Informing the COVID-19 response: mathematicians' contributions to pandemic planning and response

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COVID-19 has changed how we live our lives, and will continue to do so for some time yet. Australia has been fortunate in many ways. We have clearly defined borders which are able to be managed effectively. We have a highly functional public health system. Despite the challenges in Victoria in mid-2020, ultimately we increased testing and contact tracing capacity enough to suppress transmission. We have, for the most part, seen coherent leadership from our state and Commonwealth political leaders.

The 'science'—from clinical and lab-based research to mathematical modelling—has been listened to and, again for the most part, acted upon.

But world class research is clearly not sufficient to manage the pandemic. The United Kingdom—the 'home', and I would argue 'intellectual powerhouse', of mathematical epidemiology—has suffered greatly. As has the United States and much of Europe.

In Australia, the field of mathematical epidemiology is still in development. It was only 2005 when Australia's National Health and Medical Research Council made its first major investment, funding a 'Capacity Building Grant' in infectious diseases modelling to support public health. I was fortunate to be appointed as a post-doctoral research fellow under the scheme, as were a number of other now well-known mathematical epidemiologists including Professor Jodie McVernon (Doherty Institute) and A/Prof James Wood (UNSW), who trained in infectious disease modelling and mathematical physics respectively. The grant was led by Professor Raina MacIntyre, a prominent epidemiologist and media figure in Australia's COVID-19 response.

From the outset, we were engaged with the Australian Government Department of Health's Office of Health Protection, the body responsible for preparedness and response to public health emergencies in Australia. At the time, the focus was on SARS and pandemic influenza.

As a mathematician, I have maintained an open dialogue with the Commonwealth for over 15 years. Through contractual research, we have developed stochastic models for border incursions, examined optimal distribution strategies for limited supplies of antivirals, estimated the volume of Personal Protection Equipment (PPE) required in a response and examined optimal strategies for vaccination. These analyses informed the development and multiple revisions of the Australian Health Management Plan for Pandemic Influenza (AHMPPI). In February 2020, with input from me and colleagues, the AHMPPI was rapidly adapted for COVID-19.

Throughout this 15-year period, we regularly visited Canberra to sit around the table with Health leadership, including four different Chief Medical Officers of Australia and their advisors. Both parties learnt a lot through that collaboration. As a mathematician I learnt how to communicate the purpose, limitations and relevance of our models. The government learnt to appreciate what models could and could not do. What policy decisions they could and could not inform. We gained a shared understanding that deeply quantitative work primarily delivered qualitative insights. And we learnt to trust each other.

Trust—not just in the science, but in the people conveying that science—is, in my view, the most fundamental requirement for the effective contribution of scientific knowledge to policy and response.

As a qualified and trusted advisor, I have contributed in two ways. With my team, we have undertaken mathematical analyses and delivered those results to government. But my responsibilities also include interpretation and evaluation of the (global and emerging) literature. Can Imperial College's COVID-19 modelling on 'lockdowns' be applied to Australia? Are optimal vaccination strategies developed for other countries applicable here? Are real-time analysis methods for a well-established outbreak—like those developed at the London School of Hygiene and Tropical Medicine—applicable to Australian case data?

I believe that Australia benefited from the deep engagement and trust developed between academics and the Commonwealth over 15 years. The trust lies not just with the advisors, such as me. The trust extends through to a cultivated broader trust in the scientific research performed by others and interpreted and evaluated by those advisors.

And with that, where does mathematical analysis make a difference?

Often, it is in what we (as mathematicians) may perceive as surprisingly simple points.

Epidemic theory describes how a pathogen spreads through the community. Scaling out the average duration of infectiousness, and ignoring some biological subtleties, the rate of change in prevalence I (the proportion of individuals who are **I**nfectious in the population) is described by a non-linear ordinary differential equation:

$$\frac{\mathrm{d}I}{\mathrm{d}t} = (R_0 S - 1)I,$$

where R_0 is the 'basic **R**eproduction number', the number of secondary cases arising from a single case in an otherwise fully susceptible population, and S is the proportion of the population that is **S**usceptible.

With $R_0 > 1$ and S sufficiently large (as it is at the beginning of an epidemic), prevalence (that is, I) grows exponentially and S decreases (as $dS/dt = -R_0 S I$).

Eventually, depletion of the susceptible pool (S) modified the dynamics. The resultant non-linear dynamics are what make infectious diseases both mathematically interesting, and conceptually challenging for public health policy makers to respond to.

In early 2020, my team delivered a report to government which explored the possible change in the total number of infections over the course of an epidemic due to various percentage reductions in transmissibility. For our purposes here, this is as simple as considering how the size of an epidemic depends upon R_0, although we did not report the analysis in this way to government.

A textbook analysis yields the 'final size equation', which relates R_0 to the size (as $t \to \infty$) of the epidemic, $Z_\infty = 1 - S(t \to \infty)$:

$$Z_\infty = 1 - e^{R_0 Z_\infty}$$

This is a non-linear relationship. By February 2020, we suspected the R_0 for COVID-19 was in the range $1.5 - -3$. At the upper end of this range, a 50% reduction (due to say, some level of physical distancing) has an important but fundamentally challenging effect – an epidemic with a modified reproduction number of $3/2 = 1.5$ still spreads explosively, resulting in a vast number of infections. But if COVID-19's reproduction number was at the lower end, a 50% reduction would prevent the virus from spreading entirely as $1.5/2 = 0.75 < 1$ and transmission cannot be sustained.

Such results are entirely unsurprising to us as mathematicians. We understand the importance of non-linearities and of features such as bifurcations. It is natural for us to view the transmission of an infectious disease as a dynamical system. But these important points are anything but intuitive and easily missed by decision makers.

With trust and open communication channels, important findings, as well as viewing the entire pandemic and our response to it as a dynamical system, proved influential in Australia's early response.

Simple analyses emphasised the value of mathematical reasoning. They highlighted the risks of 'intuitive linear thinking' but they also demonstrated how mathematical analysis can overcome that limitation. Models can be used to anticipate or reason on the (positive or negative) impacts of alternative response strategies.

Subsequent scenario analyses (with more 'realistic' and nuanced models calibrated to COVID-19 epidemiology) laid the groundwork for our initial response and for the monitoring and evaluation of the 'effective reproduction number' of COVID-19 throughout 2020 and into 2021. Collectively, these mathematical capabilities have contributed to the Australian government's risk-assessment process for managing the pandemic.

National policy guidance relies upon in-depth mathematical modelling and analyses, conducted both in-house, nationally and around the world. But while necessary, the existence of that research is not sufficient to have impact. To have impact, to be effective, also requires relationships, 'translators' and, above all, (mutual) trust.