. *Nature* columnist Richard van Noorden points out that interdisciplinary papers tend to have fewer citations than the norm in the short term but gain more than the normal number of citations over the longer term (thirteen years) and 'can have broad societal and economic impacts that are not captured by citations'.[7] This is an argument against mindless use of metrics (more on this in Chapter 7). By the way, one interesting piece of data in van Noorden's article is that countries in eastern Asia, India, China (including Taiwan)

and South Korea were the most interdisciplinary nations by one type of analysis, and Australian interdisciplinary research was also above the world average. National medical research funders will need to keep reviewing and adjusting their systems to address this expanding interdisciplinarity in medical research.

What can funders do to make reviewing easier?

It can take anything from a couple of hours to a full day to review a single grant application, depending on the complexity of the research proposed, what the funding agency is seeking from the reviewer and the diligence of the reviewer. A review committee member therefore faces a huge workload. They may have a dozen or so applications to review and understand in detail as the spokesperson – the person who will introduce the application to the committee meeting, speak to its strengths and weaknesses and summarise the comments of the external reviewers (they will have had to digest and understand these beforehand). They will also need to read all the other applications and the external reviewers' comments so that they are ready to discuss them during the meeting and vote.

This is a huge undertaking. Finding willing scientists is a major job for funding bodies. Statistics on this are rare, but the difficulty of recruiting reviewers is a common item of discussion between funders. There is always a small number of senior scientists who just never accept a request to join a peer review committee. However, most scientists understand that it is part of their obligation to one another, a philosophy of 'I will review these applications because I know that others are being asked to review mine.' On the plus side, the committee camaraderie is

usually enjoyable, you learn about new methodologies and techniques, and new collaborations with other committee members often arise.

There are things that funding bodies can do to help. One is to ask first for short summary applications, usually called Expressions of Interest or Letters of Intent. This is especially helpful if the success rates are very low. These Expressions of Interest are peer reviewed and then only a small subset of the best applicants is invited to submit a full application. For example, if the final success rate is likely to be about 10 per cent, then only the best 20 to 30 per cent of the initial Expressions of Interest might be invited to submit a full application. This two-stage process is mostly welcomed by researchers, and reviewing Expressions of Interest normally takes less time. Overall, however, it does not necessarily reduce greatly the total amount of peer reviewing needed, because the Expressions of Interest still need to be peer reviewed as well as the full applications. It also increases the administrative work of the funder.

Funding bodies can also consider carefully what they send reviewers. Often, they request far too many experimental details, and reviewers must wade through pages and pages of techniques and methodology. This can result in reviewers over-focusing on minutia while paying less attention to the potential gains in knowledge. It helps greatly if funders have a good, simple, intuitive online reviewing system. On this, mea culpa for the NHMRC's Research Grants Management System, which has now been replaced with a new management system, Sapphire. (The lesson? Never fully trust the promises of an IT service.)

One minor but important way to reduce reviewing workloads is to stop asking supervisors for references for fellowship applicants. Having looked at many thousands of these, I have rarely seen one that I thought was fully frank and honest. Supervisors universally extol the applicant's virtues, sometimes to a scarcely credible extent, but the applicant's

weaknesses are rarely mentioned. This is understandable because supervisors want to do the best for their students and postdocs, but it is regrettable because it disadvantages applicants whose supervisors are more honest. Unless all supervisors are completely frank about applicants' weaknesses as well as their strengths, those applicants with supervisors who are franker and less effusive will be unfairly disadvantaged.

This problem has led to 'coding' of criticism, the use of innocuous words and phrases that are meant as a subtle signal about an applicant's weakness. The problem with this is that everyone needs to know the code and how to interpret it. But they don't. Words have different meanings, nuances and implications to different people: to men and women, across generations, and certainly across different scientific and national cultures, including those whose native language is not the language of the review. Those from different cultures also write in different ways. I am oversimplifying, but, at the risk of caricature, some American supervisors are extravagant in their use of adjectives and adverbs, while reviewers from less exuberant cultures are, well, less exuberant. Then there is the evidence that women use less 'hype' than men.[8] Better to do away with supervisor references entirely, or reduce them to simple yes-or-no questions.

Scientists need to be vigilant about financial cutbacks that affect peer review quality. Successive Australian governments have cut NHMRC and ARC budgets for administration of peer review systems every year for more than a decade. Dishonestly, governments pretend that these cuts are 'efficiency dividends' when they are nothing of the kind. In my time at the NHMRC, we lost 20 per cent of our staff during which application numbers doubled. Government Departments of Finance do not seem to understand that quality peer review is absolutely essential

for the best use of public funds. Cutbacks impact on the rigour of peer review, threaten the quality of funding decisions and diminish the research community's trust in the fairness of the system. Researchers should always question why changes in peer review are made.

'Success rate' is not a marker of the science

There is never enough money to support all worthy applications and there probably never will be. Government funding is always finite and there are always lots of highly motivated scientists competing for it. The NHMRC was only able to fund 14.8 per cent of applications for its Investigator Research Grants in 2021, just 254 of 1722 applications. The ARC was able to fund only 587 of 3095 applications for its Discovery Grants, also less than 20 per cent. The situation is similar internationally. The NIH funded only 11,332 of 55,038 extramural applications (20.6 per cent).[9] At the International Human Frontier Science program, we are able to fund fewer than 4 per cent of initial applications each year.

Researchers will have spent many summer days preparing applications for NHMRC and ARC grants, sending them off full of confidence that they have written compelling proposals while their families and friends were enjoying their holidays. It is dispiriting to receive, months later, a 'I regret to inform you that your application was unsuccessful' missive. It is hard not to feel that it is you who is unsuccessful as a scientist. A few such emails in a row can break one's enthusiasm for medical research and end careers.

In these dispiriting moments, it can be hard to remember that 'success rate' relates to money and it is not a description of the ideas in the application, or scientific ability. In fact, experience at the NHMRC has shown that at least two-thirds of the applications will be judged

as worthy of funding under peer review, in terms of the quality of the science and the scientists' likelihood of achieving the research goals. That is, two-thirds of applications are worth funding, but there is money for less than 20 per cent.

Maintaining the independence of peer review

Politicians should never have the power to overrule peer review decisions.

A democratically elected government is responsible for setting the broad strategies for spending taxpayer funds. They must decide whether to spend on research for health improvement, for space, for agricultural or Antarctic science, and to decide the amount of funding for each. To make these strategic decisions, wise governments will seek expert advice.

Once the broad policy has been set, however, it has long been the norm in advanced scientific countries that governments do not decide to fund a specific person or specific institution. Instead, funding decisions are made independently via peer review, at arm's length from government. To have it otherwise would lead to pork barrelling, as in any other area of spending without similar safeguards. It would be vested interests that determine where the money goes. Wise politicians understand, too, that it is not in their interests to have this power, because it opens them up to endless special pleading and lobbying and potentially to accusations of favouritism and even corruption.

In Australia, the NHMRC has this independence. The Minister for Health does not have discretion to change the NHMRC's funding recommendations. This was codified in the *National Health and Medical Research Council Act 1992*. The NHMRC has been around for almost

100 years, but it was only in the early 1990s when the Minister for Health and Aged Care, Brian Howe, decided that the council needed the protection of an Act of Parliament. I remember being in a meeting with him and John Funder and asking him why the NHMRC needed an Act at all, given that it had flourished for more than half a century without one. He replied that we might not need it now, but one day we would need its protection, and so the *NHMRC Act* contains provisions against ministerial intervention. It states that 'Directions given by the Minister … must be of a general nature only, and, in particular, the Minister is not entitled to direct the CEO, the Council or a Principal Committee: (a) to recommend the allocation of research funds to a particular person, organisation, State or Territory; or (b) as to the manner of the CEO, Council or Principal Committee's treatment of particular scientific, technical or ethical issues.' Minister Howe was prescient in his concern. Unlike the *NHMRC Act*, the *Medical Research Future Fund Act 2015* is silent on the protection of decisions made scientifically through peer review. More on this in Chapters 4 and 8.

However, an Act of Parliament apparently is not always a guarantee against government interference in scientific review in Australia. The Australian Research Council Act states: 'The Minister must not direct the CEO … to recommend that a particular proposal should, or should not, be approved as deserving financial assistance.' So it is very odd that Coalition government ministers have interfered in ARC funding decisions for more than two decades, including in 2017, 2018, 2020 and 2021, earning the strong condemnation of researchers. In 2014 budget too, the Abbott government allocated ARC funding directly to James Cook University and the Juvenile Diabetes Research Foundation.[10]

Another mistake that governments can make is when they insist on mixing non-scientific matters into peer reviewing.[11] Applicants for

Australian Research Council funding are required to state what national benefits will flow from the research: they must 'articulate the extent to which the research contributes to Australia's national interest through its potential to have economic, commercial, environmental, social or cultural benefits to the Australian community'.[12] Because the ARC mostly funds basic research, which UNESCO defines as 'experimental or theoretical work undertaken primarily to acquire new knowledge of the underlying foundations of phenomena and observable facts, without any particular application or use in view', the most important benefits are and should be the acquisition of deeper knowledge. Sure, this knowledge may lead to concrete benefits downstream eventually. But a peer reviewer of the application is unlikely to be an expert in whether the results of the research will lead to new commercial opportunities, better government decision-making, or peace and goodwill on Earth. Asking applicants to state what the national benefits will be can encourage applicants to submit half-truths, spin and bullshit, and can disadvantage truthful and modest researchers. Further, it gives an opening for politicians to interfere ideologically, as when an acting minister recently vetoed an ARC grant on climate change.[13]

* * *

Peer review is not a precision process that leads to entirely objective conclusions. It is a sapiential value judgement made by human beings well placed and knowledgeable to make such judgements. A peer review is an opinion, but an informed one.

Some funders appear ready to give up on peer review, and some commentators are calling the system 'broken'. Commentators suggest that a randomised lottery system to decide research funding would be

better, at least for some of the applications near the cut-off points. The implication is that a dice can make as good a judgement as a committee of well-credentialled scientists.

I don't agree. Rather than give up, we should work to refine and improve our systems. We should not throw up our hands, saying that as scientists we don't believe in our judgements, so we will leave it to chance. A lottery sends a dangerous message, and such a philosophy would inevitably result in political intervention. One doesn't need much imagination to envisage a politician thinking, *If you scientists can't decide what to fund, I'll do it*.

Until recently, there has been surprisingly little scholarly work on peer review, though the international Research on Research Institute (RoRI) is running a major project on the effects of lotteries in research funding decisions.[14] The results will deserve careful consideration, but to me a lottery seems wrong in principle. Instead, we should be working to improve our peer review systems, studying the flaws and unintended consequences and working to reduce them progressively.

Chapter 4

Choosing Research Priorities

Why we need to listen to scientists and avoid waste

Everyone has priorities when it comes to medical research: individual researchers, patient advocacy groups, institutions and governments. These are often in competition, and so decisions on which priorities to fund are hard.

A researcher's priority is their own area of research, whether it be cancer, autoimmune disease, depression, heart disease. After all, this is why we chose to work in that field. We think it is an important problem and that progress needs to be made, and we believe we can see a way to make progress.

The priorities of patient groups and health advocates are, understandably, to support research into a particular health issue. There are many philanthropic foundations that support medical research into a specific health problem, such as diabetes, or breast cancer, or dementia. These foundations help to bring public awareness of the problem and often raise considerable funds for research.

Institutions have priorities, too – particularly research institutes and centres that are devoted to a specific health problem.

Governments have priorities in addition to research itself. There can be a priority to build the human research capacity by offering fellowships to train epidemiologists, research nurses, clinicians, bioinformaticians or health economists. Moving research into policy and practice and into commercialisation are priorities. Priorities can include building the infrastructure needed for research, such as facilities like the Australian Synchrotron, labs and animal houses and clinical research wards, and digital and physical services such as gene sequencing and imaging.

It is human nature to consider our own research area the top priority. Most of us can remember being obsessed with our research, struggling to develop a new method, or thinking for weeks at a time about the literature in the field and trying to make coherent sense of our own latest findings. This obsession can be very unhelpful for our personal relationships. And we do also have our own personal career priorities, such as how are we going to get our next grant, get our latest paper published or build our curriculum vitae.

Research priorities in Australia using public funds should be different to priorities in the United States or in Europe. Why? Because Australia produces only a small fraction of the world's medical research output – around 3 per cent. Medical knowledge in broad areas like cancer, heart disease or type 2 diabetes expands due to the fact that researchers all around the world are working on these problems. Even a major increase in NHMRC spending or a Medical Research Future Fund (MRFF) initiative would make only a tiny difference to the total worldwide research effort, and it would divert taxpayers' funds from other research more highly rated by peer review.

People living with uncommon but debilitating health conditions often lobby the NHMRC and politicians for priority research funding. When medical research currently offers no good treatments, as is

the situation with many rare diseases, their case can seem highly compelling. It is heartbreaking (and salutary) to meet with these folk: a reminder of how people look to medical research to alleviate their suffering. However, with Australian researchers just a small fraction of the total pool of research talent, and few Australian applicants for funding for such individual conditions, it is difficult to see how priority funding for a small number of extra grants below the cut-off – a token gesture – would make a real difference. It seems more effective to encourage Australian researchers towards the growing number of international consortia for research on less common and rare diseases, for example the International Rare Diseases Research Consortium.[1] When I was at the NHMRC, I usually offered to arrange to put patient groups in contact with top Australian researchers to interest them in research into their health condition. The work that private foundations do to mobilise community support and funding is also important in raising researcher consciousness.

Real research priorities for Australia

Australia has health problems that are ours alone, problems that we cannot reasonably expect scientists in other countries to research for us. These do deserve funding priority.

The most important of these is research to improve the health of First Nations peoples, the state of which is our national shame. The health burden comes largely from the weight of prejudice and racism, from poverty and disadvantage, from barriers to services and marginalisation. These are social determinants of health, and so the research needs to be conducted with full involvement from the relevant communities.

I wish I could say that I had been more successful in bringing about tangible health outcomes here. During my tenure, the NHMRC dedicated at least 5 per cent of funding directly for Aboriginal and Torres Strait Islander health and capacity building of First Nations researchers. However, the findings of the Close the Gap reports show that little progress in achieving the key health targets has been made, and so medical research has not yet made much difference. It was not from a lack of goodwill, or from a lack of health research scientists wishing to dedicate their skills to this area and conducting excellent research. It was certainly not from a lack of health problems to be tackled.

Perhaps the most useful thing we did was to try to build research capacity by providing flexible funding opportunities that focused on research training and career development. This type of funding, such as Centres of Research Excellence and Synergy grants, gives researchers the discretion to use funds in ways that are most needed at the time, without having to specify at the time of preparing a funding application exactly where the funds will go. That is, researchers are not tied to a predetermined protocol but are awarded the funding on the importance of the problem and the judged ability of the group of researchers to identify and conduct the research needed. This flexibility is especially important for Aboriginal and Torres Strait Islander health research, where the consent of the community and their involvement in the research is crucial to its success.

We also tried to make sure that credentialism was not a barrier. For example, when conducting research in remote areas, the most important person may well be a community nurse who never had a chance to gain formal research qualifications. They are crucial to the research, though, because they know their community well and are trusted by individuals in that community, so they can help to gain the genuine

consent and active participation of the community. Seeking consent and participation is not only the right thing to do but it also makes the research go better and faster, producing more accurate results. It is more likely to have the greatest impact, too: when a community is involved in the research, they want to know what the outcome is and are much more likely to implement or embrace the implementation of the findings of the research.

This process of involving participants in the planning and conduct of research began long before I took up my position. Here and across the globe, First Nation peoples taught researchers and funders to see that true respectful consultation was necessary.

The second real Australian research priority is to improve the delivery of healthcare. Health systems differ country to country, and our national health system has many unique features and challenges. No other country has the same population characteristics, geographic spread, peculiar mix of state (hospitals) and Commonwealth (general practitioner and aged care) systems and funding, or particular blend of universal healthcare and private insurance. Research into the policies and practices of healthcare delivery requires partnerships with local, state and territory, and national decision-makers. One way to do that is the NHMRC's Partnership Projects and Partnership Centres, introduced more than a decade ago, to ensure collaborative research, with involvement from the care delivery organisations and state governments.[2]

A third priority is to implement research-based evidence to improve disease prevention and patient care. With 97 per cent of medical research being done elsewhere in the world, Australia needs 'receptors' to take up that knowledge and put it into practice here. So there needs to be research-trained and research-active individuals delivering healthcare and setting health policies. Doctors and other healthcare

professionals need to be supported in their jobs and absorb international research and influence local practices. Systems to achieve this had been recommended by many reviews of medical research, to little avail. At the NHMRC I worked to introduce Advanced Health Research and Translation Centres, which aimed to enlist healthcare institutions, state and territory Health departments and universities in this task. No money was available, and the Commonwealth Department of Health was wary of the plan. Eventually, we achieved the first iteration in 2014. The NHMRC has persisted with the idea, and the Medical Research Future Fund has added a little funding to keep the program going. But much more needs to be done if we hope to see the benefits of global research output in Australian healthcare delivery.

The research priorities that science reveals

There is a world of difference between the need for research into a particular problem and whether something worthwhile is likely to be achieved by this research.

No matter how important a health problem is, only scientists can see where there are truly opportunities for scientific research to make a difference – research that is likely to make real advances in knowledge.

Everyone, including our elected representatives, can recognise the need for research in, for example, dementia and depression, to reduce suffering and the huge and growing burden on individuals, their carers and the health system. But what research? The best scientists are capable of looking at problems from a new angle and know when a field requires a fundamental change in direction and when 'more of the same' type of research is a waste. Only other researchers will be able to judge which of competing applications are best poised to

make progress in understanding the causes or developing treatments, if the proposed research is promising or likely to lead to a dead-end, and whether the skills and knowledge of the research team are right for the task.

The mRNA 'miracle' COVID vaccine story is especially instructive. It began six decades ago with the discovery of mRNA, and continued with the first delivery of liposome-wrapped mRNA into cells in the 1970s.[3] It is a quintessential story of how the accumulation of fundamental knowledge and the insight of trained scientific minds eventually led to the 'overnight success' of the vaccines. Thousands of scientists across the globe contributed to this success over decades, and they were supported through the standard competitive peer review mechanisms without official designation as a priority.[4] That is, talented researchers gave mRNA biology priority over the years. Without their insights and wise peer reviewer support, successful mRNA vaccines would still be only a dream.

Or consider the Human Genome Project. Scientists glimpsed the potential for human health as soon as Watson and Crick published the structure of DNA in 1953, but the Project took years and years of hard basic science. Researchers could see the value of understanding genetics at a fundamental level and struggled for years with methods that now seem primitive. Their vision and persistence have resulted in the benefits of personalised medicine and have transformed medical research itself.

By the early 2010s, many countries were considering how to integrate the knowledge from genetics and genomics research into healthcare and thinking about how to pay for it. The Department of Health in Australia could see the benefits of personalised medicine but was worried about the costs of widespread uptake of genetic testing and

genomic analysis. I thought the most useful thing to do was to set up partnerships between NHMRC researchers and state health authorities. I convinced the NHMRC's Research Committee to set aside around AU$25 million for a five-year grant for research into how genomics can be best integrated into Australian health systems. Professor Kathryn North, a leading research geneticist, gathered together a powerful group of top researchers and health authorities. It is incredibly gratifying to see what wonderful success she and her colleagues have made of this national research and translation alliance in genomic medicine.[5]

Serendipity can sometime play a part in major research advances, but chance favours only the prepared mind, as Louis Pasteur said in 1854. True breakthroughs always depend on other existing knowledge, a mountain created over decades. Very often it is only after many years that the most valuable research becomes apparent. Think of the essential work of basic scientists who toiled away at understanding the immune system and its role in cancer at a fundamental molecular and cell biology level, funded through open competitive research grant schemes. It was only after decades of this research that other scientists used this knowledge to produce game-changing immunotherapies, a whole new way of treating cancers.

It is always important for funders and peer reviewers to keep in mind that really innovative and transformative ideas can come from researchers outside the mainstream. Australia's most famous examples are Robin Warren and Barry Marshall, who won the Nobel Prize for Physiology or Medicine in 2005. Robin Warren was a careful and dedicated scientist and pathologist, expert in the bacteriological knowledge produced by a century of previous research. He did not accept the assumptions of the majority of gastrointestinal scientists, who at that time believed that ulceration of the stomach was mainly

due to hydrochloric acid secreted by the stomach wall in response to stress. Warren's careful work led him to propose a completely different cause: gastric infection with a *Helicobacter* bacterium. However, his idea would probably just have stayed an idea were it not for the unique personality of Barry Marshall, who was brave and smart enough to realise that Robin Warren's well-evidenced hypothesis was exciting and possibly true. Barry was willing to risk his own health on a pilot study, drinking a beaker of *Helicobacter pylori* bacterium fluid to show that it indeed could produce stomach inflammation. Self-experimentation has a long record in medical research.[6] At the NHMRC, I introduced the Marshall and Warren Grant Award to remind peer review committees to value ideas that were outside the mainstream but potentially transformative.

To say that priorities on what particular research to fund should be mainly determined by researchers sounds and is elitist in the sense that it aims to fund the best research. That said, there is nothing but gain from involving members of the broader community in the whole funding decision process. They can be highly valuable on review committees, not the least as watchdogs on the behaviour and processes of the committee. They bring a wider perspective to strategic and policy decisions on research funding. In translational research, their insights add depth and breadth to the review of applications for funding.

People as priorities

Other than their own research, many medical researchers would identify attracting great young people to medical research as the top priority. Fortunately, research sparks a fire in lots of young undergraduates in biomedical science, medicine, nursing and other health sciences.

Seeing this happen is truly one of the wonderful parts of being a teaching academic.

Young scientists are often the most creative.[7] We have plenty of Australian examples. Graeme Clark was in his thirties when he did the important research work that led to the bionic ear, successfully commercialised by Cochlear. Colin Sullivan was in his early thirties when he first tried positive airway pressure on a patient in his University of Sydney lab, kickstarting ResMed's successful commercialisation of his findings with the development of continuous positive airway pressure (CPAP) devices for sleep apnea. Ian Fraser and Jian Zhou were in their thirties, too, when they filed the patent that resulted in Gardasil, the effective vaccine against cervical cancers.

The mean age of Nobel winners in Physiology or Medicine is around forty years old.[8] Australian Nobel Prize winners Peter Doherty, Elizabeth Blackburn and Barry Marshall were all in their thirties when they conducted their award-winning research, though Robin Warren was in his early forties and Sir Macfarlane Burnet was in his fifties. I am confident that there are twenty- or thirty-something Australian researchers who right now are doing the research that will win them a Nobel Prize. Given the present-day profile of young Australian medical researchers, it is likely statistically that they will be female and from more diverse backgrounds than in the past.

An important responsibility for a national funding body such as the NHMRC is to attract gifted young PhD students into medical research. It is difficult to work out the right number of postdoc fellowships to offer, though. There are enormous numbers of graduating PhDs in medicine, public health and biomedicine around Australia, and it is not possible for every one of them to have a career in health and medical research. There are simply not enough research grants for that. I made

that obvious point to a journalist once and then had a very angry phone call from the vice-chancellor of one of our Group of Eight universities. He said (loudly) to me that my message, that not everyone who wanted a medical research career can have one, would discourage young scientists from applying for postdoctoral positions at his university. But honesty seemed then and now to be the best policy, and really bright people who want a research career and who are passionate about a health or scientific problem are not going to be put off by a few words of caution from the head of the NHMRC. A vice-chancellor's responsibility might be to better prepare potential postdocs for both the ups and downs of embarking on a research career.

Australia doesn't yet have good ways of supporting enough individuals to combine active professional healthcare careers with active medical research. We need trained, high-quality researchers in patient care, in designing and administering the health system, in designing human services to reduce the social determinants of health, and in the biotech and innovative industries, as well as in the lab. The NHMRC Practitioner Fellowships, which offer support for clinicians and other health services professionals to undertake research linked to their practice or policy, is one model, as is the MRFF's Clinical Researcher scheme. But it is only a fraction of what is needed.

Infrastructure as a priority

Medical researchers need resources to conduct their research. This might be physical things, such as labs, microscopes, gene sequencers and synchrotrons, or virtual resources, such as databases (for example, the Ensembl genome database, the Human Protein Atlas, human genomics data through the Global Alliance for Genomics and Health), or access

to public and private health or welfare data or clinical registers. The 'infrastructure' can include people with specific technical skills – such as informatics, programming, specialty research nursing or animal care technology – or recruiting research participants, supporting a valuable cohort and translating the protocols for research participants. Researchers also need journal subscriptions, animal houses, and essential but mundane things such as electricity and water and data storage facilities.

Australia has had many schemes to address gaps in scientific infrastructure, such as the National Collaborative Research Infrastructure Strategy (NCRIS). Over the years, some national needs, such as the Australian Synchrotron and the Australian Animal Health Laboratory for research on dangerous infectious organisms, have been funded as one-off projects, often without provision for ongoing financial support for researchers to use the facilities. This can mean less-than-optimal use and so be wasteful.

One area where we have done well in Australia is building laboratories for medical research. The Atlantic Philanthropies invested hundreds of millions of dollars in research labs for medical research institutes, first in Brisbane and then Melbourne and Sydney. The Howard government also funded two rounds of capital works for the independent medical research institutes. This meant that, into the first decade of the twenty-first century, a divide began to develop between the quality of labs at the institutes and those at universities. Since then, universities have also invested in building new state-of-the-art facilities, and Australia now has many top research buildings right across the sector. Indeed, some of these are incredible architectural statements and wonderful places to work in, such as the South Australian Medical Research Institute, the Garvan Institute for Medical Research and the Peter Doherty Institute.

It is great to have these new state-of-the-art buildings, though their running costs are high. Unlike in many other countries, research funds from the NHMRC and the ARC are mandated to be used for the direct costs of research. Funding for these other costs, so-called indirect costs, must be found elsewhere. This is distorting medical research in Australia, as we shall see in more detail later. In response to the independent Medical Research Institute sector's pleas for support of indirect costs, in 2014 the then Health minister, Peter Dutton, established an enquiry into this issue. However, only a bland report was eventually issued and no actions taken.

The Morrison government also treated universities and institutes differently during the COVID-19 pandemic, when it illogically gave independent research institutes but not universities access to JobKeeper funds. Universities shed thousands of talented researchers and support staff as a result.

Priorities in the philanthropic sector

Not all the money to fund medical research comes from government. There are many wonderful charities funded by people with a commitment to finding cures and treatments for specific diseases. Organisations such as the Cancer Council, the National Heart Foundation of Australia, the Juvenile Diabetes Research Foundation and the National Breast Cancer Foundation provide valuable extra funds for researchers. These organisations can take a different perspective from a government funding agency and deliver money differently, such as the Endowed Chair grants of the National Breast Cancer Foundation – two ten-year research grants of AU$5 million each, including a co-contribution from the recipients' host institutions.[9] They also play an important

role in increasing the awareness of medical research in the community through their outreach and fundraising work.

Even a small charitable organisation with relatively limited funds can be very valuable. Its very existence can draw the attention of good researchers who otherwise might not be thinking about the research possibilities in the field.

There are three broad options for charitable foundations when deciding what research to support. The first is to run its own application and review processes. But this can be costly and, for a small organisation, use up precious donated funds. There is a risk that their administration will be swamped with hundreds of applications for a limited number of grants or fellowships.

A second, and often better, option is to ask the NHMRC to run the peer review process and then hand the review outcomes back to the foundation to make final decisions.

The third, and worst, option is to just rely on the advice of one or two favourite medical researchers. Avoiding capture by scientists is always a challenge for charitable foundations, and it can be hard, often impossible, to avoid conflicts of interest. Many foundations have a leading researcher in the field of interest as their president, chief scientific adviser or chair of their research advisory committee. Human nature can make it difficult to disentangle this person's interests from the interests of the foundation and its donors.

Prioritising commercial development of medical research

I have lost count of the number of government schemes over the last thirty years that have aimed to accelerate the transformation of scientific research in Australia into commercial development. Only a few large

viable private companies have been built on the outcomes of Australian medical research.

CSL is our outstanding success story. I am hardly an expert in knowing why it has been so successful, but the outstanding leadership of Dr Brian McNamee AO and his recruitment of talented staff is often cited. CSL has been responsible for one of the great success stories of groundbreaking Australian basic science: turning Ian Fraser, Jian Zhou and Xiao-Yi Sun's research into a commercial product, a vaccine against human papilloma virus that saves lives around the world. (By the way, Ian Fraser exemplifies all that is good about medical research. He is a wholly decent human being, motivated to do good for his fellow beings, combining innovative basic research through to its translation into a new vaccine to prevent an awful disease. Ian never fails to mention that his colleagues Jian Zhou and Xiao-Yi Sun were also responsible for the discoveries. Tragically, Jian died at a young age, just as the impact of his and Ian's research work was emerging.)

Cochlear, too, is a wonderful Australian story, from the visionary, indefatigable, inspiring Graeme Clark, through to outstanding company leadership by Chris Roberts.

CSL and Cochlear have most of their sales overseas. The small domestic market in Australia acts an inhibitor for the development of new drugs and treatment, as does the lack of capital. State governments, particularly in Victoria and Queensland, have tried to make up for this lack over the years.

The NHMRC is not able to fund commercialisation research, but I introduced two schemes that pointed towards that direction without contravening the *NHMRC Act*. Industry Development Grants supported medical research when there was a demonstrated interest by a potential commercial development partner. Industry Career

Development Fellowships were introduced for young postdocs to do research in a private company rather than a university.

Almost eighty years ago, American engineer and administrator Vannevar Bush, whose report to US President Roosevelt laid the foundation for the success of US science and the world-leading industries built upon it, wrote: 'The most important ways in which the Government can promote industrial research is to increase the flow of new scientific knowledge through support of basic research, and to aid in the development of scientific talent.'[10] This is still true. When the G7 presidents and prime ministers established the International Human Frontier Science Program in 1987, it was to fund basic research into 'the sophisticated and complex mechanisms of living organisms' for 'the benefit of all humankind'.[11] This mission has been re-confirmed every three years by the now fourteen member countries and the European Union. As I mentioned earlier, HFSP awardees have gone on to win twenty-eight Nobel Prizes.

Governments should set only broad priorities

My view is that governments should set only broad priorities for scientific research and do so based on wise, independent and informed analysis of the need and the opportunity. Otherwise, strategic decisions will be primarily political. Lobbyists and people close to the government minister will set strategy. It is even worse if governments interfere in what particular research to fund and which researchers should get funding.

Most countries prevent or limit the direct government interference in their medical research agencies. In the United Kingdom, the Haldane Principle, developed progressively following a 1919 report

from a government committee chaired by Robert Burdon Haldane, a philosopher-politician, holds that independent research councils, rather that politicians and government departments, should make decisions on research funding. The general principle has long been adhered to by governments regarding medical research. The Haldane Report was issued in 1919. The principle was restated in 2018 by the UK Secretary of State for Innovation, Universities and Skills:

> … in the 21st century, I think three fundamental elements remain entirely valid.
>
> – That researchers are best placed to determine detailed priorities.
> – That the government's role is to set the over-arching strategy; and
> – That the research councils are 'guardians of the independence of science'.[12]

In forming the UK Research and Innovation institute in 2018, which includes the Medical Research Council, the parliamentary *Higher Education and Research Act 2017* formally incorporated the Haldane Principle.[13]

In the United States, Congress gives only broad strategies when voting on funding for the National Institutes of Health, and the decisions on how the funding is used are made by the organisation's scientific leadership, with all grant decisions for both intramural and extramural research made by peer review.

However, governments love 'announceables', and the time that it takes from discoveries to new treatments and commercial products frustrates many politicians. Prime ministers and Health ministers like to

announce research initiatives that they believe will fast-track practical outcomes, ideally before the next election. But medical researchers know that breakthroughs are never based on one piece of research. This is not how science works, and it is certainly not how new findings are translated into health and medical policies and practices. It all takes time: replications, analyses, syntheses and more and more research, until the accumulated evidence seems reliable and substantial enough for clinical decisions to be based on it. In fact, it is more accurate to think of the evidence for clinical actions as never being quite settled, always being subject to what we learn as new research emerges. This leaves clinicians and policymakers in difficult positions: what is the best evidence-based advice right now? This problem remains unsolved, though the work of the Cochrane Collaboration, some clinical research societies and groups such as the Australian Living Evidence Consortium do excellent work to rigorously incorporate new evidence as quickly as possible into clinical guidance.

When a government announces a special new research initiative, it is often a smallish bucket of money, too little and of too short a duration to make any discernible difference to the problem. On other occasions, it is tempted to set up a whole parallel organisation to the NHMRC, such as the National Breast Cancer Centre or Cancer Australia. These organisations could have simply duplicated NHMRC cancer research efforts, but wise leadership of each over the years has developed them into useful broader organisations offering information and advice, beyond just research funding. Though the NHMRC remains the biggest funder of cancer research in Australia.

Then, in 2014, the Abbott government set up a huge new funding scheme parallel to the NHMRC: the Medical Research Future Fund (MRFF).

The Medical Research Future Fund: a missed opportunity?

The MRFF is an international outlier in terms of government control of its operations. It was born in the contentious first budget of the Abbott government. It was a singular piece of good news in a budget that has been sometimes described as a 'horror'.[14] The establishment of the MRFF reflected both the government's strong support for medical research in general and its frustration at not being able to control what the NHMRC did.

The Senate Community Affairs Committee set up an inquiry into the draft MRFF legislation in 2015. The Senate Committee's report recommended passing the legislation, but there were reservations. A supplementary report by the Australian Labor Party expressed concern, stating:

> Labor Senators do not agree that decisions regarding the projects and programs awarded funding should sit wholly with the Minister of the day. This is inconsistent with the way existing grants are awarded by the NHMRC and inconsistent with international best practice in awarding grants to the highest quality projects based on a process of peer review … Labor Senators do not support a discretionary funding mechanism through which the Minister for Health of the day can allocate funding based on a broad set of parameters – as defined by contested and inadequate definitions of 'medical research' and 'medical innovation'.[15]

These concerns were prescient.

The Leader of the Government in the Senate, Mathias Cormann, said in his Second Reading speech on 12 August 2015, 'it is important to ensure that the framework for setting the priorities within which the government has to operate is independent, that it is based on expert advice and that that expert advice is informed by appropriate consultation with consumer groups and medical research stakeholders'.[16] It is depressing how far the government had deviated from this.

I wrote in *The Conversation* in April 2015: 'It will be especially important to be vigilant as the Medical Research Future Fund is rolled out. Decisions must be made through peer review, and it was reassuring to hear the prime minister say that "the vast majority of disbursements from the fund will be in the hands of the National Health and Medical Research Council".'[17] Unfortunately, the reassurances have turned out to be in vain. Decisions regarding the projects and programs do sit with the Health minister using 'a discretionary funding mechanism'. There is a highly credentialled advisory board, but its role seems to me to simply be to advise on overall general MRFF strategies.

The *Medical Research Future Fund Act 2015* states: 'The Australian Medical Research Advisory Board is established to determine the Australian Medical Research and Innovation Strategy and the Australian Medical Research and Innovation Priorities. The Health Minister takes the Priorities into account in making decisions about the financial assistance that is provided from the Medical Research Future Fund Special Account.'[18] This gives the minister of the day decision-making discretion, and there is no evidence in the minutes of the Board that it is called on to advise the minister before they announce a funding call.[19] It might be that ministers have drawn on advice from their department, but if so this process is not clear or transparent, and the scientific and medical credentials of the departmental officers

are unknown. My experience in Canberra was that the Department of Health had wonderful public servants, but few had experience working in healthcare and very few had scientific research backgrounds. Compare this to the NHMRC, with its combinations of scientists, health officials and community health representatives, and with decades of experience conducting rigorous review of applications and administration of awards.

As far as I can tell, most MRFF calls for applications do involve peer review, mostly organised by the NHMRC, but there is little transparency in whether the Health minister follows the peer reviewers' advice. There is room to worry about this because other ministers in recent governments have sometimes ignored their departmental advice on grants.[20] Nor is it transparent how ethical guidelines (on human and animal subjects and research integrity) are applied, how allegations of research misconduct are handled by the Department of Health, and whether open access policies are mandated and monitored. Few statistics are reported, limiting judgement of the MRFF's impact.

The MRFF's annual funding is now of similar size to that of the NHMRC. MRFF decisions are therefore hugely influential in Australian medical research. If the fund is used wisely, it will have many benefits. But any funding scheme run within a government department under the command of a politician risks being politicised. If political lobbying were to become decisive, it would privilege the 'haves' with inside knowledge and corrupt the way that decisions about science are made. Furthermore, the NHMRC budget has stalled as the MRFF's has risen, with success rates for NHMRC grants falling. The Abbott government's aim to increase Australian medical research was laudatory. How they did it was not so great.

With two large but separate bodies funding medical research, gaps and duplication are inevitable. Already there has been an abrupt change in the research balance. For many years, Australia's medical research funding through the NHMRC was split roughly fifty-fifty between funding for basic discovery research and funding for applied or translational research. In contrast, the MRFF funds translational research, and this means that basic research is now a much smaller proportion of total Australian medical research funding – the ratio sits at around 25 per cent basic to 75 per cent applied. Basic research is often mistakenly thought to be only laboratory-based biological and life science research. But there is equally important investigator-driven research into basic principles, methodology and philosophies in public health and health services research.

In June 2023, Mark Butler, the Health Minister in the Albanese government, seems to have recognised the problems with the MRFF and issued a national consultation paper on 'optimising outcomes from government investment through the governance and administration of the Medical Research Future Fund and the National Health and Medical Research Council's Medical Research Endowment Account'.[21] Three models are proposed, two of which could lead to better coordinated national strategy, transparency and accountability. A national strategy needs collaboration with the states and territories, who are responsible for healthcare under the Australian Constitution.

MRFF grant lists to date show that most MRFF funding recipients are senior, well-established individuals, mainly professors. A coordinated national strategy can build future human research capacity by supporting new and emerging researchers.

* * *

When he was Opposition leader, Tony Abbott announced that his government would commission research into the health effects of wind farms. Back then, as turbines were being built around the countryside, claims began to emerge that they were harmful to health and caused headaches, vertigo, depression and even cancer. Wind farms became politicised. The federal Treasurer, Joe Hockey, reflected the views of some landholders when he said that he found the wind farm at Lake George near Canberra 'utterly offensive' and a 'blight on the landscape'.[22] The issue grew and grew, so much so that a Senate Select Committee on Wind Turbines was set up in 2015.

With a newly elected Abbott government committed to research on the issue, I felt the NHMRC should be the body commissioning this research. This would ensure that applications from real scientific experts were elicited, and that the review system would be rigorous and scientific, the process transparent and the research independent. The alternative would have been for the government to commission a commercial consultancy firm that would likely not be transparent or engage the best researchers, and that would be suspected of delivering findings that suited the government.

As the first step, I set up an expert committee to review the existing scientific evidence. Receiving their report, NHMRC concluded, 'After careful consideration and deliberation of the body of evidence, NHMRC concludes that there is currently no consistent evidence that wind farms cause adverse health effects in humans.' However, it also concluded that more research was needed: 'Given the poor quality of current direct evidence and the concern expressed by some members of the community, high quality research into possible health effects of wind farms, particularly within 1,500 metres (m), is warranted.'[23]

When I announced that the NHMRC would commission research, some in the public health community were outraged. They seemed to feel that even asking the question, even commissioning good research, gave the critics too much ammunition against the development of wind farms as alternative renewable energy sources. Public health research doyen Professor Simon Chapman was quoted as saying, 'It's really quite disgraceful – it's money literally poured down the drain.'[24]

I remain unrepentant. If an elected government had promised the research, then it was best that the NHMRC conducted it. It was especially important to do after a scientifically expert NHMRC committee called for it. On the other hand, perhaps I am just still feeling hurt because here the criticism was from people that I deeply respect.

But I did enjoy the farewell gift from one of my NHMRC staff members when I finished up in the role: a carry bag decorated with wind turbine emblems.

Chapter 5

Medical Research Careers

Barriers for women and emerging researchers

Insecurity is inherent in medical research. Scientific talent is not evenly distributed and the awarding of public funding must be merit-based. Not all who want to be medical researchers have the talent to do so. This is tough on individuals if, after years of training, postgraduate positions and a developing career, they cannot obtain competitive research grant funding.

Full-time researchers live precariously. They rarely have long-term security of employment at their university or institute. Their salaries depend on repeated success in securing funding, in competition against other researchers. This combination of frequent competitive funding rounds and short-term appointments means that they live in the knowledge that their research careers can end very abruptly if their application is unsuccessful.

Full-time researchers do have an advantage in that they have more time for research than part-time researchers, who are professionals employed to provide healthcare or teach university students. These professionals can be seen to be less 'productive' (meaning they publish fewer papers) than full-time researchers. On the plus side, though,

they have the advantage of greater income security through their professional job. If their medical research funding peters out, the mortgage can still be paid.

I do not know what proportion of Australian researchers have an alternative profession to fall back on when research funding runs out. The NHMRC is excellent at collecting information on those it funds, but if information existed on the total Australian medical research effort, it would help planning and reduce the insecurity in the system. Research on medical research itself is surprisingly rare, so the Research on Research Institute established by Wellcome, Digital Science and the Universities of Leiden and Sheffield is an exciting international development. Perhaps an Australian charitable foundation would like to establish something similar for Australian research.

The situation for young full-time researchers is particularly precarious in Australia. In many other countries, universities and large research institutions, such as the institutes of the Max Planck Society in Germany, have formal systems that move successful emerging researchers from short-term contracts to more secure tenured positions. There is no equivalent of this in Australia. Full-time medical researchers may remain dependent on short-term contracts, relying on competitive renewal of their salary every three to five years, from their first postdoctoral fellowship through to retirement decades later. This particularly disadvantages women and others with care-giving responsibilities. Research institutions should provide more security for emerging researchers by giving them a secure contract for seven to ten years. More on that in the final chapter.

It would help a lot, too, if Australia had more and larger alternative sources of salary support and research funding outside the NHMRC, as there are in the United States and in Europe. The philanthropic

bodies we do have are mostly small, and many provide only 'starter' research grants or short-term fellowships.

Particularly insecure for basic science postdocs

The biggest group of precariously employed medical researchers are the basic science postdocs without another profession. The maths on their chances of a long-term, full-time career in research is challenging. Most graduating PhDs are not going to be able to become tenured academics. Just as an example to give the scale of the issue, we had about twenty graduating PhDs each year in Monash's Physiology department when I was its head fifteen years ago. However, we had only two new academic appointments to fill over a ten-year period. This mismatch was similar to that of other Australian bioscience departments. The good news, though, is that many of our Monash PhD graduates went on to have spectacular careers in finance, public administration and healthcare, using all that a PhD teaches about thinking, planning, analysis, self-reliance, networking and communication. So this is not an argument for departments to reduce their PhD intake, just make sure that all the post-graduation opportunities are explained to students.

Postdocs do much of the hands-on work in research groups. This is of benefit to both them and to the rest of the lab group. The postdocs learn under and train with the more senior members of the group, and they provide more brains and hands for the group. However, this can lead to postdocs being exploited. Some senior researchers and institutions succumb to a temptation to lure as many postdocs as possible, without consideration of each postdoc's prospects for a long-term research career. In one instance in the last decade, an institution reportedly appointed 100 new postdocs in a single year,

with the implied or explicit advice that they could then go on to the NHMRC fellowships scheme. Did many of them know that there were only about 100 NHMRC fellowships available across Australia, so the likelihood of all of them gaining NHMRC support was zero?

The postdoc years can be the best and worst of times. You can learn new fields and methods, work overseas in a great research group in one of the exciting research institutions and cities of the world, and build a network that can last a lifetime. It is a special thrill when your first presentation at an international meeting evokes interest from scientists whose work you admire. We often form lifelong friendships and networks from our postdoc years, and gather indelible scientific and social memories.

The NHMRC has run fellowship schemes offering two years overseas and two years back in Australia for more than fifty years. However, not all postdocs want, or are able to, move overseas. Many are in their late twenties or early thirties and have family obligations and responsibilities. In the 1990s, the NHMRC introduced a scheme to support postdocs who wanted to stay in Australia – but there was a requirement to move away from their PhD research group and institution. The reasoning behind this was that everyone in science benefits from expanding their experiences and methodologies and undergoing a change in research group cultures.

The worst of times is when the postdoc is exploited. A bad postdoc supervisor can regard a postdoc as just a 'cheap pair of hands', rather than as a mind with the potential to be developed. Some postdocs in the United States, for instance, find that they are just one of 100 or more in the biggest labs in the country, asked to work on a narrow topic and given little help to expand their scientific horizons and develop their skill sets. For the most part, though, scientists take seriously their

responsibilities for nurturing and developing postdocs' talents. Most successful researchers will agree that the mentorship of their postdoc supervisors has been crucial to their careers.

Particularly insecure for women scientists

The numbers of women working as postdocs have increased in recent decades. The NHMRC reports that women were 58 per cent of applicants for the lower levels of postdoc awards in 2021. The proportion of women graduating with medical degrees has also surpassed 50 per cent.[1] However, powerful forces are driving women away from careers in medical research. The NHMRC's data shows that 'far fewer women than men apply for the senior fellowship levels … [even though] women make up the majority of applicants at the junior levels'.[2] We have a system-wide problem that we must address so we don't keep losing all that talent. Funding bodies can play their part, but the universities, institutes and hospitals have the greater responsibility.

A career in research is particularly tough for women with young kids. Working towards a successful career usually demands long hours, which are often irregular. Cultured cells and lab animals don't work nine to five; clinical responsibilities and undergraduate teaching disrupt the orderly scheduling of the day. Long days and out-of-hours work are almost impossible when your kids are young. It remains only too true that society expects female partners to provide the bulk of care when the kids have caught yet another bug from the crèche, need a lift to footy practice, or have to be picked up from after-school care or a playdate. It is more difficult, too, for primary caregivers to travel to national and international meetings to raise their visibility and develop their network, and to find time for writing grant and fellowship applications and research papers.

Postdocs and younger scientists do not have high salaries, so the option of full-time paid care of children in the home is usually not possible. Government childcare support for preschoolers can make a huge difference, and Scandinavian and some European countries are well in advance of Australia and the United States with this. Postdocs with preschool age children can face spending most of their salaries on childcare, and the costs are rising faster than salaries. Unless funding bodies, government and employers address this specifically and rigorously, women who have children face a double set of barriers to a long career in medical research compared to men.

One useful policy that some universities have is to employ another researcher to carry on the research while a mother is on maternity leave and working restricted hours on her return. On-site childcare can also be transformative. And there have been some other innovative policies. For instance, the Walter and Eliza Hall Institute of Medical Research has forbidden scientific meetings before 9.30am and after 4.30pm to maintain 'family-friendly meeting times'.[3]

Of course, many women with kids do go on to reach the top of their fields, but we ask more of senior women than of most men, and too many do not go on with their careers, as the NHMRC data shows. It would be useful to collect statistics to assess the extent of disadvantage caregivers with dependent children or parents face professionally in order to think about how to make improvements in the system.

Shifting expectations of a career

Postdocs graduating in 2021 have different expectations from previous generations. Rather than embark on a linear research career, they are more likely to want to take time out from research to do other things:

travel; change fields; combine their main job with another, such as working for an environmental cause or creating a start-up. This can challenge those of us who expect everyone's career path to mimic our own.

It is a challenge for peer review systems to figure out how to compare such scientists with those on a traditional step-by-step march up the ladder. We must find ways to better value talented early career researchers who spend their time moving between working in biotech, fintech, NGOs and medical research. Peer reviewers need to be more flexible in their judgements of less-conventional career trajectories. Likewise, greater flexibility would help more doctors and other health professionals to combine research and clinical training with volunteering for health NGOs here and overseas (such as Médecins Sans Frontières or the United Nations High Commissioner for Refugees) or completing professional college training.

Postdocs and emerging researchers come from much more diverse backgrounds than decades ago. This means that appointment and promotion committees need to reflect this diversity and to guard against biases, conscious and unconscious. It would be valuable for universities and institutes to monitor if the drop-out rate of minority researchers is greater than average, to be able to identify and remedy the causes. Medical research benefits from diversity in all its aspects, so let's make sure that outdated habits of judging achievements and track records don't get in the way.

* * *

When I first went to the United States in the 1970s, I was surprised to see that some scientists in their eighties were still active, and moreover

were often in key leadership positions. It is admirable that some scientists wish to stay involved well into their old age, but I would argue that it is not good they keep leadership positions. Organisations rarely benefit from long-term leadership by one person. There are exceptions, but in general most organisations ensure that an appointment is long enough for leadership to be exhibited (at least five years) but not so long that the leadership becomes rigid and reactionary. Australian vice-chancellors usually serve between five and ten years, and deans of Science and of Medicine about the same.

Prime ministers usually last far less than that, but that is an entirely different story.

Chapter 6

Trouble in the Lab

How sloppiness, ignorance, cheating and fakery are undermining trust

Like all humans, scientists vary in their motivation, skills, psychology, formative histories, wealth and privilege, gender, age and ratio of optimism to pessimism. I contended in Chapter 1 that the quanta of honesty, compassion, intelligence, cooperative spirit and generosity are well above average among medical researchers. Almost all the people that I have met in medical research stand out as having principled motivations, caring about the wellbeing of other humans and seeking a deeper and better understanding of good health and ill health. Admittedly I am biased, but a better lot of people would be hard to find.

But we are still human, with all the complexity of motivation that comes with that. Some of our less than admirable human tendencies can be amplified by the competitive nature of medical research funding and the rewards of prestige and money that can follow. By taking into account human nature, funding bodies have developed practices and guidelines over the decades that improve the process of awarding

grants by developing systems for unbiased peer review and avoidance of conflicts of interest. Decades of work by medical researchers has improved the openness and conduct of clinical trials.[1] Ethical rules have been developed for research on other humans, after the medical experiments by the Nazis and others during World War II, and egregious scandals such as the Tuskegee Syphilis Study, which took place between 1932 and 1972 and was designed to observe the effects of syphilis in African-American males when left untreated, leading to the deaths of more than 100 participants. Rules for the use of animals in research have been developed too, once outside criticism and scientists' own ethical qualms led to a recognition that, essential though this research often is, there must be limits on animal suffering. Policies are being developed to give citizens and taxpayers who paid for the research better and faster access to results through the open access movement. Scientists have led the work on better ways to assess people for appointments and promotions – for example, the Declaration on Research Assessment (DORA).[2]

Medical researchers have led these changes because we know that our scientific work is built on trust – in each other's findings and by those who provide the money. It is in our own interests to maintain the trust of the taxpayers and their governments – governments fund medical research more handsomely than most other types of science because they have faith that we can help with society's health problems. Most working medical researchers grumble about bureaucracy, but in ethics this benefits us. Human ethics committees help maintain public trust in medical research using other humans. Animal ethics committees ensure that when animals need to be used, it is within an ethical framework. Trust can be easily broken, and disadvantaged and minority populations who have experienced

medical research as exploitative do not always trust researchers to be fair with them.

Most of all, medical researchers need to be able to trust one another's work when we are designing and conducting our research. Unfortunately, we cannot always do that.

The pressures on researchers in the third decade of the twenty-first century are greater than even a couple of decades ago. There are immense competitive pressures to win research funds, get promoted and even gain some clinical appointments.[3] We are pressured to publish with impact, to earn recognition from our peers, to improve our personal 'metrics' and to win funding for ourselves and our teams in the face of low success rates. Sadly, these pressures can lead some researchers away from the principles of science, resulting in poor and error-strewn science, and even fraud.

Poor and error-strewn science often comes from poor training and poor or absent supervision, rather than from deliberate bad behaviour. While this is not acceptable, the perpetrators can sometimes be re-trained and the problems remediated (for instance, the retraction of publications).

Then there is deliberately fraudulent research. This is cheating – the aim is to get a step ahead of competitors, win more grants and increase one's prestige. Cheating can include omitting some results that 'don't fit', leaving out a key methodological step or two in publications so that others cannot build upon your findings, inventing phantom patients for clinical trials, faking the results to suit your hypothesis, or perhaps never having done the experiments at all. Not many scientists are outright fraudsters, but a few are.

Both poor and sloppy science and fraudulent science damage medical research. When researchers set out to deliberately cheat, to publish

deliberately fraudulent research results, there is simply no excuse. However, despite the different motivations of the researchers and the added culpability in the case of fraud, the malign effects of sloppy science can be as great as those of deliberate cheating. Both transgress against the tenets of science, and both harm the reputation of medical research and undermine trust. Worse, both can harm patients and put at risk volunteers in clinical trials. They can result in error-laden public health policies and waste the resources of companies trying to commercialise.

Sloppy and error-strewn science

In 2012, Glenn Begley and Lee Ellis, then at biopharmaceutical company Amgen, published a bombshell article in *Nature*. They had tried to replicate fifty-three published experiments, interested in whether these previously published results could be developed commercially. To their surprise, they could successfully replicate the findings in only six of the fifty-three. They called this 'a shocking result', and it is indeed hard to argue with that.

Their description of the difference between the six replicable results and the forty-seven that could not be was telling:

> In studies for which findings could be reproduced, authors had paid close attention to controls, reagents, investigator bias and describing the complete data set. For results that could not be reproduced, however, data were not routinely analysed by investigators blinded to the experimental versus control groups. Investigators frequently presented the results of one experiment, such as a single Western-blot analysis.[4]

In short, good science existed in the reproducible papers, but methodological flaws were evident in the forty-seven, leading to results that were not able to be reproduced.

It is worth quoting from Begley's follow-up paper in 2015, as it sums up the problem perfectly:

> Medical and scientific advances are predicated on new knowledge that is robust and reliable and that serves as a solid foundation on which further advances can be built. In biomedical research, we are in the midst of a revolution with the generation of new data and scientific publications at a previously unprecedented rate.
>
> However, unfortunately, there is compelling evidence that the majority of these discoveries will not stand the test of time.
>
> To a large extent, this reproducibility crisis in basic and preclinical research may be as a result of failure to adhere to good scientific practice and the desperation to publish or perish.
>
> This is a multifaceted, multistakeholder problem. No single party is solely responsible, and no single solution will suffice.[5]

The problems are seen in both human and pre-clinical animal research. For example, Alexander Aarts and colleagues looked at the replications of 100 published experiments in high-ranking psychology journals. They found that, at most, only 50 per cent of the original findings were observed in the replications.[6] Yasunori Park, Jennifer A. Byrne and colleagues found that 712 articles across seventy-eight journals 'described at least one wrongly identified nucleotide sequence, with a total of 1,535 wrongly identified sequences'. The more than 3400 articles they examined had been highly cited (>17,000 times), including in reports of clinical trials. They warned that because the publications

'may misinform the future development of human therapies', 'urgent measures are required to address unreliable gene research articles'.[7]

Many scientists have worked to make improvements in clinical trials, such as pre-registration on websites such as clinicaltrials.gov, but the problems of reproducibility persist. For example, in the area of critical care, David Niven and colleagues studied the reports of sixty-six clinical practices and found that less than 50 per cent of replication studies had findings consistent with the original papers. An effective treatment reported in the original paper was found not to be effective in almost one-third of replication studies.[8]

Steve Perrin, chief scientific officer at the ALS Therapy Development Institute in Cambridge, Massachusetts, has pointed out that '[a]nimal models of disease are frequently condemned as poor predictors of whether an experimental drug can become an effective treatment [in human beings]. Often, though, the real reason is that the preclinical experiments were not rigorously designed.' He referenced an earlier study by Sean Scott and colleagues, who analysed why the efficacy of dozens of agents identified in transgenic mice models of familial amyotrophic lateral sclerosis, a progressive motor neuron disease, were not efficacious in human clinical trials. They had concluded that poor pre-clinical experimental design, especially uncontrolled confounding variables, was the main reason why these agents were ineffective when later tested in adequately designed and powered repeat studies.[9]

Recently, Timothy M. Errington and colleagues looked at replicability in fifty papers in the field of cancer biology. Their results were, in the words of the editorial in *Nature*, 'disquieting' – 'fewer than half of the experiments assessed stood up to scrutiny'.[10] One of the most shocking of their findings was that only 26 per cent of the authors of the papers examined were helpful to Errington and his colleagues

by providing further experimental details when these were not in the original papers. This might suggest that the majority thought it was just not important to ensure replicability or had something to hide.

Soon after Glenn Begley and Lee Ellis's 2012 *Nature* article appeared, the influential international weekly magazine *The Economist* published a feature article entitled 'Trouble at the lab' (to which my chapter title pays tribute). It is a comprehensive, thoughtful and damning article, canvassing the many reasons that might account for the inability to replicate results, most of them scientifically inexcusable.

Two points made in the article are especially important. The first is about trust and government funding. The article noted: 'The governments of the OECD, a club of mostly rich countries, spent $59 billion on biomedical research in 2012, nearly double the figure in 2000. One of the justifications for this is that basic-science results provided by governments form the basis for private drug-development work. If companies cannot rely on academic research, that reasoning breaks down.'

The second is about our responsibilities as scientists. The article quotes Bruce Alberts, a previous editor of *Science*, the prestigious journal of the American Association for the Advancement of Science. He makes the important point that scientists themselves 'need to develop a value system where simply moving on from one's mistakes without publicly acknowledging them severely damages, rather than protects, a scientific reputation'. *The Economist* concurred: 'This will not be easy. But if science is to stay on its tracks and be worthy of the trust so widely invested in it, it may be necessary.'[11]

Many scientists are now trying to address the problem, for example via the Reproducibility Project of the Open Science Collaboration. Yet some scientists are untroubled by this issue of lack of reproducibility

in medical research. They point out that biology is inherently variable and so some of the variation in results in replications studies is simply due to that. There is of course some truth in this, but with funders rarely supporting projects to test replication and with the difficulty of publishing negative results, this argument cannot serve to dismiss the problem. There is simply too much evidence that poor and incompetent science is a serious problem and is only too prevalent.

Gross research misconduct

What we call research misconduct could equally well be called fraud and cheating. It is a deliberate attempt to beat colleagues, get more grant money and increase personal prestige and influence. It is transgressing the tenets of science. It is inexcusable.

Most of us will have heard about some of the more notorious cases, here and abroad, but for a fuller account I recommend *Scholarly Misconduct: Law, Regulation and Practice* by Ian Freckelton, a respected barrister and legal scholar who was recently inducted into the Australian Academy of Health and Medical Sciences.[12]

Formal definitions of research misconduct vary across national borders. Earlier definitions tended to focus only on the major issues of fabrication, falsification and plagiarism, and these remain the definitions of the US Office of Research Integrity. Progressively, definitions of research misconduct have become more detailed, complex and sophisticated. At the heart, though, is motive: acting in a way the perpetrator knows is wrong.

The system of investigating whether research misconduct has occurred and the penalties and sanctions vary widely across the world. However, most funders require the research institution to conduct an

investigation when an allegation of misconduct is made against one of its researchers. The logic of this is that institutions have the legal employment contractual basis upon which to conduct investigations, and they can apply sanctions such as compulsory training or dismissal when needed.

However, institutions also have a conflict of interest. Many senior administrators see a case of misconduct as just bad publicity, and this can lead to poor investigatory processes or even to sweeping the problem under the rug. Institutions' fears of bad publicity are real, but that must never be an excuse for poor investigation of claims of misconduct. Institutional attempts to cover up misconduct often backfire, anyhow.

The Australian Code for the Responsible Conduct of Research (developed by the NHMRC, the ARC and Universities Australia) has cast the issue in terms of deviations from responsible research behaviours. The latest (2018) edition of the code states that breaches of the principles of the code occur 'on a spectrum from minor breaches to those that are more serious'. This approach of conceptualising the problem as a spectrum from less serious through to serious is better than having a simple threshold for research misconduct. When there is a single threshold definition, the implication is that it is either research misconduct or it is not, with the unfortunate idea that poor practices just short of the definitional threshold are somehow acceptable.[13]

There is no national mandate in Australia on how to investigate research misconduct. The current Australian code provides only a 'guide to managing and investigating potential breaches of the code' – 'a model for institutions to use to investigate and manage potential breaches, determine any corrective actions to ensure the integrity of the research record and when a finding of research misconduct may

be made'. But how can we know if this voluntary system is adhered to, given institutions' conflicts of interest and the absence of mandated reporting?

Some people argue that Australia needs a legislated system to investigate research misconduct via a statutory body, notably Professor David Vaux, a medical researcher at the Walter and Eliza Hall Institute who has championed integrity in science for many years.[14] Whether this is a good idea depends on the nature of the legislation and the statutory body. Instead of the usual criminal court adversarial system, it would be more useful for any investigatory processes to fit with the principles and ethics of science even if, subsequently, criminal proceedings might be warranted eventually. Rather than just finding guilt or not, a scientific adjudicating body can seek to understand and analyse why the misconduct occurred, remedy the harm caused and recommend preventative practices. There is also a risk that making the investigation of research misconduct subject immediately to law, raising the potential for criminal penalties, might just cause breaches to be hidden more often. It might exacerbate the hesitancy to report misconduct – it would be a daunting step for a junior researcher to report a fellow scientist, for instance, if that might end everyone up in a court.

However, there are different ways in which a legal process for misconduct allegations could run. Perhaps a coroner's court might be a model to explore. A coroner's court can investigate the situation first; they are not adversarial like other courts, and they can make recommendations for change and improvement.[15]

My colleague Kerry Breen, previously chair of the Australian Health Ethics Committee of the NHMRC and a member of the Australian Research Integrity Committee, is sceptical of the role

universities seemed to have played in the most recent revision of the Australian Code for the Responsible Conduct of Research.[16] He predicts that governments will turn to the legal system and criminal sanctions the next time that a university handles an egregious case of research misconduct poorly. This happened recently in Sweden, when a distressing case of research misconduct at the Karolinska Institute was found to have put patients' health at risk and to have been poorly managed by this prestigious institute.[17] Sweden established a new national legal process for scientific misconduct. After its first year of operation, the new centralised system had completed twenty-five investigations. Of these, only four researchers were found guilty of misconduct, with one of these convictions later overturned on appeal.

The United States has had a legal process for dealing with serious scientific misconduct for many years, but its effectiveness has been often questioned. In a wide-ranging report, the US National Academies of Science, Engineering and Medicine have called for the establishment of an independent Research Integrity Advisory Board, pointing out that 'no permanent organizational focus for efforts to foster research integrity at a national level currently exists'.[18] *Science* comments that the report's underlying message was, 'The US research community needs to do a better job of both investigating misconduct allegations and promoting ethical conduct – or the government might act unilaterally in ways that scientists won't like.'[19] In short, a legislated investigative body, the Office for Research Integrity (ORI), has not solved the problem in the United States. It is surprising that ORI completed just ninety-three investigations in 2021 for the whole country (considering the numbers for Sweden above), with just three findings of research misconduct.[20]

Australia already has a national research misconduct body, the Australian Research Integrity Committee (ARIC), a joint body of the NHMRC and the ARC, though not many researchers seem to be aware of its role. It will consider appeals from either the accused or the accuser about any investigation conducted by a university or research institute. It cannot conduct its own inquiry into the misconduct allegation, only into the processes that the research institutions used. Unfortunately, these processes are no longer specified in the code. The ARIC does not have sanctioning powers but it reports to the CEOs of the NHMRC and the ARC, who do have such powers. The ARIC could be readily strengthened, incorporating its expanded functions into a stronger Australian Code for the Responsible Conduct of Research with mandated reporting – more on this in the final chapter. For now, just let me say that it would help if research institutions made their staff more aware of the ARIC's role and their right to appeal to it.

Penalties and remediation

Penalties should suit the seriousness of the findings of an investigation. Minor and accidental mistakes may call for remedial actions. For example, if an early career scientist has made a mistake due to ignorance or lack of experience, they could undergo better education and training and work under close supervision for a period, as well as retracting or issuing corrections to affected publications.

There are practical reasons for fitting the response to the gravity of the misconduct. If all findings end careers, this can give potential whistleblowers pause. They might hesitate to bring misconduct to attention if they are worried that exposure of a relatively minor mistake due to ignorance could end the career of a young scientist.

However, proven deliberate faking of results should result in the researcher leaving public-funded research. Perpetrators may also be in legal jeopardy. The wrongful use of government funds in other walks of life is normally regarded as fraud and is liable to criminal prosecution. Section 134.2 of the Australian *Criminal Code Act 1995* covers 'obtaining a financial advantage by deception'. An example could be knowingly including fraudulent results in a grant application to the NHMRC or the ARC. In the United States, researchers have been jailed for gaining NIH and NSF funds falsely. Patients might even have been exposed to harm in a clinical trial based on findings from fraudulent pre-clinical research.

The Collins Dictionary defines reckless endangerment as 'a crime whereby a person behaves in a reckless manner which creates a substantial risk of serious physical injury to another person'. It can result in criminal penalties in many legal jurisdictions. The QIMR Berghofer Medical Research Institute recently referred a finding of research misconduct by one of its staff to the Queensland Crime and Corruption Commission.[21]

Prevention

Prevention is the responsibility of each and every person in medical research: individual researchers, research group heads, vice-chancellors and research institute directors, scientific societies and publishers.

Prevention starts at the individual research group level, with the long-agreed norms of science being adhered to and constantly reinforced. Wherever they are in the world, good research groups have rigour, openness, self-scrutiny and undeviating honesty. They have regular rituals that make individuals' fraud hard to conceal,

such as weekly group research-in-progress meetings, departmental research seminars and frequent sessions when students and postdocs sit with their supervisors and go through their results in detail. Most research group leaders model good practice and build a strong group culture. They make sure that everyone knows they value the highest standards of scientific behaviour and will not tolerate less. These good group practices make it hard for an individual researcher to hide false results, crop out 'inconvenient' data points, manipulate images, use the wrong statistical methods and then misinterpret them, or selectively choose what to publish and what not to.

Medical research does mostly work like this. However, good research group practices can decay and fragment when a research group gets too large, or when the lab or group head is distracted with other tasks or is just spread too thinly with too many students and postdocs.

The *sine qua non* of prevention should be that everybody new to medical research gets proper training. This must not just be technical and methodological training as part of their PhD studies, but also teaching what constitutes proper behaviour before, during and after research.

Medical research leaders should advocate that their institution has rigorous internal research integrity procedures. Many of the most high-profile research misconduct stories are the result of an institution's lack of a proper system for handling complaints, trying to minimise the seriousness of allegations, or pressuring whistleblowers and conducting enquiries surreptitiously and suppressing the findings. If you are a researcher and do not know the system at your institution, check it out. If it is hidden, designed to be defensive, and not properly resourced, call it out.

Scientific societies and professional groups could step up their prevention efforts too, identifying the standards that they expect in their fields, disciplines and professions.

Research integrity policies are best developed by national medical research funders, rather than by governments or research institutions. This occurs in Australia (the NHMRC and the ARC), but not everywhere.[22] Research funders can avoid regulations that are out of touch with contemporary science and so needlessly impede research or permit outdated concepts to linger. The best systems will set out who is responsible for what, define what is not acceptable, give guidance of good practices and set out clearly what their expectations of research institutions in investigations are, as well as ways to appeal.

What about the responsibilities of scientific journals, where fraudulent research first sees the light of day? Until now, regrettably, the journals as a group have been disappointing. This is despite the sincere efforts of many, especially COPE, the Committee on Publication Ethics. Publishers must do more. This is a highly profitable industry and they can afford to help keep the scientific record straight. They need transparent, energetic and timely ways of responding to allegations and to findings of misconduct. It is essential, too, that they clearly and promptly mark papers that have been retracted. Journal inaction means that too many zombie papers circulate despite retraction, even when the authors voluntarily and responsibly alert their retractions.[23] *The Economist* article 'Trouble at the lab' pointed out that one of Dr Eric Poehlman's papers (on the composition of women's bodies) had been cited 400 times since it was retracted, even after he was imprisoned for using fabricated results.

Honesty and truthfulness remain essential in science and medical research, but they have lost ground in the wider society in recent years, and it is probably too much to expect that this will not have affected some scientists. There is evidence that it is already happening, with

studies reporting increased hype in research publication titles and abstracts, and in grant applications.

Peer reviewers, be vigilant.

Reporting and openness

Management thinker Peter Drucker once said, 'If you can't measure it, you can't improve it.' In Australia and almost everywhere else in the world, the public is in the dark about how often allegations of research misconduct arise and whether they are found to be valid. Unless reporting is mandated, we cannot know how large the scale of the problem is, and we do not know how well our preventative measures are working.

In Australia, the NHMRC and the ARC could insist that research institutions report annually to the ARIC. The reports should at a minimum include the number of allegations made and investigated, and a summary of findings and the actions taken (while protecting whistleblowers and the wrongly accused). Currently, the NHMRC reports annually on the ARIC's work. Its 2020–2021 annual report mentions that the ARIC 'was asked to review 2 new matters' and 'continued and finalised 4 reviews that commenced in the 2019–20 reporting period'.

Meanwhile, it falls to individuals like those who run organisations such as PubPeer, Retraction Watch and For Better Science, and the remarkable Dutch microbiologist and scientific integrity consultant Elisabeth Bik, to monitor the system as best they can. They do a thankless but highly valuable task in the absence of rigorous monitoring and reporting by journals and research institutions around the world.

Facing up to the problems

It has always been difficult for me to admit that we have a genuine and substantial problem of fraud and rubbish science in medical research. I suspect this is true for most scientists. We want to think of science as being free from half-truths and fake news. We hope that the high moral purpose of medical research will guard against wrongdoing, that it will weigh on our minds so heavily that we all take care to work and publish honestly and competently.

We know that scientists sometimes make unintentional mistakes due to ignorance, but we also know in our hearts that some people are so ambitious that they push the envelope, stretch the truth and take shortcuts. We know, too, that a few others go further and get carried away by the prospects of scientific and financial rewards and so cheat, commit fraud and lie in publications. This is what some humans do in all walks of life.

We know all this, but it is fair to say that we generally do not want to face up to it. Jennifer Byrne at the University of Sydney put it well when she wrote that we tend to overlook the research fraud issue 'because the scientific community has been unwilling to have frank and open discussions about it'. It is awkward to admit even to oneself that some of us do not uphold the values of science that we so admire:

> Fraud departs from community norms, so scientists do not want to think about it, let alone talk about it … This becomes a vicious cycle: because fraud is not discussed, people don't learn about it, so they don't consider it, or they think it's so rare that it's unlikely to affect them, and so papers are less likely to come under scrutiny. Thinking and talking about systematic fraud is essential to solving this problem.[24]

When challenged about the incidence of fraud in medical research, many scientists tend to take defensive positions. We might contend that the usual self-correcting methods of science, replication of experiments and peer review will solve the problem. But we know that peer review is not honed to detect fraud reliably (though it can do), that replication of experiments is something that most of us are not very interested in doing (and it rarely gets supported by funders anyhow) and that a negative result from replication research will struggle to get published.

All medical researchers should talk more about research misconduct because it is we who have most at stake: our reputations, the reputation of medical research itself, and our time and resources when we spend months or years on a project based on what turns out to have been fraudulent research.

So, what should we do as scientists to better own the problem and guard medical research? One way, I contend, is for medical research to become a true profession.

Medical research should be a self-regulating profession

Medical research is not a profession, even though it demands a high level of professionalism. Anyone can call themselves a medical researcher. There are no processes that affirm an individual has reached some agreed level of expertise, proficiency and reliability. There is no specific training and no accreditation program. There is no requirement to learn a designated set of skills and knowledge, such as the proper use of statistics, what good research practices are or what the ethical obligations are. There is no equivalent of the Australian Health Practitioner Regulation Agency and the national- and state-based medical boards. There is no need for registration and demonstration

of training. There is not even a set of stated principles that we expect every medical researcher to share.

Other groups of people who train to be expert, whose jobs involve individual responsibilities and can be hazardous to others, have professional bodies that manage accreditation or are accredited by government. Such fields have training and competency entry requirements, and they usually require ongoing training and education. They have formal ways to withdraw recognition and accreditation when their members act in ways that harm their customers or patients and tarnish the reputation of the profession itself. Why should medical research be different to doctors, dentists, physiotherapists and vets? Why don't we have a professional certification system in medical research that requires achievement and maintenance of competency and ethical standards and could remove accreditation when misconduct is proven?

I am indebted to Dr Glenn Begley for his thinking on this. When his 2015 paper on the problem of pre-clinical experiment replication appeared, I contacted him and found that we had similar ideas. Glenn pointed out to me that when he had storm damage to his house in California, the plumbers, electricians and others that he needed to fix it were certified by professional organisations and so he could trust that they were competent. He and I have tried to publish our views on this issue in some of the leading medical journals but have not been successful.

Many readers will point out that there is in fact a type of entry to medical research, and it's called a PhD. A PhD certainly does demand good scholarship and competence in the methodology and techniques of the particular field of study, but it rarely requires demonstrated knowledge and competence in the broader aspects of being a responsible medical researcher. Furthermore, once a PhD has been awarded, a

lifetime as a medical researcher is possible. In this way, a PhD is more like an honour, such as a fellowship of a learned academy or an Order of Australia, than a professional title. Once the degree is bestowed, the title is there for a lifetime.

Most scientists' instincts will be to quickly reject the idea that a form of professional accreditation is necessary. They will groan at the prospect of more red tape and will dread the thought of needing to regularly renew their accreditation. Some will point out that some of the most creative stars of research have been 'wildcards' and will argue that something as creative as research will suffer from such an accreditation process. Others will argue that membership of scientific and research societies is a form of accreditation, like the Australian and New Zealand Society for Immunology, the Health Services Research Society of Australia and New Zealand, the Public Health Association of Australia and the Australian Society for Biochemistry and Molecular Biology. I would contend that these are probably better thought of as semi-professional rather than professional. They rarely require ongoing demonstration of competence or adherence to any professional or ethical standards, and they do not have protocols for expelling a member for misconduct.

Is there a role for learned academies such as the Academy of Science, the Australian Academy of Health and Medical Sciences, the Academy of Technology and Engineering or the Academy of the Social Sciences? Memberships of these are awarded on recognition of previous meritorious achievement, not current research competence. The medical academies rarely play a role in the ethics of the profession, here or internationally. However, nothing prevents them from considering standards for the behaviour and competence of those who conduct medical research. Could the Australian Academy of Health

and Medical Sciences be the guardian of good medical research practice in Australia if it were suitably resourced? I write more on this in Chapter 11.

Obviously, accrediting medical researchers is not a step that could or should be taken lightly. There are many questions. What would the accreditation standards be, and what training would be required? What are the core values to be upheld? Would funding agencies such as the NHMRC and the ARC require accreditation? Could loss of the accreditation be the punishment for proven research misconduct of a serious nature?

For me, there is only one compelling reason for medical research not to be accredited: if it would impede creativity. This could occur if some of the most creative souls in medical research were put off by needing to be accredited, or if the accreditation became too bureaucratic, lengthy or arbitrary. Many will also be hesitant if the accreditation were led by government rather than by a scientific and research organisation.

However, it would bring the oversight of who does research and the standards expected of them back to scientists themselves and their organisation. The standards could adapt and change as science demands. It would be costly to administer, and an academy or other body would need to be provided with the funds to do this role, but it would be worthwhile.

So, let's discuss the need for professionalisation of medical research and what it would mean, before the reputation of medical research becomes more damaged through poor and incompetent science and research misconduct.

* * *

I have written this chapter with some trepidation. Some of my colleagues fear that any internal criticism of the methods and procedures of medical research will be seized upon by critics, especially politicians, to attack scientists and medical research itself and potentially even take control of funding.

I understand this concern, but the bigger risk in the medium to long term is to not address the problems ourselves. After all, if scientific training teaches us anything, it is how to critically examine everything – methodology, results, applications for funding, proposed publications, PhD theses, seminars and conference presentations – and then to find solutions.

The danger signs are already flashing. Richard Smith, a previous editor of *The BMJ*, wrote recently about clinical trials: 'We have now reached a point where those doing systematic reviews must start by assuming that a study is fraudulent until they can have some evidence to the contrary.'[25] When someone as experienced as Smith makes such a statement, it is past time for us to put our house in order.

Chapter 7

Publishing Medical Research

Transitioning to better ways

Many of the biggest challenges in medical research arise from problems with publication of our results. The way that we publish and our use of publications in peer review has become increasingly dysfunctional. This view is widely held among scientists, but it has been hard to break away from the current systems. Problems include restricted access to published papers, a mistaken belief that equates journal prestige with the quality of individual papers, that poor and fraudulent research continues to be published, and that fake journals are proliferating.

Publishing has a long legacy from the days of print, and we are now in an awkward and unsatisfactory transition between these old ways and what is possible now. Happily, transformative ideas have begun to emerge.

Expensive and restricted access to published research

Medical research publishing is dominated by large private for-profit corporations such as Elsevier, Wiley-Blackwell, Lippincott Williams &

Wilkins and Springer Nature, and by scientific and medical professional societies such as the American Medical Association, the American Public Health Association, the Massachusetts Medical Society, the American Society of Nephrology and the Australian Medical Association. The scientific and medical publishers mostly operate similarly to the private publishers, but journal profits are often used to support their other professional and scientific activities.[1]

Journal publishing operates within a capitalist framework. Scientific papers are valuable, so it is logical that publishers will want to make money from them. It is hard to criticise publishers for that, but their profits are built upon the funding of the research by the taxpayer, or those who have donated to charitable research foundations. By handing over the publishing of our science to for-profit companies, we are giving away control, and providing journal publishers with a valuable resource that they will understandably wish to use to maximise value and minimise costs. The for-profit publishers are reported to be 'staggeringly profitable'.[2]

An expensive subscription is usually needed to access published papers, and researchers must hope that their employing university or healthcare network subscribes. This means that many researchers in low-resource regions of the world do not have such access. It is galling, too, when the people who paid for the research, the tax-paying public, cannot read the results. Vitally interested patient health groups, consumer health activists and NGOs cannot afford the high journal subscription fees. This may not be such a problem in some non-health-related sciences, where the research is not directly relevant to the general public (particle physics springs to mind), but it is a big problem in medical research, which is expressly funded and conducted for public health benefit.

Changes are underway

With the arrival of electronic publishing, scientists began to advocate that research publications should be open to all. The drive to remove journal paywalls gathered momentum through the 1990s, and the Public Library of Science began publishing the open access *PLOS Biology* in 2003 and *PLOS ONE* in 2006. Open access journals free to read now number almost 20,000 in total.[3]

The commercial publishers have been under pressure to remove their paywalls but have found another way to maintain their profitable businesses – levelling an article processing charge on authors who wish their articles to be open access. This works particularly well for the 'high prestige' journals, because we scientists still too often equate the quality of the article with the journal name. But the charges, again, disadvantage researchers in low-resource settings.[4] The for-profit model has also stimulated the rapid growth of so-called 'predatory journals', discussed later in this chapter.

The open access movement has been gradually eliminating paywalls over two decades, but two recent policies are likely to finally demolish them. In 2018, an influential group of research funders calling themselves cOAlition S adopted 'Plan S'.[5] Its aim is that 'all scholarly publications on the results from research funded by public or private grants provided by national, regional and international research councils and funding bodies, must be published in Open Access Journals, on Open Access Platforms, or made immediately available through Open Access Repositories without embargo'. Recently, this coalition went further. In a major and far-reaching development, it announced that they regard scholarly work that has been peer reviewed but not published in a traditional journal as of 'equivalent merit and status'. They mentioned such services as Peer Community In (PCI), Next

Generation Repositories, Notify Project, PREreview and Review Commons, where peer review takes place 'independently from publication in journals or on platforms': 'These innovative developments turn attention away from the prestige of the journal or platform to focus on the intrinsic value of the peer-reviewed article itself.'[6]

Then, mid-2022, the White House Office of Science and Technology Policy announced that in the United States 'publications and their supporting data resulting from federally funded research [must be made] publicly accessible without an embargo on their free and public release'.[7] There is a deadline of 2025 for implementation. Together, the Plan S policies and this White House announcement look set to overcome the restrictions on access to publicly funded research and data.

The preprint servers are also challenging the traditional publication model. Around for more than a decade, they achieved a significant profile during the COVID-19 pandemic. Papers appeared rapidly on the servers, helping other scientists and public health officials to respond to the sudden epidemic. It is possible to see a future system in which the traditional journal publishers will be bypassed, when scientists simply post their papers (articles? manuscripts?) on a server. The authors could modify publications as needed in response to other scientists' reviews, or when later additional research requires it. How could peer review be arranged? A 'community model' is usually suggested, where registered reviewers review and rate preprints. Other suggestions include self-organising peer review, which can utilise blockchain technology.[8]

The value that journal publishers add is also being called into question. There is evidence that there are few differences (other than formatting) between the preprint and the journal versions.[9] We already know that traditional journal peer review is not a reliable way to pick up fraud. This was amply demonstrated by the Surgisphere scandal

during the COVID-19 pandemic. The prestigious journals *The Lancet* and *The New England Journal of Medicine* published apparently large international trials of anti-COVID-19 agents after the manuscript had undergone peer review, but many researchers quickly pointed out that the articles were fraudulent.[10] Scientists agree that peer review is essential, but what added value did the peer review by the two prestigious journals bring?

An even more disruptive change has been suggested recently by Stuart Richie, from King's College London, who proposes doing away with the scientific paper completely, replacing it with online notebooks and living documents. This would allow for frequent updates and direct links to the data, and could allow direct review by other researchers at any time. It is probably a step too far at this time, but I cannot help but agree with him that '[w]e've made astonishing progress in so many areas of science, and yet we're still stuck with the old, flawed model of publishing research. Indeed, even the name "paper" harkens back to a bygone age.'[11]

In short, the landscape is changing fast. However, the traditional publishers will try to protect their profits. What should researchers do in this environment? When we are peer reviewing, we must judge the content of papers, not their place of publication. We should participate in community reviewing systems for preprint servers where they exist in our field. We should actively support policies that mandate open access, such as Plan S. We should regard it as one of our responsibilities to always share the results of our taxpayer-funded research fully with other scientists and with the general public. We should stop equating the value of a paper with the name of the journal in which it is published.

Misuse of publications metrics to judge the quality of published research

Journal Impact Factor prestige

Statistics can illuminate and they can obscure. The rise of metrics in science journal publishing has had adverse effects on scholarly peer review.

In the 1960s, bibliographer Eugene Garfield invented the Journal Impact Factor to rank journals for commercial advertising advantage. Soon, peer reviewers and administrators began to equate the quality and scientific impact of a paper with the impact factor of the journal in which it was published. In that way, Journal Impact Factor became the de facto, but flawed, arbiter of scientific value. Overwhelmed by work, reviewers will too often look only at the impact factors of the journals in which an applicant has published (this takes just a few minutes), rather than reading the papers themselves to understand their scientific significance and the quality of the approach, methodology and analysis of the results (which can take hours). Phrases like 'He is an outstanding researcher – he's published two *Nature* papers' have been heard too often in appointment and peer review meetings. There are even rumours that some institutions and countries give researchers substantial cash bonuses for publishing in a journal with a high Journal Impact Factor.[12]

It should be obvious to anyone that any metric for a whole journal publishing hundreds or thousands of papers per year tells you almost nothing about the metrics of an individual paper. Within any journal, a few papers are highly cited, the majority much less often and some hardly at all.[13]

The problems with the Journal Impact Factor were well described by the scientists who in 2012 developed the San Francisco Declaration on Research Assessment (DORA), one of the most important demonstrations of scientific leadership in the last two decades. They itemised the following:

> These limitations include: A) citation distributions within journals are highly skewed [1–3]; B) the properties of the Journal Impact Factor are field-specific: it is a composite of multiple, highly diverse article types, including primary research papers and reviews; C) Journal Impact Factors can be manipulated (or 'gamed') by editorial policy; and D) data used to calculate the Journal Impact Factors are neither transparent nor openly available to the public.

For funders, the DORA principles include:

1. Do not use journal-based metrics, such as Journal Impact Factors, as a surrogate measure of the quality of individual research articles, to assess an individual scientist's contributions, or in hiring, promotion, or funding decisions.
2. Be explicit about the criteria used in evaluating the scientific productivity of grant applicants and clearly highlight, especially for early-stage investigators, that the scientific content of a paper is much more important than publication citation or the identity of the journal in which it was published.
3. For the purposes of research assessment, consider the value and impact of all research outputs (including datasets and

> software) in addition to research publications, and consider a broad range of impact measures including qualitative indicators of research impact, such as influence on policy and practice.[14]

Excellent principles, but effective and practical implementation of the principles has not been straightforward. The scientists behind the DORA principles are developing a toolkit for use in implementing the principles to assist organisations.[15] Many research organisations are also seriously grappling with how to best implement the principles, including the European Molecular Biology Laboratory and University College London.

Supplementary codes designed to combat the misuse of bibliometrics when evaluating scientific research have also been developed. The Leiden Manifesto for Research Metrics, formulated in 2014, provides ten principles 'for the appropriate use of metrics in research evaluation', and in July 2022 the European Commission published an agreement on reforming researcher assessment.[16]

In short, the Journal Impact Factor does not describe an individual paper's impact, and journals with a high impact factor do not necessarily offer better quality peer review. When we use it to judge an individual paper or person, we are not being scientific. We are responding to marketing.

Citations of individual papers

Another way that the importance of an individual paper is sometimes assessed is to count the number of times that other authors have cited it. This is a little more reliable than using the Journal Impact Factor because it is at least related to one type of impact that an individual

paper has had – other researchers have felt the need to cite the article in their paper.

However, it is still misleading. A paper's impact on other researchers, as measured by citations over two years or so, is not the same as its true importance. The real impact can often only be appreciated over many years, after it has become an enduring contribution to knowledge, caused a shift in a scientific paradigm, affected policy and practice in health, or led to commercial products. Often, the original paper might be almost forgotten, but it was an essential link in a chain. In contrast, the citations that a paper gets in the first couple of years may turn out to just be a flash in the pan.

A system based on citations is also open to gaming. Scientists are human, and so personal and non-scientific factors can influence whether another researcher's paper is cited. The effect of non-scientific factors on citation practices has been well studied and described.[17] For instance, we are more likely to cite important people in the field (hoping, perhaps, *If I quote you, you might get to know who I am and even cite my papers*). Friends quote each other and even set up cartels.[18]

Then there is the serious problem of unfair practices in authorship that distort citation analyses. Women in research teams are significantly less likely to be credited with authorship than men.[19] An infamous example is Rosalind Franklin, who was left off perhaps the most celebrated biomedical publication of all time, which revealed the structure of DNA. If you are not an author, you can't be cited.

True conceptual breakthroughs may take much longer than usual to be recognised and so they are underrepresented in shorter-term citation statistics. In their 2017 paper 'Bias against novelty in science: A cautionary tale for users of bibliometric indicators', Wang, Veugelers

and Stephane concluded, 'These findings suggest that science policy, in particular funding decisions which rely on bibliometric indicators based on short-term citation counts and Journal Impact Factors, may be biased against "high risk/high gain" novel research.'[20]

There are also fashions in medical research. Sometimes a 'hot' research field elicits an initial flood of papers and citations but signifies very little in the end. On the other hand, a technical paper may be of little interest to other researchers but of great interest to an entrepreneur who recognises it as the first step in the commercial development of an innovative technology.

Sometimes, important papers are never cited. For example, when an article shows that a method other scientists have been using is faulty, that line of research just stops. It might have saved years of fruitless research by others, but there is no longer anyone in that field to cite the paper. It is also well known that a paper with important but negative results, showing that something we have believed to be true is not so, is also less likely to find its way into top-cited journals. It is reassuring, though, to see that papers which stimulate others to publish negative and critical views do seem to be cited normally.[21]

Another conceptual problem is that the major journals are oriented to Europe and North America. Editors and reviewers are disproportionally from these two continents, as are citations.

The NHMRC monitors the citation performance of all Australian medical research through its 'Measuring up' series. It reports retrospectively at five-year intervals, the most recent covering the period from 2008 to 2012. It gives an overview of the performance of different medical research sectors and disciplines and specific NHMRC funding schemes. The analysis is robust at this national rather than individual researcher level. The most recent version showed that Australian

researchers contributed 3.6 per cent of the world's publications; that multidisciplinary, bioengineering and public health research were increasing most rapidly here; and that university researchers contributed more than two-thirds of the total. NHMRC-supported research was cited well above the world average (68 per cent above). This was particularly the case for NHMRC Practitioner Fellowships and the (now discontinued) Program Grant schemes. More than 40 per cent of NHMRC-supported publications had international co-authors, from more than 135 different countries.[22]

Judging quality rather than quantity

On a peer review committee, assessors are faced with dozens or even hundreds of papers published by each applicant. It is a fantasy to pretend that we can assess all those papers. Think of the maths. If there were, say, ten applicants with an average of ten papers each per year over five years, that's five hundred papers. There is no chance that any of us could read and assess them all. The only feasible thing to do for most assessors, understandably but regrettably, is to simply count of the numbers of papers, scan the Journal Impact Factor or use some other flawed metric.

Here is a radical proposal, and one I am advocating for in this book for the second time. It assumes that we want to identify researchers who can conduct and publish important research, not the ones who can publish the most papers. Let's judge the very best that the applicant is capable of by reviewing in detail just their single best publication. If we ask each applicant to nominate their best paper and to say why, we can review its quality and analytic rigour in depth, determining whether it is novel or 'me too science', and its significance. The applicant's choice

of paper will carry other forms of significance, such as whether their best work is recent or from long ago. This is a practical and realistic solution to otherwise needing to judge hundreds of papers.

Perhaps considering just one paper per applicant is too radical? Maybe then their two self-identified best ones. But keep the number small enough that it is reasonable to expect reviewers to read them thoroughly and assess their quality and impacts on knowledge. Hopefully this model can be trialled in some of the work now underway on how to implement the high ideals but practical challenges of DORA.

* * *

Because publishing medical research is profitable, fake and predatory journals now litter the scientific landscape. Unscrupulous publishers have exploited the open access movement, setting up fee-for-publish journals, usually with little or no peer review. Predatory journals have been defined as 'entities that prioritize self-interest at the expense of scholarship and are characterized by false or misleading information, deviation from best editorial and publication practices, a lack of transparency, and/or the use of aggressive and indiscriminate solicitation practices'.[23] All researchers will have had experience with being approached by these, where fast publication is offered for a price. There are at least 10,000 such journals now, and they can be hard to spot. There are lists available, though they have been criticised as unreliable.[24]

The problem of fake journals will not go away so long as science publishing is profitable. There is not much that we as individual scientists can do about these journals, except to warn our staff and students about them.

More importantly, we can actively support some of the transformative changes underway in publishing, insist that funders assess publications consistent with the DORA principles and stop prizing numbers. We can advocate for a better system of scientific publishing overall, with safeguards in place to avoid bad science being published by predatory journals.

Chapter 8

Politics and Australian Research

Political interference and nationalism in funding decisions

Surprisingly, government intervention in research funding has become a special problem in Australia – and many researchers are unhappy about it.[1] As I wrote in Chapter 4, there was no transparency on how the Minister for Health in the former Coalition government decided the initiatives of the huge new Medical Research Future Fund or on the final funding decisions. At the ARC, Ministers of Education in Coalition governments have been vetoing grants that the ARC, through its peer review process, recommended to be funded. Just before Christmas 2022, for example, the ARC announced that six applications recommended for funding after peer review were not approved by Minister Stuart Robert.[2]

Previously, the most significant government involvement in medical research was over using human embryos and cells from aborted foetuses in stem-cell research. The Howard government needed the vote of independent Tasmanian senator Brian Harradine to pass legislation. Senator Harradine was implacably opposed to embryonic stem-cell research because of the destruction of pre-implantation embryos. As a

result, initial Australian legislation in 2002 was highly restrictive and unworkable. However, a determined Senator Kay Paterson convinced the prime minister in 2006 to allow her to introduce a private member's bill to amend the Act to bring it more in line with scientific knowledge and community attitudes. The other hero (unsung) was Dr Clive Morris at the NHMRC, who had scientific, bureaucratic and political skills to help the senator achieve her aim.

A lot of political and bureaucratic time was wasted on developing these two detailed pieces of legislation. It would have been better if, from the beginning, the legislation had simply required self-regulation through the NHMRC's Australian Health Ethics Committee, with majority membership of non-researchers, as the *NHMRC Act* requires open and consequential community consultation for all its guidelines and regulatory recommendations.[3] This is how the NHMRC's National Statement on Ethical Conduct in Human Research has successfully set ethical and sapiential guidelines for years without the need for legislation on such difficult issues as medical research with participants who are pregnant, have cognitive impairment or mental illness, or who might be involved in illegal activities, and animal-to-human xeno-transplantation. With self-regulation, working within the guidelines of the *NHMRC Act*, the rules can be changed quickly when needed. This is not possible once a detailed procedure is set in legislation (and politicised). This model of self-regulatory guidelines is already used by Australian states in relation to animal experimentation ethics. State laws require adherence to the NHMRC/ARC Australian Code for the Care and Use of Animals for Scientific Purposes.[4] This code can be updated regularly as scientific knowledge and community attitudes change.

The controversy over stem cells diminished worldwide following Dr Shinya Yamanaka's discovery that mature cells from adults can

be reprogrammed to become pluripotent. The 2020–2021 NHMRC annual report mentions that there was just one application for a licence to conduct research involving human embryos in progress with NHMRC's Embryo Research Licensing Committee, with twelve approvals of variations of previously licensed research.[5] The exception is the United States, where some members of the public opposed the mRNA vaccines on the grounds that human foetal cells were used in some of the early research to develop it.[6]

Political use of science in the pandemic

The business of using science in public policymaking is important, difficult and fraught. We heard a lot of politicians saying 'We have followed "the science"' during the COVID-19 pandemic. To their credit, Australian politicians did almost always act on the advice of their Chief Health Officers early in the pandemic, and they also sought input from experts at the Doherty Institute, Monash, the Kirby Institute, the University of Sydney and others. We would have had many more deaths and cases of long COVID had they not done so. This is in contrast with some leaders elsewhere, such as in Brazil and Florida, who basically boasted that they were ignoring science.[7] With a population only a little smaller than Australia's, Florida had nearly 60,000 COVID-19-related deaths up to November 2021, compared to less than 2000 in Australia. Donald Trump frequently claimed that the virus was fading when in fact COVID cases were rising sharply; that children were immune to the virus; and that hydroxychloroquine was a safe and effective treatment – all against the advice of his scientists.

Without question, it was salutary that politicians in Australia and most other places followed expert advice, but there are reasons to be

wary about the longer-term effects of the rhetoric of justifying political action solely on the basis of scientific advice.

First, there is no such thing as 'The Science', with a capital T and capital S. There is science, and there are scientists and scientific methods. But there is no agreed entity in the same way there is 'The Great Barrier Reef', 'The Governor-General' or 'The Australian Academy of Science'.

Second, public policies can never be purely based on science, especially when dealing with a novel coronavirus where much is unknown. When the world first saw that a deadly virus was spreading rapidly, public health officials and government policymakers had to make decisions based on what little was known scientifically. Policy mistakes were made because politicians and public health advisers were working with very limited research evidence. New publications were streaming out in great numbers on preprint servers. For example, it took some months for scientific advice to emerge that the virus could be spread through aerosols and not just droplets (credit for this should go especially to Lidia Morawska at Queensland University of Technology).[8] As time went on and research evidence accumulated, the scientific advice necessarily changed. But it can be confusing for the public when political leaders change their decisions while still saying that they are following 'The Science'.

I am not aiming to criticise the pandemic response, but rather to warn of possible unintended consequences. When new threats appear, governments have to use the evidence that they have, 'the-science-available-at-that-time'. The risk is that the community might think that 'The Science' is immutable, like the Second Law of Thermodynamics, rather than a changeable thing where conclusions alter as more evidence emerges. So when public officials change their advice because new

scientific evidence demands it, while still (correctly) saying 'we are following The Science', our critics and the anti-science movement can seize on this and claim, 'See, Science got it wrong anyhow, so why trust scientists in the future?'

In an emergency, when there is scant real science to go on, it would be better if politicians simply say that they are following 'scientific advice' or 'advice from scientists', signal that scientists will be providing more information in the future and so the current advice might need to change. That is, they are acting on specific advice from specific scientists and not acting on the command of some grand edifice called 'The Science'. Everyone can understand that individuals (even scientists) can be wrong, but if 'The Science' turns out to have been wrong, some will use it to undermine confidence in the very notion of empirical evidence.

I would also make a plea in turn for scientists to understand the pressures that the Chief Health Officers and Medical Officers came under. The route from scientific evidence to public policy is hazardous and complex. Political judgement will always be necessary, at least in democracies. What good public health officials do is to take the whole public health situation into account. As well as what is known and not known about the virus, they need to think about the consequences for the population's mental health and the effects of delaying treatments for other diseases. Politicians have, in fact, an even harder set of decisions to make. They need to consider not only the science-based public health advice, but also the effects on the economy, on the delivery of essential goods and on the provision of essential services. There is never a perfect balance.

Nationalism and internationalism

Science itself is universal, without national borders. It is one of the joys of a medical research career that you have colleagues scattered around the world in many different countries. We can work on projects together, exchange students and postdocs, publish together, visit one another and attend conferences in a range of locations, all without needing to account for nationality.

However, the funding for international collaborations comes mostly from national sources, mostly national governments. This can be an impediment to research collaboration across borders. National research funders almost always have rules restricting their funds being used outside the country. So while there are no international barriers in discussing and planning collaborative research, the research will typically be funded by a national funding agency and be governed by that funder's rules and policies (for example, policies on research misconduct). Occasionally, funders do make an agreement to support collaborative research (for example, the NHMRC has ten current international collaborative initiatives),[9] but even then, each funding body usually supports the parts of the research to be conducted in their own country.

Despite these restrictions, individual scientists find ways around national funding restrictions, and international collaboration flourishes. For example, 42 per cent of all NHMRC publications between 2008 and 2012 were collaborations between Australian and overseas co-authors.[10] I always supported allowing NHMRC funding to be spent outside Australia, provided the project's chief investigator was an Australian and the money was administered through and overseen by an Australian university or research institute.

The remarkable International Human Frontier Science Program (HFSP) Organization is the only significant example of a funding

scheme that allows scientists from any country to apply and be funded. HFSP has been funding multi-country teams of scientists for more than thirty years. The circumstances of HFSP's birth help explain this wonderful no-borders-in-science approach. HFSP arose towards the end of the Cold War, from an idea proposed by Japan. After advice from a group of leading scientists from seven nations and the European Union, the presidents and prime ministers of these countries, Margaret Thatcher and Ronald Reagan among them, founded the program for international research collaboration in basic life science. Now, with Japan still the most generous donor, fourteen countries and the European Union put money into a common pot for basic life science research and fellowships. There are no restrictions on who can apply: any life scientist anywhere can be a HFSP research grantee or a HFSP postdoctoral fellow. Decisions on funding are made entirely through international peer review, with no country quotas.[11] It has been a remarkable success, and since 1989 twenty-eight awardees have gone on to win a Nobel Prize.[12]

The EU's European Research Council has some similarities to the HFSP model, but on a European-wide rather than global scale. Special mention must be made, too, of the Bill and Melinda Gates Foundation and its borderless approach to funding research.

As nationalism rises in many countries, we should be on guard for barriers being erected against collaboration and open scientific exchange. Perhaps we can understand that governments might want to put restrictions on collaborations in some research areas such as physics or engineering, for military and defence reasons. Some medical research can be hazardous too, and the results perhaps even weaponised, such as gain-of-function research with infectious agents. But rather than discouraging certain forms of international

collaboration altogether, it would be better to have internationally accepted rules and the requirement for full transparency about such research projects.

A significant downside of national funding of medical research is that some diseases are neglected because they occur largely in low- and middle-income countries. Though our human biology is a common possession, our exposure to the factors that cause ill health is not evenly or fairly distributed across the world.[13] Governments and scientists in wealthy countries tend to research diseases of most burden for their citizens (for example, dementia, Type 2 diabetes, breast cancer, cardiovascular disease). So when the infectious diseases of HIV/AIDS and COVID-19 infected their citizens, wealthy countries responded with significant research funding. Meanwhile, about 3.2 billion people – almost half of the world's population – are at risk of malaria.[14] Tuberculous is the leading infectious cause of death worldwide: ten million people had TB in 2017 and 1.6 million died, including 230,000 children.[15] There are about fifty million cases of dengue infection across the globe each year, with 22,000 deaths, mostly children.[16] At least 220 million people are infected with schistosomiasis worldwide.[17] These diseases hardly affect us in Australia and our researchers seek less funding for these than for the diseases that Australians mostly suffer from. There are honourable exceptions – individual medical researchers who have dedicated their careers to research on the diseases more common in low-resource countries, such as Professors Allan Cowman, Brendan Crabb, Michael Good, Ruth Bishop and Don McManus, among others.[18]

* * *

Being able to talk, collaborate or share a meal or coffee with a researcher from anywhere in the world is one of the best parts of medical research. Or from almost everywhere: scientists in North Korea and Myanmar do have impermeable borders. And the squabbles over the origin of COVID-19, concerns about China's Thousand Talents program, tensions between China and the United States, and the sidelining of Russian scientists due to of the war in Ukraine are all examples of how politics can intervene to build national barriers to collaboration.[19] But these current setbacks will not deter researchers from wanting to share their knowledge with others worldwide and to collaborate in research to improve health everywhere.

English is the lingua franca of international collaboration in science. Will this still be true in twenty to thirty years as the number of Chinese-language papers further increases? Or will artificial intelligence make it possible to read an article in any language, with the nuances usually needed in scientific writing? Whatever the outcome, international collaboration, across political borders, is a defining and admirable feature of medical research.

Chapter 9

Data

Making more of our biggest infrastructure asset

Digitisation has changed most things in medical research, just as it has for almost every other area of life. We collect research data electronically; we contribute our data to biodata bases and curated biodata resources, and we use them frequently. Some medical researchers do *in silico* research only, using the rich data resources from discovery science. Informaticians are employed everywhere in medical research, from the gene labs to health systems research. More and more funders and journals mandate that research data be openly accessible to all.

You could think of all these data as collectively forming a very large, distributed piece of infrastructure. How large? No one knows, but the Global Biodata Coalition (GBC) has estimated that research funding organisations spend at least US$500 million every year supporting biodata resources.[1] The GBC recently released a thorough inventory that identified 3112 biodata resources around the world, supported by more than 1700 funding agencies.[2] The number and size of the resources is growing fast, and further growth acceleration is expected as funders and journals mandate open data.

The financial support of the globally used data resources is fragile and fragmented. Too often, it is short-term and indirect, through research grants. Even some of the most-used data resources rely on a patchwork of different funders. Others have introduced or are contemplating a user-pays model. This is understandable, but it disadvantages researchers in low-resource regions.

The financial pressures on the biodata resources were well described by Philip Bourne and his colleagues, who point out that the world needs to develop more equitable funding models. They suggest:

> The first step is for funding agencies to communicate more effectively about data science problems and to seek collaborative solutions. Working from the bottom up, scientists have been doing this for a long time. Sustaining the biomedical big-data ecosystem is the responsibility of all stakeholders, and will require coordinated efforts among data generators, data maintainers, data users, funders, publishers and others in the private sector.[3]

The genetics and genomics fields have been data leaders. From the beginning, the scientists of the Human Genome Project adopted the philosophy that data from their work should be available to everyone. Since then, a group of far-sighted and dedicated scientists have been developing the Global Alliance for Genomics and Health (GA4GH), which has made impressive progress on the technical, ethical and regulatory issues in human genetic and genomic data.[4] Many medical researchers contribute to its work programs, including the development of the Framework for Responsible Sharing of Genomic and Health-Related Data.[5] GA4GH is currently funded by Genome Canada, the Canadian Institute of Health Research, NIH's National Human

Genome Research Institute, Wellcome, the UK Medical Research Council and the UK National Institutes of Health Research.

The International HundredK+ Cohorts Consortium (IHCC) supported by NIH and Wellcome is another example of medical researchers cooperating internationally to share data. Cohorts are powerful scientific tools in medical research, but as the IHCC says, 'each cohort is constrained … by its size, ancestral origins, and geographical boundaries, which limit the subgroups, exposures, outcomes, and interactions it can examine'. Therefore, '[l]inking data across large cohorts provides a vast digital resource of diverse data to address questions that none of these cohorts can answer alone, enhancing the value of each cohort and leveraging the enormous investments made in them to date'.[6]

Epidemiology and clinical trials generate large datasets, too. Some medical researchers argued for many years that the data from clinical trials should be available. The movement gained momentum in the 1990s, with the US Congress passing a law requiring that clinical trials be registered, and the NIH launched a similar policy in 2000. Australia's ClinicalTrials.gov.au is a joint initiative between the NHMRC and the Department of Industry, Innovation and Science. Scrutiny from other researchers is needed to check the validity of conclusions, to allow others to replicate the findings, and for secondary research. Registration of trials also allows a follow-up check on whether the results have ever been published – this is important because the results of unsuccessful drug trials are not always published.[7]

The researcher-led collaborative initiatives I have mentioned are to improve the use of data generated from identifiable human beings, where respect of privacy is central to the work. However, there is a massive amount of other data that is not subject to privacy concerns

but is crucial for everyday laboratory medical research. These data are remarkably diverse. For example, there are biodata resources for enzymes, macromolecules, proteins, nucleotides, and other vertebrate and non-vertebrate gene sequences.[8] There are also resources for the common model animals in research, such as *Drosophila* (fruit flies) and *C. elegans* (roundworms), as well as yeasts (*Schizosaccharomyces*), the classic model plant (*Arabidopsis*) and much more. Researchers everywhere in the world use one or more of these data resources. However, the funding of these is complex and fragile, with most being supported by only a narrow group of funders.

The GBC aims to better coordinate the development of these biodata resources and ensure sustainable financial support.[9] This coalition includes many of the world's leading biomedical and life-science research-funding organisations. It is currently supported financially and in-kind by the NIH's National Human Genome Research Institute, the US National Science Foundation, Wellcome, the State Secretariat for Education Research and Innovation (Switzerland), the NHMRC, the UK Biotechnology and Biological Sciences Research Council, the Research Council of Norway, Genome Canada and the Chan Zuckerberg Initiative. The International Human Frontier Science Program (HFSP) has been the midwife for the birth of GBC, beginning with a HFSP workshop held in 2016 in Strasbourg. The GBC model is built on the far-sighted ELIXIR initiative in Europe, led by the European Molecular Biology Lab's European Bioinformatics Institute.[10]

The Global Biodata Coalition, ELIXIR, GA4GH and IHCC are all examples of the research community's self-starting recognition that data infrastructure is at the heart of science today. One day, perhaps, the life sciences will be able to marshal data infrastructure support

comparable to that of the physical scientists, who have convinced governments to invest billions in research infrastructure and the tools they need, such as CERN, the James Webb Space Telescope and the International Thermonuclear Experimental Reactor (ITER). It will happen if biomedical researchers organise to promote the need and lobby successfully, as their physical scientist colleagues have done.

Chapter 10

Fake Science

Our responsibility to call it out

Nearly five centuries after Galileo, 250 years after Lavoisier, 150 years after Pasteur, Semmelweis and Lister, and more than half a century after Salk and Sabin, Watson and Crick, it is frustrating that many of our fellow human beings and some of our political leaders reject science, and that vested interests misuse science in health and medicine.

In the long term, those who are anti-science cannot win because, well, their arguments are not scientific. You can believe that the world is flat, but this will not have any effect on intercontinental flights, satellites or world shipping. You can teach creation science to your children rather than evolution, and this will have an impact on your children's education, but organisms will continue to evolve. You can believe that COVID-19 is a left- or a right-wing conspiracy, but that will not stop the virus from circulating.

Anti-science forces have tended to be at the margins of most societies, but many worry that social media is now empowering them.[1] It was a shock for many in the scientific community when Donald Trump was elected US President, with his known anti-science and anti-vaccination views.[2]

Misuse of science by powerful vested interests

Powerful vested interests are coming to understand that, when science has exposed the public health dangers of their products and public opposition has begun to threaten their businesses, they need to be seen to be 'scientific'. When a company or even a whole industry (the fossil fuel industry and the tobacco industry are two that come to mind) realises that ignoring calls for change will no longer work, they often try to counter the claims against them by misusing science. They develop material that selectively draws on published scientific work to support their case and influence the public and policymakers – like research findings that purported to show smoking can have positive effects on some diseases (but Cancer Council Victoria's comprehensive summary of the true situation reveals a different story[3]). They recruit some scientists to their cause and pay them to speak and to give evidence in court, and they develop their own 'scientific-looking' documents for lobbying politicians and influencers. This aims to give a respectable front to their less salubrious activities, such as intimidating and destroying the reputations of public health scientists who oppose them. A prime example is the University of East Anglia's climate scientists, who, following a series of hacked emails, were accused by climate deniers and some in the media of manipulating climate data, an allegation that was later proven false.[4] Such misuse of science often delays government decisions for decades.

This is a large topic, explored compellingly in the book *Merchants of Doubt* by Naomi Oreskes and Eric M. Conway.[5] I recommend this book if you want to learn more about how vested interests can misuse science to prevent governmental action. The authors discuss examples such as cigarettes causing cancer, acid rain due to coal use, the hole in the ozone layer caused by the use of chlorofluorocarbons and DDT, and global warming from fossil fuels.

Scams, quackery and pseudoscience

A common misuse of science is in the complementary and alternative medicine industry, where some companies wrap themselves in a cloak of pseudoscience. This is a large and profitable industry, selling products that claim to have a positive effect on health. The global complementary and alternative medicine market has been estimated at more than US$80 billion, with a predicted annual growth of more than 20 per cent between 2023 and 2030.[6] One 2018 study showed that almost two-thirds of Australians used complementary medicine, with around one-third also consulting a practitioner.[7]

Many products are marketed with 'sciencey' images such as people in lab coats. Some ads use 'sciencey' terms such as 'supports immune system health', 'healing with care' and 'detoxifies the body'. These imply, rather than state outright, that the product is therapeutic. In this way, these companies stay just within the Therapeutic Goods Administration rules.[8]

Doubtless, medical research will show that some of the products are effective, and there are many well-meaning people and companies within the industry. But there are also charlatans, claiming their products and therapies offer benefits that real science has disproven. It is one thing when people sell ineffective products to the worried well.[9] That is mostly just a waste of money, even perhaps a little beneficial placebo effect, without harm. But it is an entirely different matter when people who are sick with a treatable illness are pushed towards products and 'therapies' that do not work. As the English journalist John Diamond wrote in *The Independent*, there is no such thing as alternative medicine: either it works, in which case it is medicine, or it doesn't, in which case it isn't.[10]

There are great resources for people to consult, such as the NIH's National Centre for Complementary and Integrative Health, the

Therapeutic Goods Administration, the UK National Health Service, Quackwatch.org, Australian Friends of Science in Medicine and the US-based Science-based Medicine.[11] State health departments also often offer information about reliable treatments and public health organisations. We all have a responsibility to recommend these resources, helping to ensure that those who do not have a background in science do not get taken in by marketing and seduced by the lure of magic beans.

Chapter 11

Ideas for Change

Where to from here?

Medical research will continue to deliver human-made miracles, as some of the best people on the planet dedicate their lives to research to improve the lot of their fellow human beings. But as we have seen, some of our long-established practices no longer serve us well. Reforms are needed, and medical researchers must lead them.

Here are some suggestions, all intended to bolster the values of science and increase trust. Some are already underway, some would be quite simple to implement, some would be a challenge, some are generic and some are international in scope, while others are specific to Australia. A few might even seem utopian, but I believe that we have the commitment to the values of science and strength to achieve them.

Agree on the defining principles of medical research

What do we believe in, as medical researchers?

Here are some of the principles I believed would be expected of me when I was training to become a medical researcher.

- I would always be honest and truthful.
- I would learn to accurately and reliably use all the methodology needed for my research, and I would keep learning new methodology to improve my research.
- I would respect the participants in my research and know the ethical rules.
- I would credit all who helped in my research fully and accurately.
- I would participate in peer review as a mutual obligation to other researchers.
- I would publish the true results of my work, present them accurately, and mentor students and postdocs to do the same.

None of my expectations will seem odd to most medical researchers. Being human, I undoubtedly fell short of these expectations from time to time, though I hope not when it came to questions of honesty and integrity.

Should we develop a formal declaration of the defining principles – a statement that we commit to live up to?[1] Could we decide on an oath that reflects what we believe and which emerging researchers agree to uphold? Such an oath should be simple – and be more poetic than my list above. It could be made as part of the conferral of a doctorate.

Critics may dismiss a medical research declaration of principles as meaningless, and of course it would only be symbolic rather than having a legal status. But that is not to dismiss the importance of declarations. They are serious statements of intent. They symbolise that the individual swearing to uphold the principles is aware of their responsibilities and the standards to be protected. New Australians make a pledge of allegiance to Australia when they become citizens. Oaths are used in court to signify the seriousness of giving evidence

and the responsibility of the individual giving it. There are oaths of office for Australian parliamentarians and for the Governor-General. A declaration or an oath says to the community that these are the principles you should expect us to uphold, and we will undertake to do so. It is a form of covenant.

The idea of a declaration of principles for scientists is not new. Individuals as distinguished as philosopher of science Sir Karl Popper, British biologist Sir John Sulston and Polish-British physicist Sir Joseph Rotblat have suggested a generic statement for all scientists, perhaps an adaption of the Hippocratic Oath, while others have suggested an oath for medical science.[2]

Make medical research a true profession

As discussed in Chapter 8, medical research is not recognised as a profession by a professional body. Anyone can call themselves a medical researcher. There are no processes to affirm that a researcher has reached an agreed level of expertise, proficiency and reliability. Other groups whose jobs involve highly technical knowledge and particular responsibilities are usually self-organised as a profession, with training and competency requirements and recognition through some form of accreditation. They have formal processes to withdraw recognition and accreditation when their members act in ways that harm their customers or patients and the reputation of the profession itself. Why should medical research be different? Surely medical research is as important as the work of lawyers, plumbers, electricians, doctors, nurses, dentists, physiotherapists and vets? So why don't we have a professional certification system in medical research, one that we ourselves establish and regulate?

There is a lot involved in setting up self-regulation. First, researchers should discuss and identify the core knowledge and training that someone wishing to be accredited should have. As well as having a doctorate to prove expertise in their field, we could expect knowledge of the principles of good research practice, of statistics and of ethical guidelines. We could agree the responsibilities that researchers who lead research groups should accept, in science and in human relationships. We could set out what continuing education should entail, with some of this generic and some tailored to the research discipline. Accreditation as a medical research professional could involve the formal declaration mentioned above.

Accreditation as a medical research professional should not be dependent on holding grants or on publication metrics. The aim is instead to promote responsible professional behaviour, rather than to be an index of research productivity or publication excellence. Accreditation would therefore involve quite different criteria to those a learned academy uses to award fellowships.

It would also be necessary to establish the ways that accreditation can be lost. For medical research, this should be proven research misconduct. The consequences of loss of accreditation should be equivalent to that of other professions and could mean loss of the right to be a principal or chief investigator. Funders could make accreditation a requirement for holding a grant with public funds.

The body responsible for self-regulation must be trusted by medical researchers and independent; it should not be a government body. In many countries, it could be the national academy of medical science – for example, the Australian Academy of Health and Medical Sciences here in Australia.[3] If the national academy did not wish to take on this role, a 'college' could be set up, perhaps along the lines of the College of Physicians or the College of Surgeons. Other models to consider

might include Engineers Australia, or the Animal Health Australia program for veterinarian accreditation.[4]

A softer model would leave development of a professional medical research regime to the universities, with some sort of core curriculum and obligatory continuing education. But I would not urge this. Medical researchers ourselves need to take control of what it means to be a professional, just as physicians, anaesthetists, surgeons, pathologists and many others do. *We* need to set the standards, not universities and research institutes.

I realise that I am suggesting a transformative change. Even if everyone agreed that it is necessary, it would take years to implement. But let's begin to think about it. The best place to start a discussion within Australia, I suggest, is the Australian Academy of Health and Medical Sciences.

Recognise and properly reward peer review work

Apart from the research itself, nothing is more central to science than peer review. To undertake peer review well requires knowledge, insight, generosity of spirit, a commitment to take the time needed to do it thoroughly, and a commitment to truth and fairness. But too often it seems like one extra burden in a medical researcher's busy life. We do it in the crevices of our weeks, between our other professional and personal activities.

We should value this work more highly. We should recognise formally that reviewing a grant or a fellowship application or a paper submitted for publication is a truly scholarly activity. It takes knowledge, thought and time to do it well and thoroughly. It is a core part of the work of a medical researcher and so should have a formal status alongside

activities such as publishing research, supervising students and giving service to our fields. The quality and quantity of peer reviewing should be assessed in academic appointments and promotions and in research funding. It should be one of the criteria for any researcher when seeking a job or a grant. If scientists know that their reviews are being judged for quality and that the quality and number of their reviews matter in appointments, promotions and grant applications, their willingness to participate and to write quality reviews will increase.

Work will be needed to make this happen. We will need to determine how to record, document and evaluate the quantity and quality of peer review. Indicators of the quality of the reviews will need to be developed by funders and journals. There are many ways to do that but, as an example, research funders could ask their review committees to give a simple rating on the written reviews, such as A = excellent, B = good, C = fair, D = poor. Journal editors could instigate a similar practice.

Peer reviewing is a core scholarly activity upon which medical research (and science generally) depends. Let's give it the status it deserves.

Improve how we judge quality

When judging an applicant for a research grant, we rely on their previous publications to assess their research capability. However, an applicant might have published 100 papers or more in the last five years, and it is simply impossible to read and properly evaluate every one of them. Too often, we default to simply counting the number of publications. We say to ourselves 'this shows how productive they are, right?' Then we make a judgement about quality based on our personal views on where these papers were published ('papers in *BMJ* are always higher

quality than in *MJA*, right?') or we use the Journal Impact Factor or citations or some other metric, which is not really judging quality at all.

We can do better.

First, let's do away entirely with the total number of publications when we review research applications. This is more an indicator of the resources available to the applicant and is poorly correlated to quality. Large research groups will produce more co-authored papers. Laboratory heads with big egos often, unethically, insist on having their names on everything, whether they were directly involved in the research or not. Women are too often left off authorships.[5] Having many clinical trials publications might just show that the researcher is a good recruiter of patients. Busy health practitioners and university lecturers have less time available for research than full-time researchers, and the same goes for researchers who have been ill, have disabilities or have major caregiving responsibilities.

Instead of quantity, let's judge quality. As I suggested in Chapter 7, let's assess how well a candidate can do by asking them to nominate the one publication that they believe shows them at their best and explain why they chose it. Reviewers can then read the paper in full and come to a conclusion on its scholarly merit, use of best methods, rigour of interpretation of results and significance to the field. It is impossible to do that for all an applicant's dozens or hundreds of papers.

There are a lot of factors to think through here too, but this approach would be more scientific and more intellectually honest than what most of us do now. It could be first introduced on an experimental basis for, say, mid-career fellowships.

One important benefit is that it would help level the playing field for researchers with fewer resources, or with limited time for research (for example, those with dependent children or elderly parents, busy

health professionals). It would make career gaps less important. It would also reduce the pressure on medical researchers to publish more and more papers and instead encourage fewer but more substantial ones.

Along the same lines of thinking, perhaps all CVs in applications for funding or for promotion should be restricted to listing, say, five publications. This would be a way to counter the endless escalation in paper numbers, and be a disincentive to salami-slicing, honorary authorship and the proliferation of dodgy journals.

Leave interpretation of metrics to experts

It is now ten years since the Declaration of Research Assessment folk published the core principle: 'Do not use journal-based metrics, such as Journal Impact Factors, as a surrogate measure of the quality of individual research articles, to assess an individual scientist's contributions, or in hiring, promotion, or funding decisions.'

We should object to any appointment and promotion committee or funding body that still uses journal metrics and does not adhere to DORA principles. We should stop using these metrics ourselves. Interpretation of metrics should be left to qualified scientometricians and informaticians[6] because, in my experience, few medical researchers understand the science of, and the limitations of, metrics.[7]

The DORA folk and other organisations are developing better ways of assessing the quality and true impacts of research.[8] We should support them, in our own interest and in the interest of science. Only twenty-two organisations in Australia appear to have signed up to DORA. These include the NHMRC, the Australian Academy of Science, the Association of Australian Medical Research Institutes and several individual institutes, but only one university, the University of Melbourne.

In contrast, more than eighty UK universities have signed. Australian researchers might enquire why their universities are hesitating.

Insist on best funding practice

Here is a summary of what I believe researchers should expect of funders, government and non-government, as discussed in Chapter 3.

- State clearly the intent for each funding scheme, align peer review criteria to these aims and implement the DORA principles in assessing applications.
- Take great care in establishing peer review committees: brief the members well; have an independent, impartial but well-regarded chair; and have a diverse membership (not just the old and stale).
- Always use review committees to make the final decisions, as this ensures individual reviewers are accountable to other scientists.
- Have clear and rigorous rules on both perceived and real conflicts of interest. Nothing undermines trust more quickly than a belief that the system runs on 'who you know, not what you know'.
- Avoid unnecessary bureaucracy.
- Review the peer review processes and systems frequently.

Funders cannot aim for best peer review practices if they do not have the necessary administrative funds. Governments must provide better administrative funding to the ARC and the NHMRC, to maintain researchers' trust in the fairness and rigour of the review processes.

Support the coming changes in publication

First, a reminder about the main problems described in Chapter 7. Publication of research, the primary outcome of our work, is expensive, with big profits for journal publishers. Many scientists and most of the public (who pay for the research) cannot gain access because these publications are behind paywalls. It is becoming debatable whether journal publishers really add much value over preprints – studies show that few articles are substantially changed between preprint and final publication.[9] The review processes that they manage should be adding value, but even top journals miss clearly fraudulent manuscripts. Zombie retracted papers circulate among us. Entirely fake journals proliferate.

Fortunately, there are lots of laudable activities underway to improve this situation, some described in Chapter 7, all more congruent with the digital age. Solutions will be multiple. It looks certain that scientists twenty years from now will publish their work very differently.

It is in our interest that, as researchers who support this coming revolution in publishing, those changes better reflect the values of science.

Boost scientific values and help prevent poor practices and research misconduct

Incompetent and fraudulent research are not someone else's problems – they are our problems.

The remedy is simple in one sense: scientific values need to be the basis of all we do. At the institutional level, we all must make sure that everyone who begins a research project is well trained. This training should include the technology they will use, their responsibilities

to research subjects (human, animal, environmental) and the high expectations of personal integrity that come with being a scientist. These need to be taught to beginners so they know what is expected from the start of their careers[10] and modelled by supervisors. We must insist that our university or institute has no tolerance for research misconduct and ensure that everyone knows what to do when doubts arise. If we do not have confidence in our university's processes for dealing with allegations of research misconduct, we must do something about it.

On a personal level, too, the values and established processes of science are our guide. We must have good, open and honest examination of our research and results within our research group. There should be frequent research-in-progress meetings of the whole group, where everyone is expected to share their results and discuss those of others, and rigorous questioning is encouraged. Supervisors must meet with individual researchers often and scrutinise primary data. They must impress on everyone the ethics of science and be ready to act at the first indication of a problem. We must all accept that it is our responsibility to speak up when there is wrongdoing.

In short, the solutions are largely in our hands. Our responsibility to medical research and to all those who hope to benefit from medical research is personal. We must tolerate nothing but the best science and personal behaviour in ourselves and others and be ready to help colleagues to understand what is expected of them.

Strengthen Australia's research integrity system

Medical researchers resent how those who engage in misconduct harm the reputation of research, undermine public trust and put public health as risk. They waste our time and resources when we base our

own projects on science that turns out to have been fraudulent. It is in our own interest that misconduct is reduced and transgressors held accountable.

As with most other major research countries, cases of grievous research fraud continue to occur in Australia. We should strengthen Australia's research integrity system by revising the Australian Code for the Responsible Conduct of Research, making it ready for legal incorporation. It is essential, too, that the powers of the Australian Research Integrity Committee (ARIC) are broadened and specified in the code.

It is time to incorporate the code into broader state, territory and Commonwealth legislation. This model has worked well for the welfare of research animals. The Australian Code for the Care and Use of Animals for Scientific Purposes, revised regularly under NHMRC and ARC leadership, is incorporated into relevant state and territory legislation. This combination of setting out principles and processes in a code under legislated power has advantages over both just a voluntary code and a purely legislative approach. A code can be reviewed, revised and updated frequently as science practices and community attitudes change. Legislation requires that the code be adhered to but a code avoids the cumbersome process of amendments to the law if scientific circumstances change, and counters the politicisation of the issue and the risk of a law that becomes progressively out of date as science progresses.

Regardless of the system, the first step in the investigation of any allegation of research misconduct should remain the responsibility of the employing institution. However, institutions have a conflict of interest, hoping to minimise impacts on their reputations. For that reason, the processes for investigation should be mandated in the

Australian Code for the Responsible Conduct of Research, and there should be compulsory reporting of the findings to the ARIC. In turn, the ARIC should be able to query these institutional findings, require re-reviews and take appeals. The ARIC should make its findings public (while protecting privacy of individuals as needed) and it should be able to recommend that funding support be withdrawn from researchers or even institutions. The ARIC should require institutions to report regularly too, so that we can better know the extent of the problem, whether preventative measures are working and how the code might need to be revised.

For this to work, the ARIC will need to be funded by governments. No longer should its resources come from the hard-pressed administrative budgets of the NHMRC and the ARC. It would not be expensive. The US Office of Research Integrity has an annual budget of less than US$10 million, so AU$5 million each year should do handily for ARIC. Though it should be government-funded, appointments to the ARIC and to code revision committees should continue to be made by the funders, the NHMRC and the ARC.

Some may ask: why not go all the way to a fully legislated system, as has happened in Sweden? Perhaps, but let's wait until we see how it works out for them, a smaller country, without states and with fewer universities. Other systems should also be considered.[11] First, though, we should build on what we already have, by strengthening the provisions of the Australian Code for the Responsible Conduct of Research and hardening its implementation by incorporating it under legislation.

I have argued that we ought to develop medical research as a profession. If we did that, one powerful sanction of misconduct could be loss of accreditation as a medical research professional. The potential

loss of reputation would itself be powerful, and it would be more impactful if perpetrators were barred from research.

Make more from research data

Data from medical research, in depositories, databases and curated data resources, is collectively the medical research community's largest infrastructure asset. The NIH estimated in 2015 that it alone was spending over US$100 million on data.[12]

We have not been making the most of its value. The medical-research equivalent to investments in CERN (the European Organization for Nuclear Research), ITER (the world's largest fusion project), and the Hubble and Webb telescopes would be investments to better capture data, curate it, link it up and make it available globally (while protecting personal privacy). This will require work and planning, but so too did CERN, established in 1954 and still expanding today. So did the new James Webb telescope, conceived in the 1990s, launched on Christmas Day 2021, and expected to work for the next two decades.

There is important work already underway by groups of scientists, such as the Global Alliance for Genomic Health, the Global Biodata Coalition, the International HundredK+ Cohorts Consortium, the NIH's BD2K programme, the European Open Science Cloud and ELIXIR (European Life-Science Infrastructure). Public health researchers have long been convincing authorities of the need to bring health data together for analysis – for example, by the Australian Institute for Health and Welfare and the World Health Organization's Global Health Observatory.[13]

Making more of the data from medical research will be a huge and complex task. There are many different types of data, on many different

platforms, in many different languages, and there are many different national and funder protocols regarding it. But it is not going to get any easier, and the benefits will be huge, so let's start the conversation.

Give emerging Australian researchers fixed seven- to ten-year contracts

A successful career in medical research will always be insecure as it requires continued competition for funding. Research funding from the taxpayer is not guaranteed; a researcher has to keep coming up with the best ideas for research, conduct successful research and apply anew.

As we saw in Chapter 5, early career scientists experience the greatest insecurity, especially those who do not have a professional degree such as medicine, nursing or public administration to fall back on. Paradoxically, this is the career stage when they might be most innovative. Most early career researchers have only short-term employment arrangements and are dependent on winning competitive fellowships or grants. If their funding application fails, they can be suddenly out of work, with no income.

The insecurity cannot be fixed by the NHMRC and funding agencies. These organisations need to continue to fund the best research and fellows judged on merit. Rather, the insecurity needs to be addressed by the universities and research institutes who recruit early career researchers.

My idea is that institutions should offer early career scientists a firm fixed-term contract for, say, seven to ten years to give them security of income during their early creative years. The contract should be long enough for the emerging researcher to be well mentored, build

their skill set and track record and be ready to become an established independent researcher. Contracts should not be dependent on winning an NHMRC or ARC fellowship or grant, though such researchers should be expected to apply for these. They would of course be subject to all the normal employment requirements and rules of the institution.

Institutions will need to budget for this, so they are likely to offer contracts only to those postdocs who show the potential to become successful medical researchers. Away from the intense competitive environment of NHMRC-fellowship-or-bust, institutions could structure these contracts in flexible and creative ways. Parents with young children could switch to part-time for a few years if they wanted, health professionals could continue to work in healthcare, 'gap years' could be factored in. This will not remove the competitive pressure they will face at the end of the contract, but meanwhile they can be creative and innovative. When a researcher fears an abrupt end to their career and immediate loss of income, they can be tempted to stick to safe and reliable projects only.

Remove the indirect costs distortion

The NHMRC and the ARC pay only the direct costs of the research, in accord with longstanding government policy. The money needed to pay the electricity, salaries, subscriptions to publications, the animal house and so on has to come from somewhere else. It is estimated that these indirect administrative costs amount to about twice the direct costs.

It is not a level playing field and this inclines researchers to play games to maximise their support. It can inhibit collaboration across universities and institutes. The Commonwealth government's Research

Infrastructure Block Grant system for universities provides just twenty cents or so for every NHMRC or ARC dollar won. Universities need to find the rest, mainly from fees that overseas students pay for their education. Most state governments give independent medical research institutes some support through formula-driven funding schemes, and there is a special indirect-costs NHMRC scheme for institutes only, which was established by the Howard government. Another difference in the treatment of universities and independent institutes is that institutes are usually also registered charities and so they can offer more-attractive, 'tax-effective' salaries to their staff. In another difference, the Morrison federal government authorised medical research institutes to use JobKeeper (a COVID-19 pandemic scheme that helped keep Australians in jobs), but not universities. The loss of overseas student income during the pandemic also dramatically eroded universities' ability to cross-subsidise research.

Hospital-employed researchers are the most disadvantaged. They have no defined system to support indirect costs, though some can access university support if they also hold an academic appointment.

The solution is for the federal and state governments to work together to fund the NHMRC and the ARC to pay full indirect costs in all their grants.

Encourage more research in hospitals and other clinical care settings

As far back as 2009, the Rudd government's National Health and Hospital Reform Commission concluded that Australia had gone too far in separating clinical care from medical research.[14] The commission stated:

> Valuing clinical leadership and embedding a culture which frees health professionals to invest time in quality improvement may be as important as structural change in achieving health reform … Providing health professionals with opportunities to combine teaching and research with their service responsibilities builds a culture of quality and is demonstrated to lead to better uptake of new knowledge and better outcomes.

The McKeon committee report reinforced this in 2013.[15] The Medical Research Future Fund also identifies this need in its strategy.[16]

Apart from the NHMRC's longstanding Centres of Research Excellence scheme, some interesting things are happening in the states' tertiary hospital sites to bring research evidence to healthcare. This is also occurring through the Advanced Health Research and Translation Centres and altruistic researcher-clinician initiatives such as the Australian Living Evidence Consortium.[17] It is heartening to see more health professional groups being introduced to research – for example, my ambulance paramedic nephew has completed a well-designed and well-supervised Master's research project at Monash.

However, the overall situation does not look much different now, a decade and a half after the commission's report. Health professionals are rarely provided with research opportunities to 'build a culture of quality' for better health outcomes.

The Commonwealth and state governments need to develop a shared vision for research in healthcare delivery settings. A start could be giving the states a role in the governance of the MRFF.

Develop a national strategy

Australia conducts just a tiny percentage of the world's medical research, so we need to be canny and forward thinking. We need an overall medical research strategy to maximise our resources, prevent duplication and waste, and plan for the future. We have two major but separate medical research funding programs, the NHMRC and the MRFF. We have piecemeal policies on the indirect costs of research. The six states and two territories have separate policies on research, especially in hospitals and in public health. We do not have a national policy on participating in major international medical research projects, with the honourable exception of the NHMRC. We have a too-weak approach to research integrity and we have an uncoordinated and episodic approach to research infrastructure.

A national strategy can come only through national government leadership with the states and territories. The strategy should aim to be as visionary for the 2020s as the Wills Report was twenty-five years ago. Perhaps it will emerge from consultation on the new discussion paper, improving alignment and coordination between the Medical Research Future Fund and NHMRC's Medical Research Endowment Account.

Analyse our performance with rigour

Australian needs a rigorous, independent, scholarly organisation that collects and analyses data and information on the inputs, outputs and outcomes of all medical research (not just the NHMRC), including on workforce.[18] At regular intervals, it should provide the public and governments with an independent analysis of how well or how poorly Australian research in doing against international standards and

comparable countries. Are we indeed 'punching above our weight', as we often contend, and if so, by how much in relation to comparable countries such as Canada?

Without such a rigorous independent body, research policymaking will continue to rely on partial (in both senses of the word) analysis, self-interested advocacy and self-congratulation.

Roadmap for the future

- **Adopt a formal declaration of principles for all medical researchers**
- **Make medical research a true profession**
- **Bolster peer review by formally recognising peer reviewing in appointments, promotions and research applications**
- **Value publication quality rather than quantity, implement the DORA Principles and drop journal metrics entirely**
- **Reform Australia's research integrity system**
- **Increase career security for early career researchers**
- **Adopt an Australian national medical research strategy and an ongoing rigorous analysis of our research performance.**

It is up to us

The system of medical research is not broken. The many life-enhancing discoveries that occur every day attest to its health and success. It is because I believe fervently in its importance and its values that I am

suggesting where it could be better and where there are amber flashing lights in the system, where trust is eroding.

My appeal is for scientists to lead, to address the problems and to find the best solutions. The interests of our research institutions will not always align with those of the researchers. Our funders are government bodies and so, properly, they are constrained in what they can say and do. So change is up to us.

Notes

Chapter 1: Trust and Honesty

1 Australian Institute of Health and Welfare, 'Coronary Heart Disease', Australian Government, 9 February 2023, www.aihw.gov.au/reports/australias-health/coronary-heart-disease. Coronary heart disease nevertheless remains the leading cause of death in Australia.

2 W. Anderson and M.A. Perry, 'Australian animal ethics committees: we have come a long way', *Cambridge Quarterly of Healthcare Ethics* 8(1), 1999, pp. 80–86, doi:10.1017/S0963180199801121.

3 The Declaration on Research Assessment (DORA), developed in 2021 in San Francisco, 'recognizes the need to improve the ways in which the outputs of scholarly research are evaluated'; see 'About DORA', DORA, https://sfdora.org/. The Research on Research Institute (RoRI) is a group of 21 partners drawn from 13 countries, led by a core team based in the United Kingdom (at Wellcome and the University of Sheffield) and the Netherlands (Leiden University); see 'About RoRI', RoRI, https://researchonresearch.org/about.

Chapter 2: Public Funding Success

1 'A short history of the National Institutes of Health', National Institutes of Health Office of NIH History & Stetten Museum, https://history.nih.gov/display/history/A+Short+History+of+the+National+Institutes+of+Health; 'History of MRC', UKRI, www.ukri.org/about-us; 'About us', Chinese Academy of Sciences, https://english.cas.cn/about_us/introduction/201501/t20150114_135284.shtml; 'NSFC at a Glance', National Natural Science Foundation of China, www.nsfc.gov.cn/english/site_1/about/6.html.

2 See, for example, S. Rusakaniko et. al, 'Strengthening national health research systems in the WHO African Region – progress towards universal health coverage', *Globalization and Health* 15(50), 2019, https://doi.org/10.1186/s12992-019-0492-8.

3 Matt Hourihan, 'In the age of Trump, Congress keeps boosting science funding', *AAAS*, 18 December 2019, www.aaas.org/news/update-age-trump-congress-keeps-boosting-science-funding.

4 'Foundation fact sheet', Bill & Melinda Gates Foundation, https://www.gatesfoundation.org/about/foundation-fact-sheet; Janelia Research

Campus, http://www.janelia.org/. For more on philanthropic investment in medical research funding, see 'Enlisting philanthropies to invest in basic medical research', Lasker Foundation, 2016, https://laskerfoundation.org/enlisting-philanthropies-to-invest-in-basic-medical-research/.

5 'Collaborate Against Cancer', Mindaroo, www.minderoo.org/collaborate-against-cancer/#overview; 'Research Australia's collaborative strategy', Research Australia, https://researchaustralia.org/a-collaborative-strategy/.

6 'About us', National Institute for Health and Care Research, www.nihr.ac.uk/about-us/; 'Partnership Projects', NMHRC, www.nhmrc.gov.au/funding/find-funding/partnership-projects; 'Recognised Research Translation Centres', www.nhmrc.gov.au/research-policy/research-translation/recognised-research-translation-centres; 'Health research and innovation', European Commission, https://research-and-innovation.ec.europa.eu/research-area/health_en.

7 See, for example, Kim Humphery, 'Setting the Rules: The Development of the NHMRC Guidelines on Ethical Matters in Aboriginal and Torres Strait Islander Health Research', *NZ Bioethics*, February 2003, pp. 14–19, www.nzlii.org/nz/journals/NZBioethJl/2003/6.pdf.

8 Peter Eichhorn and Ian Towers, *Principles of Management, Efficiency and Effectiveness in the Private and Public Sector*, Springer, New York, 2018.

9 Roderick F. Viergever and Thom C.C. Hendriks, 'The 10 largest public and philanthropic funders of health research in the world: what they fund and how they distribute their funds', *Health Research Policy and Systems* 14, https://health-policy-systems.biomedcentral.com/articles/10.1186/s12961-015-0074-z; Department of Finance, 'Medical Research Future Fund', Australian Government, www.finance.gov.au/government/australian-government-investment-funds/medical-research-future-fund; Department of Health and Aged Care, 'Medical Research Future Fund grant recipients', 5 April 2023, www.health.gov.au/resources/publications/medical-research-future-fund-mrff-grant-recipients.

10 Australian Research Council, 'About the ARC', Australian Government, www.arc.gov.au/about-arc.

11 In a report released by the Australian Society for Medical Research in 2014, Deloitte estimated that '… for every dollar spent on additional NHMRC R&D, seven cents would be returned in health expenditure savings in the future'.

12 National Institutes of Health, 'Budget', 18 August 2022, www.nih.gov/about-nih/what-we-do/budget. Note that other US government departments also fund medical research in the United States – such as the Department of Energy, with US$300 million for biomedical research, especially genomic research. See Department of Energy, 'Department of Energy FY 2019 Congressional Budget Request' 4, United States of

America, March 2018, www.energy.gov/sites/default/files/2018/03/f49/DOE-FY2019-Budget-Volume-4_0.pdf.

13 'Annual report 2020–21', NHRMC, www.nhmrc.gov.au/about-us/publications/annual-report-2020-21

14 'Papua New Guinea' and 'Australia', John Hopkins University and Medicine Coronavirus Resource Center, 10 March 2023, https://coronavirus.jhu.edu/region/papua-new-guinea.

15 World Health Organization, 'Life expectancy and healthy life expectancy – data by country', Global Health Observatory data repository, 2020, https://apps.who.int/gho/data/node.main.688.

16 'Mortality Analyses', John Hopkins University and Medicine Coronavirus Resource Center, 10 March 2023, https://coronavirus.jhu.edu/data/mortality.

Chapter 3: Deciding What to Fund

1 See, for example, Julia Belluz, Brad Plumer and Brian Resnick, 'The 7 biggest problems facing science, according to 270 scientists', *Vox*, 7 September 2016, www.vox.com/2016/7/14/12016710/science-challeges-research-funding-peer-review-process.

2 Editorial, '*Nature* is trialling transparent peer review – the early results are encouraging', 1 March 2022, www.nature.com/articles/d41586-022-00493-w.

3 NWO, 'Open Science Fund project proposals published today', 31 January 2022, https://www.nwo.nl/en/news/open-science-fund-project-proposals-published-today and Wellcome, 'Open Research Fund: project proposals submitted to Wellcome', https://wellcome.org/grant-funding/open-research-fund-project-proposals-submitted-wellcome. See also Serge Horbach, Joeri K. Tijdink and Lex Bouter, 'Research funders should be more transparent: a plea for open applications', OSF Preprints, CC0 1.0 Universal, https://osf.io/37tsu/.

4 Australian National Audit Office, 'Administration of grants at the National Health and Medical Research Council', 2009, www.anao.gov.au/work/performance-audit/administration-grants-national-health-and-medical-research-council.

5 Richard Van Noorden, 'Interdisciplinary research by the numbers', *Nature* 525, 16 September 2015, www.nature.com/articles/525306a.

6 Guntram Bauer, 'Challenges for international peer reviewing of research proposals', *Technology & Innovation* 12, no. 3, 2010, https://doi.org/10.3727/194982410X12895770313998.

7 Richard Van Noorden, 'Interdisciplinary research by the numbers'.

8 Marc J. Lerchenmueller et al., 'Gender differences in how scientists present the importance of their research: observational study', *BMJ* 367, 2019, www.bmj.com/content/367/bmj.l6573 and Chris Woolston, 'Male authors boost research impact through self-hyping studies', *Nature*, 31 January 2020, www.nature.com/articles/d41586-020-00266-3.

9 NHMRC, 'Outcomes of funding rounds', 2 February 2022, www.nhmrc.gov.au/funding/data-research/outcomes; Australian Research Council, 'Selection Outcome Reports', Australian Government, www.arc.gov.au/grants/grant-outcomes/selection-outcome-reports; NIH Research Portfolio Online Reporting Tools, https://report.nih.gov/funding/nih-budget-and-spending-data-past-fiscal-years/success-rates.

10 Tim Brennan and Dr Hazel Ferguson, 'Independence of the Australian Research Council', Parliament of Australia, 3 June 2022, www.aph.gov.au/About_Parliament/Parliamentary_Departments/Parliamentary_Library/FlagPost/2022/June/ARC_Independence; Bianca Nogrady, 'Australian researchers push to end politicians' power to veto grants', *Nature*, 10 March 2022, https://doi.org/10.1038/d41586-022-00682-7; Department of Education, 'ARC Budget Statements 2014–15', Australian Government, 13 May 2014, www.dese.gov.au/about-us/resources/arc-budget-statements-2014-15.

11 Australian Research Council, 'National Interest Test Statements', Australian Government, 2022, www.arc.gov.au/national-interest-test-statements.

12 'National Interest Test', The University of Melbourne, 2022, www.arc.gov.au/national-interest-test-statements.

13 The acting minister was Stuart Robert MP, acting in the Education portfolio. See Philippa Collin et al., '"Disappointment and disbelief" after Morrison government vetoes research into student climate activism', *The Conversation*, 13 January 2022, https://theconversation.com/disappointment-and-disbelief-after-morrison-government-vetoes-research-into-student-climate-activism-174699.

14 'RoRI RANDOMISATION project', Research on Research Institute, 2022, https://researchonresearch.org/projects#!/tab/273951116-6.

Chapter 4: Choosing Research Priorities

1 See their website at https://irdirc.org/

2 See, for example, 'Partnerships for better health', NHMRC, 2023, www.nhmrc.gov.au/research-policy/research-translation-and-impact/partnership-centres-better-health

3 Elin Dolgin, 'The tangled history of mRNA vaccines', *Nature*, 22 October 2021.

4 Ibid.

5 See Australian Genomics, www.australiangenomics.org.au/.

6 Esther Landhuis, 'Do it yourself? When the researcher becomes the subject', *Science*, 5 December 2016, www.science.org/content/article/do-it-yourself-when-researcher-becomes-subject.

7 See Benjamin Jones et al., 'Age and scientific genius', NBER Working Papers Series, National Bureau of Economic Research, Cambridge, January 2014, www.nber.org/system/files/working_papers/w19866/w19866.pdf.

8 Benjamin F. Jones and Bruce A. Weinberg, 'Age dynamics in scientific creativity', *PNAS*, 7 November 2011, www.pnas.org/doi/10.1073/pnas.1102895108.
9 'Endowed Chairs Program', National Breast Cancer Foundation, 2023, https://nbcf.org.au/research/endowed-chairs-program/.
10 Vannevar Bush, 'Science: the endless frontier – a report to the President on a program for post-war scientific research', Washington, DC, July 1945, https://apo.org.au/sites/default/files/resource-files/1945-06/apo-nid62466.pdf.
11 'Governance', Human Frontier Science Program, 13 January 2020, https://www.hfsp.org/about/governance/hfspo-statutes.
12 'The Haldane Principle', *Putting Science and Engineering at the Heart of Government Policy*, Innovation, Universities, Science and Skills Committee – Eighth Report, House of Commons, UK Parliament, 8 July 2009, https://publications.parliament.uk/pa/cm200809/cmselect/cmdius/168/16807.htm.
13 Section 103, *Higher Education and Research Act 2017*, https://www.legislation.gov.uk/ukpga/2017/29/section/103/enacted.
14 Michelle Grattan, 'Horror budget gets a bitter reaction from public and premiers', *The Conversation*, 19 May 2014, https://theconversation.com/horror-budget-gets-a-bitter-reaction-from-public-and-premiers-26857.
15 'Report: Medical Research Future Fund Bill 2015 and Medical Research Future Fund (Consequential Amendments) Bill 2015', Parliament of Australia, 10 August 2015, www.aph.gov.au/Parliamentary_Business/Committees/Senate/Community_Affairs/Future_Fund/Report.
16 'Report: Medical Research Future Fund Bill 2015 and Medical Research Future Fund (Consequential Amendments) Bill 2015', Parliament of Australia, 10 August 2015, https://parlinfo.aph.gov.au/parlInfo/search/display/display.w3p;query=Id%3A%22chamber%2Fhansards%2Ff1265e70-9604-44a1-b4f1-791cd1c9adcc%2F0036%22.
17 Warwick Anderson, 'Six challenges facing Australia's medical research sector', *The Conversation*, 15 April 2015, https://theconversation.com/six-challenges-facing-australias-medical-research-sector-40222.
18 'Simplified outline of this act', *Medical Research Future Fund Act 2015*, Parliament of Australia, 12 December 2019, www.legislation.gov.au/Details/C2020C00008.
19 See, for example, 'Australian Medical Research Advisory Board – Communiques', https://www.health.gov.au/resources/collections/australian-medical-research-advisory-board-communiques?language=en.
20 See 'Award of Funding under the Community Sport Infrastructure Program', Australian National Audit Office, 15 January 2020, www.anao.gov.au/work/performance-audit/award-funding-under-the-community-sport-infrastructure-program.

21 Mark Butler, 'Charting the way forward for medical research funding', Department of Health and Aged Care, 5 June 2023, www.health.gov.au/ministers/the-hon-mark-butler-mp/media/charting-the-way-forward-for-medical-research-funding.
22 James Glenday, 'Wind farms are ruining the landscape and are "appalling", Treasurer Joe Hockey says', *ABC News*, 16 September 2014, www.abc.net.au/news/2014-09-16/wind-farms-ruin-the-landscape-and-look-appalling:-hockey/5748346?nw=0&r=HtmlFragment.
23 'NHMRC statement: evidence on wind farms and human health', National Health and Medical Research Council, Australian Government, February 2015, www.nhmrc.gov.au/about-us/publications/nhmrc-statement-evidence-wind-farms-and-human-health#block-views-block-file-attachments-content-block-1.
24 Sophie Vorrath, 'NHMRC pours another $3.3m into wind turbine and health research', *Renew Economy*, 22 March 2016.

Chapter 5: Medical Research Careers

1 'Student Statistics Report 2021', Medical Deans Australia and New Zealand, 2021, https://medicaldeans.org.au/md/2021/11/MDANZ-Student-Statistics-Report-2021.pdf.
2 Gender Equality Strategy 2018–2021, https://www.nhmrc.gov.au/sites/default/files/documents/Gender-Equality-Strategy-2018-2021.pdf.
3 'Benefits', Walter and Eliza Hall Institute of Medical Research, 2023, www.wehi.edu.au/about/career-opportunities/benefits.

Chapter 6: Trouble in the Lab

1 A major step occurred when ClinicalTrials.gov was launched by the National Institutes of Health in February 2000, designed to provide the public with information about ongoing and completed clinical trials.
2 'What is DORA?', DORA, 2023, https://sfdora.org/.
3 This is true not only in Australia but in the United Kingdom and elsewhere. See, for example, C. Roche, 'The research conduct spectrum for surgeons: your career in their rule bending hands?', *The Bulletin of the Royal College of Surgeons of England*, vol. 104, no. 6, September 2022, https://publishing.rcseng.ac.uk/doi/epdf/10.1308/rcsbull.2022.112.
4 C. Glenn Begley and Lee M. Ellis, 'Raise standards for preclinical cancer research', *Nature*, 28 March 2012, www.nature.com/articles/483531a.
5 C. Glenn Begley and John P.A. Ioannidis, 'Reproducibility in science: improving the standard for basic and preclinical research', *Circulation Research*, vol. 116, no. 1, 2 January 2015, www.ahajournals.org/doi/10.1161/CIRCRESAHA.114.303819.
6 Open Science Collaboration, 'Estimating the reproducibility of psychological science', *Science*, 28 August 2015, www.science.org/doi/10.1126/science.aac4716.

7 Yasunori Park et al., 'Identification of human gene research articles with wrongly identified nucleotide sequences', *Life Science Alliance*, vol. 5, no. 4, April 2022, www.life-science-alliance.org/content/5/4/e202101203.

8 D.J. Niven, T.J. McCormick, S.E. Straus et al., 'Reproducibility of clinical research in critical care: a scoping review', *BMC Medicine*, vol. 16, no. 26, 2018.

9 Steve Perrin, 'Preclinical research: make mouse studies work', *Nature*, 26 March 2014, www.nature.com/articles/507423a. Perrin cites Sean Scott et al., 'Design, power, and interpretation of studies in the standard murine model of ALS', *Amyotrophic Lateral Sclerosis*, vol. 9, no. 1, 2008, www.tandfonline.com/doi/full/10.1080/17482960701856300.

10 Asher Mullard, 'Half of top cancer studies fail high-profile reproducibility effort', *Nature*, 9 December 2021, www.nature.com/articles/d41586-021-03691-0.

11 'Trouble at the lab', *The Economist*, 18 October 2013, www.economist.com/briefing/2013/10/18/trouble-at-the-lab.

12 Ian Freckelton, *Scholarly Misconduct: Law, Regulation and Practice*, Oxford University Press, 2016.

13 '2018 Australian Code for the Responsible Conduct of Research', *NHMRC*, 16 July 2021, www.nhmrc.gov.au/research-policy/research-integrity/2018-australian-code-responsible-conduct-research.

14 See, for example, David Vaux, 'Australia needs an Office for Research Integrity to catch up with the rest of the world', *The Conversation*, 3 February 2022, https://theconversation.com/australia-needs-an-office-for-research-integrity-to-catch-up-with-the-rest-of-the-world-176019 and 'The institute's policy and procedure on good scientific practice', Walter and Eliza Hall Institute Seminars, 2014, www.youtube.com/watch?v=0mXRbr8rJrI.

15 See, for example, the Coroner's Court of Victoria, www.coronerscourt.vic.gov.au/.

16 See Ron Brent and Kerry Breen, 'Harmful research misconduct: is our research integrity framework adequate?', *Pearls and Irritations*, 23 August 2020, https://johnmenadue.com/harmful-research-misconduct/.

17 Alison Abbott, 'Culture of silence and nonchalance protected disgraced trachea surgeon (updated)', *Nature*, 2 September 2016, www.nature.com/articles/nature.2016.20533.

18 The National Academy of Sciences, Engineering and Medicine, 'Fostering integrity in research', Consensus Study Report, 2017, https://nap.nationalacademies.org/catalog/21896/fostering-integrity-in-research.

19 Jeffrey Mervis, 'US report calls for research integrity board', *Science*, 11 April 2017, www.science.org/content/article/us-report-calls-research-integrity-board.

20 'ORI Case Closures', Office of Research Integrity, 9 February 2022, https://ori.hhs.gov/blog/ori-case-closures.
21 Janelle Miles, 'Leading Queensland cancer researcher Mark Smyth fabricated scientific data, review finds', ABC News, 11 January 2022, www.abc.net.au/news/2021-11-24/qld-professor-mark-smyth-stood-down-qimr-investigation/100646988.
22 The NHMRC has a comprehensive website on research integrity: www.nhmrc.gov.au/about-us/resources/nhmrc-research-integrity-and-misconduct-policy. It includes detailed information on the actions that the NHMRC might take in the case of a breach, including termination of grants and recovery of grant funds.
23 Richard van Noorden, 'Science publishing: the trouble with retractions', *Nature*, 5 October 2011, www.nature.com/articles/478026a.
24 Jennifer Byrne, 'We need to talk about systematic fraud', *Nature*, 6 February 2019, www.nature.com/articles/d41586-019-00439-9.
25 Richard Smith, 'Time to assume that health research is fraudulent until proven otherwise?', *The BMJ Opinion*, 5 July 2021, https://blogs.bmj.com/bmj/2021/07/05/time-to-assume-that-health-research-is-fraudulent-until-proved-otherwise/.

Chapter 7: Publishing Medical Research

1 See, for example, Aileen Fyfe, 'From philanthropy to business: the economics of Royal Society journal publishing in the twentieth century', *The Royal Society Publishing*, 3 August 2022, https://royalsocietypublishing.org/doi/10.1098/rsnr.2022.0021.
2 Stephen Buranyi, 'Is the staggeringly profitable business of scientific publishing bad for science?', *The Guardian*, 27 June 2017, www.theguardian.com/science/2017/jun/27/profitable-business-scientific-publishing-bad-for-science.
3 See a directory of open access journals at https://doaj.org/.
4 Richard Horton, 'Offline: the scramble for science', *The Lancet*, 24 September 2022, www.thelancet.com/journals/lancet/article/PIIS0140-6736(22)01750-0/fulltext.
5 'About Plan S', cOAlition S, www.coalition-s.org/.
6 Plan S, 'Statement on peer reviewed publications', 6 July 2022, www.coalition-s.org/statement-on-peer-reviewed-publications/.
7 Office of Science and Technology Policy, 'Ensuring Free, Immediate, and Equitable Access to Federally Funded Research', public access memo, 25 August 2022, www.whitehouse.gov/wp-content/uploads/2022/08/08-2022-OSTP-Public-Access-Memo.pdf (underline as in the original).
8 Ying He et al., 'An incentive mechanism-based framework to assure the quality of self-organizing peer review in preprint', *Data Technologies and*

Applications, 29 April 2021, www.emerald.com/insight/content/doi/10.1108/DTA-08-2020-0181/full/html.

9 Liam Brierly, 'Preprints in motion: tracking changes between preprint posting and journal publication during a pandemic', *bioRxiv*, 14 October 2021, www.biorxiv.org/content/10.1101/2021.02.20.432090v3.full.

10 Charles Piller, 'Who's to blame? These three scientists are at the heart of the Surgisphere COVID-19 scandal', *Science*, 8 June 2020, https://science.org/content/article/whos-blame-these-three-scientists-are-heart-surgisphere-covid-19-scandal.

11 Stuart Ritchie, 'The big idea: should we get rid of the scientific paper?', *The Guardian*, 11 April 2022, www.theguardian.com/books/2022/apr/11/the-big-idea-should-we-get-rid-of-the-scientific-paper.

12 Alison Abritis et al., 'Cash bonuses for peer-reviewed papers go global', *Science*, 10 August 2017, www.science.org/content/article/cash-bonuses-peer-reviewed-papers-go-global.

13 Editorial, 'Not-so-deep impact', *Nature*, 22 June 2005, https://nature.com/articles/4351003b and Ewan Callaway, 'Beat it, impact factor! Publishing elite turns against controversial metric', *Nature*, 8 July 2016, www.nature.com/articles/nature.2016.20224.

14 'San Francisco Declaration on Research Assessment', DORA, 2012, https://sfdora.org/.

15 'The Open Reviewers Toolkit', DORA, 2015, https://sfdora.org/.

16 Diana Hicks et al., 'Bibliometrics: the Leiden Manifesto for research metrics', *Nature*, 22 April 2015, https://www.nature.com/articles/520429a and Editorial, 'Research evaluation needs to change with the times', *Nature*, 11 January 2022, www.nature.com/articles/d41586-022-00056-z.

17 See, for example, Matthius Wallum Nielsen, 'Global citation inequality is on the rise', *PNAS*, 8 February 2021, www.pnas.org/doi/full/10.1073/pnas.2012208118; Paula Stephan et al., 'Reviewers are blinkered by bibliometrics', *Nature*, 27 April 2017, www.nature.com/articles/544411a; and Diana Kwon, 'The rise of citational justice: how scholars are making references fairer', *Nature*, 22 March 2022, www.nature.com/articles/d41586-022-00793-1.

18 Istok Fister Jr et al., 'Toward the discovery of citation cartels in citation networks', *Frontiers in Physics*, 16 December 2016, www.frontiersin.org/articles/10.3389/fphy.2016.00049/full and Jeffrey Brainard, 'Reviewers award higher marks when a paper's author is famous', *Science*, 13 September 2022, www.science.org/content/article/reviewers-award-higher-marks-when-paper-s-author-famous.

19 Matthew B. Ross et al., 'Women are credited less in science than men', *Nature*, 22 June 2022, www.nature.com/articles/s41586-022-04966-w.

20 Jian Wang et al., 'Bias against novelty in science: a cautionary tale for users of bibliometric indicators', *Research Policy*, vol. 46, no. 8, October 2017, www.sciencedirect.com/science/article/abs/pii/S0048733317301038?via%3Dihub.
21 Linhong Xu et al., 'Do negative citations reduce the impact of cited papers?', *Scientometrics*, vol. 127, 2022, https://link.springer.com/article/10.1007/s11192-021-04214-4.
22 NHMRC, 'Measuring up 2018: NHMRC supported research', Australian Government, 2020, www.nhmrc.gov.au/about-us/publications/measuring-2018.
23 Agnes Grudniewicz et al., 'Predatory journals: no definition, no defence', *Nature*, 11 December 2019, www.nature.com/articles/d41586-019-03759-y.
24 For a list of predatory publishers, see https://predatory-publishing.com/info/. For criticism of such lists, see Jaime A. Teixeira da Silva et al., 'What value do journal whitelists and blacklists have in academia?', *The Journal of Academic Librarianship*, vol. 44, no. 6, November 2018, www.sciencedirect.com/science/article/pii/S0099133318302490?via%20per%20cent3Dihub.

Chapter 8: Politics and Australian Research

1 'Australian researchers push to end politicians' power to veto grants', *Nature*, 10 March 2022, www.nature.com/articles/d41586-022-00682-7.
2 Australian Research Council, 'Selection Report: Discovery Projects 2022', Australian Government, 2022, www.arc.gov.au/grants/grant-outcomes/selection-outcome-reports/selection-report-discovery-projects-2022, and Daniel Hurst, 'Federal government's Christmas Eve veto of research projects labelled "McCarthyism"', *The Guardian*, 24 December 2021, www.theguardian.com/australia-news/2021/dec/24/federal-governments-christmas-eve-veto-of-research-projects-labelled-mccarthyism.
3 The *NHMRC Act* sets out in detail the public consultation that the NHMRC must undertake when developing guidelines and regulations: www.legislation.gov.au/Details/C2014C00364.
4 'Australian code for the care and use of animals for scientific purposes', NHRMC, www.nhmrc.gov.au/about-us/publications/australian-code-care-and-use-animals-scientific-purposes.
5 'Annual report 2020–21', NHRMC, www.nhmrc.gov.au/about-us/publications/annual-report-2020-21.
6 Meredith Wadman, 'Vaccines that use human fetal cells draw fire', National Library of Medicine, https://pubmed.ncbi.nlm.nih.gov/32527809/.
7 See, for example, Luke Taylor, '"We are being ignored": Brazil's researchers blame anti-science government for devastating COVID surge', *Nature*, 27 April 2021, https://academic.oup.com/cid/article/71/9/2311/5867798.

8 Lidia Morawska and Donald K. Milton, 'It is time to address airborne transmission of coronovirus disease 2019 (COVID-19)', *Clinical Infectious Diseases*, vol. 71, no. 9, 1 November 2020, pp. 2311–13.

9 'International collaborative health research funding', NHMRC, 2022, www.nhmrc.gov.au/funding/international-collaborative-health-research-funding.

10 Simon Marginson, 'Global science and national comparisons: beyond bibliometrics and scientometrics', 4 October 2021, https://www.tandfonline.com/doi/full/10.1080/03050068.2021.1981725 and NHMRC, 'Measuring up 2018: NHMRC supported research', Australian Government, 2020, www.nhmrc.gov.au/about-us/publications/measuring-2018.

11 Guntram Bauer, 'Challenges for international peer reviewing of research proposals', *Technology & Innovation*, vol. 12, no. 3, 2010, pp. 197–201.

12 'Nobel Prizes for HFSP Awardees', Human Frontier Science Program, www.hfsp.org/awardees/nobel-prizes-hfsp-awardees.

13 Theo Vos et al., 'Global burden of 369 diseases and injuries in 204 countries and territories, 1990–2019: a systematic analysis for the Global Burden of Disease Study 2019', *The Lancet*, 17 October 2020, www.thelancet.com/journals/lancet/article/PIIS0140-6736(20)30925-9/fulltext#%20.

14 'Malaria', National Institute of Allergy and Infectious Diseases, 27 June 2016, www.niaid.nih.gov/diseases-conditions/malaria.

15 'Tuberculosis', National Institute of Allergy and Infectious Diseases, 3 January 2020, www.niaid.nih.gov/diseases-conditions/tuberculosis.

16 'Dengue fever', National Institute of Allergy and Infectious Diseases, 12 May 2016, www.niaid.nih.gov/diseases-conditions/dengue-fever.

17 'Schistosomiasis (Bilharzia)', National Institute of Allergy and Infectious Diseases, 30 January 2020, www.niaid.nih.gov/diseases-conditions/schistosomiasis-bilharzia.

18 'Professor Alan Cowman', Walter and Eliza Hall Institute of Medical Research, 22 July 2021, www.wehi.edu.au/people/alan-cowman; 'Professor Brendan Crabb AC', Burnet, 2022, www.burnet.edu.au/people/66_brendan_crabb_ac; 'Professor Michael Good', Griffith University, https://experts.griffith.edu.au/18882-michael-good; 'Vale Professor Ruth Bishop AC BSc MSc PhD DSc', Murdoch Children's Research Centre, 20 May 2022, www.mcri.edu.au/news-stories/vale-professor-ruth-bishop-ac-bsc-msc-phd-dsc and Bill Gates, 'This virologist's discovery saved millions of lives and helped launch our foundation', *Gates Notes*, 8 March 2021, www.gatesnotes.com/Health/Heroes-in-the-field-Dr-Ruth-Bishop; 'Tribute to Professor Don McManus FAHMS', Australian Academy of Health and Medical Sciences, 16 November 2022, https://aahms.org/news/tribute-to-professor-don-mcmanus-fahms/.

19 James Jin Kang, 'The Thousand Talents Plan is part of China's long quest to become the global scientific leader', 1 September 2020, https://theconversation.com/the-thousand-talents-plan-is-part-of-chinas-long-quest-to-become-the-global-scientific-leader-145100; Editorial, 'How the US–China science freeze threatens climate disaster', *Nature*, 1 November 2022, www.nature.com/articles/d41586-022-03473-2; Richard van Noorden, 'The number of researchers with dual US–China affiliations is falling', *Nature*, 30 May 2022, www.nature.com/articles/d41586-022-01492-7.

Chapter 9: Data

1 'GBC Letter of Understanding', Global Biodata Coalition, 2023, https://globalbiodata.org/wp-content/uploads/GBC_Letter_of_Understanding.pdf.
2 Heidi Imker et al., 'A machine learning-enabled open biodata resource inventory from the scientific literature', Zenodo, 2023, https://zenodo.org/record/7975005.
3 Philip E. Bourne et al., 'Perspective: Sustaining the big-data ecosystem', *Nature*, 4 November 2015, www.nature.com/articles/527S16a.
4 'Enabling responsible genomic data sharing for the benefit of human health', Global Biodata Coalition, 2023, https://www.ga4gh.org/.
5 'Framework for Responsible Sharing of Genomic and Health-Related Data', 3 September 2014, www.ga4gh.org/genomic-data-toolkit/regulatory-ethics-toolkit/framework-for-responsible-sharing-of-genomic-and-health-related-data/.
6 Teri A. Manolio et al., 'The International Hundred Thousand Plus Cohort Consortium: integrating large-scale cohorts to address global scientific challenges', *The Lancet*, November 2020, www.thelancet.com/journals/landig/article/PIIS2589-7500(20)30242-9/fulltext.
7 Natalie McGauran, 'Reporting bias in medical research – a narrative review', *Trials* 11, 37 (2010), https://doi.org/10.1186/1745-6215-11-37.
8 'ELIXIR Core Data Resources', *Elixir*, 2018, https://elixir-europe.org/platforms/data/core-data-resources.
9 'Global Biodata Coalition', *Global Biodata Coalition*, 2023, https://globalbiodata.org/.
10 *Elixir*, https://elixir-europe.org/.

Chapter 10: Fake Science

1 Peter J. Hotez, 'The antiscience movement is escalating, going global and killing thousands', *Scientific American*, 29 March 2021, www.scientificamerican.com/article/the-antiscience-movement-is-escalating-going-global-and-killing-thousands/ and Aviva Philipp-Muller et al., 'Why are people antiscience, and what can we do about it?', *PNAS*, 12 July 2022, www.pnas.org/doi/full/10.1073/pnas.2120755119.

2 Jeff Tollefson, 'How Trump damaged science – and why it could take decades to recover', *Nature*, 7 October 2020, www.nature.com/articles/d41586-020-02800-9.

3 'Health "benefits" of smoking?', *Tobacco in Australia: A Comprehensive Resource*, Cancer Council Victoria, January 2023, www.tobaccoinaustralia.org.au/chapter-3-health-effects/3-28-health-benefits-of-smoking-.

4 Various authors, 'Climate wars: the story of the hacked emails', *The Guardian*, 12 February, 5 July and 7 July 2010, www.theguardian.com/environment/series/climate-wars-hacked-emails.

5 Naomi Oreskes and Erik M. Conway, *Merchants of doubt: how a handful of scientists obscured the truth on issues from tobacco smoke to global warming*, Bloomsbury, New York, 2012.

6 'Complementary and alternative medicine market size, share & trends analysis report by intervention (botanicals, mind healing, body healing, external energy, sensory healing), by distribution method, by region, and segment forecasts, 2023–2030', *Grand View Research*, 2018–21, www.grandviewresearch.com/industry-analysis/complementary-alternative-medicine-market.

7 A. Steel, E. McIntyre, J. Harnett et al., 'Complementary medicine use in the Australian population: results of a nationally-representative cross-sectional survey', *Scientific Reports*, vol. 8, 17325 (2018), https://doi.org/10.1038/s41598-018-35508-y.

8 Department of Health and Aged Care Therapeutic Goods Administration, 'What are "therapeutic goods"?', Australian Government, 28 August 2020, www.tga.gov.au/about-tga/what-we-do/what-are-therapeutic-goods.

9 Warwick Anderson, 'Six challenges facing Australia's medical research sector', *The Conversation*, 15 April 2015, https://theconversation.com/six-challenges-facing-australias-medical-research-sector-40222.

10 See Richard Dawkins, *A devil's chaplain*, Orion Publishing Group, London, 2003, Chapter 4.

11 'Know the science of complementary health approaches', National Centre for Complementary and Integrative Health, October 2022, www.nccih.nih.gov/health/providers/digest/know-the-science-of-complementary-health-approaches; Department of Health and Aged Care, 'Herbal ingredients', Australian Government, no date, www.tga.gov.au/how-we-regulate/ingredients-and-scheduling-medicines-and-chemicals/herbal-ingredients; 'Complementary therapies – safety and legal issues', *Better Health*, no date, www.betterhealth.vic.gov.au/health/conditionsandtreatments/complementary-therapies-safety-and-legal-issues; 'Complementary and alternative medicine', *National Health Service*, 2023, www.nhs.uk/conditions/complementary-and-alternative-medicine/; Quackwatch, https://quackwatch.org/; 'Quackery, obscurity, religion, and more …',

Friends of Science in Medicine, 4 May 2023, www.scienceinmedicine.org.au/; *Science-Based Medicine*, https://sciencebasedmedicine.org/.

Chapter 11: Ideas for Change

1 A declaration as defined by the Oxford Dictionary: 'The action of stating, telling, setting forth, or announcing openly, explicitly or formally; positive statement or assertion; an assertion, announcement or proclamation in emphatic, solemn, or legal terms.'
2 Kelsey E. Bettridge, 'A scientist's oath', *Molecular Cell*, 2018, https://doi.org/10.1016/j.molcel.2018.08.026.
3 Australian Academy of Health and Medical Sciences, https://aahms.org/.
4 Engineers Australia, https://www.engineersaustralia.org.au/ and Accreditation Program for Australian Veterinarians, https://animalhealthaustralia.com.au/accreditation-program-for-australian-veterinarians/.
5 Matthew B. Ross et al., 'Women are less credited in science than men', op cit.
6 International Society for Scientometrics and Informetrics, www.issi-society.org/.
7 Joseph R. Dettori et al., 'Measuring academic success: the art and science of publication metrics', *Global Spine Journal*, vol. 9, no. 2, 2019, https://journals.sagepub.com/doi/10.1177/2192568219831003.
8 D.W. Aksnes, L. Langfeldt, and P. Wouters, 'Citations, citation indicators and research quality: an overview of basic concepts and theories', *SAGE Open*, vol. 9, no. 1, https://doi.org/10.1177/2158244019829575.
9 Liam Brierley et al., 'Tracking changes between preprint posting and journal publication during a pandemic', *PLOS Biology*, 1 February 2022, https://journals.plos.org/plosbiology/article?id=10.1371/journal.pbio.3001285.
10 Rens van de Schoot, 'Examined with expert elicitation, prior-data conflicts, Bayes factors for replication effects, and the Bayes Truth Serum', *Frontiers in Psychology*, vol. 12, November 2021, www.frontiersin.org/articles/10.3389/fpsyg.2021.621547/full.
11 See Ian Freckelton, *Scholarly Misconduct*, op. cit., p. 519.
12 Philip E. Bourne, 'Perspective: Sustaining the big-data ecosystem', *Nature*, vol. 527, 2015, www.nature.com/articles/527S16a.
13 Australian Institute of Health and Welfare, 'Burden of disease', Australian Government, December 2022, www.aihw.gov.au/reports-data/health-conditions-disability-deaths/burden-of-disease/overview and 'The Global Health Observatory', World Health Organization, 2023, www.who.int/data/gho.
14 National Health and Hospitals Reform Commission, 'A healthier future for all Australians – final report', Analysis and Policy Observatory, 27 July 2009, https://apo.org.au/node/17921.

15 Simon McKeon et al., 'Strategic review of health and medical research in Australia: final report', 5 April 2013, https://apo.org.au/node/33477.
16 Department of Health and Aged Care, 'Clinical Researchers initiative', Australian Government, 26 September 2022, https://www.health.gov.au/initiatives-and-programs/clinician-researchers-initiative.
17 'One voice for better health through research', Australian Health Research Alliance, https://ahra.org.au/ and Australian Living Evidence Consortium, https://livingevidence.org.au/.
18 NHMRC publishes extensive statistics on its own schemes at www.nhmrc.gov.au/funding/data-research.

Acknowledgements

My undying thanks to Paul Korner, Cliff Barger, John Ludbrook and Max Webster, who trained me in medical research science and its ethics.

Thanks to my research colleagues, especially Roger Evans and Kate Denton, and all the students and postdocs we had together over the years. Roger and Kate exemplify all that is best about medical researchers.

Thank you, too, to all my former colleagues at the Baker Medical Research Institute and in the Monash University Department of Physiology and School of Biomedical Sciences. What a joy it was to work with them all.

Thank you to the eight ministers during my time as chair of the NHMRC's Research Committee and as NHMRC CEO: Michael Wooldridge, Kay Paterson, Tony Abbott, Nicola Roxon, Mark Butler, Tanya Plibersek, Peter Dutton and Susan Ley. Though some were more interested in medical research than others, all treated me and the NHMRC with respect. There has been bipartisan support for all the increases in funding that have occurred over the last twenty-three years. Heartfelt thanks to Jane Halton, Secretary of the Commonwealth Department of Health, and Chief Medical Officers John Horvath, Jim Bishop and Chris Baggoley.

Thanks to the many outstanding dedicated public servants at the Office of the NHMRC, with special thanks to Dr Clive Morris, Tony Kingdon, Roy Goldie and John McCallum. Thanks to all the

wise people of the council and principal committees of the NHMRC, especially council chairs John Chalmers, Richard Smallwood, Richard Larkins, Michael Good and Annabelle Bennett, Medical Research Committee chairs Judith Whitworth and John Coghlan, and Research Committee chairs James Best and Kathy North.

Thank you to the Board of Trustees and staff of the International Human Frontier Science Program Organization and Presidents Hirokawa Nobutaka and Shigekazu Nagata for their wise counsel and support.

I have benefitted greatly from the wisdom of many colleagues who have been heads of other national medical research funding bodies, including Anne Kelso, Elias Zerhouni, Francis Collins, John Savill, Jeremy Farrar, Mark Walport, Alan Bernstein and Alain Baudet, Mats Ulfendahl, Dame Bridget Ogilvie, Dr Makato Suematsu and many others.

Thanks, beyond words, to my efficient and intelligent assistants: Jan Morrison at the Baker Institute and Monash; Marilena Caputo, Phil Callan, Matt Sammels and Lyn Callan at the NHMRC; and Jill Husser at the HFSPO in Strasbourg. Administrative professionals such as these rarely get the praise or renumeration they deserve.

Finally, thanks to the taxpayers and citizens of Australia, who have always supported a stronger commitment of public funds to medical research. The ultimate aim of this book to help make sure that this support continues, so that medical research can keep on improving our health.

About the Author

Warwick Peter Anderson AO is an emeritus professor at Monash University. He was previously Secretary General of the International Human Frontier Science Program Organization and CEO of NHMRC, Australia's major governmental funding body for health and research. Before that, he headed the School of Biomedical Sciences at Monash and was Deputy Director of the Baker Medical Research Institute, following fellowships at the University of Sydney and Harvard Medical School. His research focused on renal causes of hypertension. Anderson has served on numerous national and international scientific bodies, including the Prime Minister's Science Engineering and Innovation Council, and published more than 170 peer-reviewed articles. ORCID 0000-0002-7130-3530.