

Pandemic impact

Evidence summary

This document summarises the evidence presented in:

Development of options on how to define the concept of pandemic impact for Australian purposes: Literature review, Associate Professor Jodie McVernon, Dr James McCaw Vaccine and Immunisation Research Group, Murdoch Childrens Research Institute and Melbourne School of Population Health, The University of Melbourne.

and

Development of options on how to define the concept of pandemic impact for Australian purposes: Report on simulation modelling, Associate Professor Jodie McVernon, Dr James McCaw Vaccine and Immunisation Research Group, Murdoch Childrens Research Institute and Melbourne School of Population Health, The University of Melbourne.

The full literature review and other supporting documents are available on the Australian Government Department of Health website at www.health.gov.au

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1 Evidence for assumptions regarding epidemic characteristics

1.1 Introduction

As described by Glass and colleagues and also supported by McCaw et al, two key components determine the impact of a novel pandemic strain on the population: transmissibility (the effectiveness of the spread of the disease) and clinical severity (how severely the disease affects individuals and causes serious adverse outcomes).¹

1.2 Influenza pandemic context

Until recently, pandemic response plans outlined responses based on a worst-case scenario modelled on the 1918 ‘Spanish flu’, including the AHMPPI 2008.² Recent review of the epidemiological features of 20th century influenza pandemics highlights the varied characteristics of these influenza epidemics.³ In particular, variability in clinical features relate to a number of epidemiological determinants, encompassing the roles of virus, host and environmental factors.^{4,5} For multiple-wave epidemics (three waves of Spanish flu and two waves of ‘Hong Kong flu’), transmissibility and pathogenicity of these viruses may have changed from one wave to the next.^{6,7} But it is likely that some of the changes are due to the socioeconomic and health status of the affected populations.⁶ Further to this, data from previous pandemics in 1957 and 1968 have demonstrated the potential for marked differences in the age-specific incidence of infection, with implications for the use of age-targeted strategies to reduce disease transmission.⁸ Transmissibility and clinical severity of the pandemic (H1N1) 2009 also appeared to be influenced by seasonal factors that reflected varying combinations of climatic effects,⁹ cross-protection from recent exposure to seasonal influenza strains,¹⁰ and routinely scheduled¹¹ or imposed extended interruptions to school-based mixing of children.¹²

1.3 Viral determinants of transmissibility

Transmissibility can be described using two measures that can be estimated from epidemiologic data: the initial reproduction number, R , which is the average number of secondary cases arising from each primary case; and the serial interval, which describes the time between onset of symptoms in a primary case and a secondary case.

During the pandemic (H1N1) 2009 outbreak in Mexico, early estimates of R were derived from epidemiological and genetic observations and reported to be anywhere in the range of 1.2–1.6 with a serial interval of 1.9 days (95% confidence interval [CI] 1.3, 2.7).¹³

These figures reflected substantial uncertainty, but suggested that the newly emerged strain was more transmissible than seasonal influenza.¹³ Later estimates based on data from other countries provided similar values for R . The World Health Organization estimates the serial interval for influenza at 2–4 days.¹⁴

Becker and others have estimated that R may be accurately inferred from daily incidence data with a cumulative confirmed case number of approximately 300, provided that the serial interval has been defined from at least 10 observations of documented person-to-person transmission,¹⁵ as the assumed serial interval will influence the calculated value of R .¹⁶

1.4 Pathogenicity of the novel strain

To rapidly and accurately assess pathogenicity of a novel influenza strain, we need to compare multiple data sources that describe the progression of strain-related illness in the community as well as information about presentations to a wide range of service providers. This mitigates the potential risk of numerator and denominator bias, both demonstrably problematic during the 2009 epidemic. One example was seen during the early weeks of the United States pandemic, where a community survey doorknocked in an area where a school closure was associated with an increase in presentations to emergency departments. The authors of this study observed a stable pattern of influenza-like illness (ILI) symptom reporting; more stable than had been anticipated from hospital figures. Such an approach demonstrates the potential for substantial bias in hospital and laboratory-based presentations associated with healthcare-seeking behaviours.¹⁷ Across the Atlantic, in Wales, presentations to general practitioners peaked at 100 per 100 000 general practice population during the 'first wave', falling to 65 per 100 000 during the second wave.¹⁸ In these same two periods, numbers of hospitalisations (deaths) rose markedly from 44 (1) to 379 (26), respectively. Higher consultation rates early in the pandemic were attributed to heightened community concern at a time of intensive media reporting and public health messages encouraging prompt medical attendance for ILI.¹⁸

During the 2009 pandemic in Australia, outbreak response teams, existing surveillance modalities and newly implemented systems and collaborations provided a picture of the evolving outbreak.

Australia-wide:

- Six Australian jurisdictions, in conjunction with New Zealand, established the FluCAN network to monitor the clinical course of hospitalised pandemic (H1N1) 2009 cases and so identify any change in disease clinical severity.¹⁹ The FluCAN system identified that, when compared with seasonal influenza-infected patients, hospital patients with pandemic (H1N1) 2009 were generally younger and healthier, more likely to be pregnant and more likely to need critical care support.²⁰
- Another Australian and New Zealand collaboration gathered data on intensive care unit utilisation during the course of the pandemic. It found that pandemic (H1N1) 2009 patients represented 2% of intensive care admissions during the influenza season but represented 8% of all bed stays, with 70% of these needing respiratory support.²¹
- The National Health Call Centre Network noted a bimodal peak in calls seeking information about ILI that were made by the general community.²²
- Nationally, surveillance undertaken by states and territories was reported by the NetEpi/National Notifiable Diseases Surveillance System²², showing a staggering of the epidemic course in jurisdictions across the country.²³
- National surveillance reports included information on workplace absenteeism collated from a national employer, showing absenteeism rates for 2009 were not notably different to 2007 or 2008.²²
- The Newcastle-based FluTracking system, a national weekly online survey of self-reported ILI, performed well in relation to other local surveillance processes during the 2009 pandemic and appeared less affected by presentation bias than health sector reporting.²⁴ It provided a useful denominator, including mild and non-medically attended ILI, against which to consider hospitalisation and death rates.²⁵

In Victoria:

- In the early days of Victoria's pandemic response, public health officers collected a set of detailed epidemiological data on 977 cases reported during the initial intensive case-finding 'Contain' pandemic response phase.²⁶ During this period, school-aged children comprised two-thirds of all infections, hospitalisations were rare (2%) and there were no deaths.²⁶ However, the workload associated with this degree of follow-up was intense, prompting Victoria to move to a 'Modified sustain' response prior to national downgrading of the 'Contain' phase.²⁶
- Sentinel general practice surveillance and a medical locum service reported on ILI presentations outside the hospital sector, showing that medical attendances were relatively in keeping with recent seasonal outbreaks,²⁶ in contrast to what was suggested by hospital or laboratory-based notifications. Approximately 70% of presenting attendees underwent diagnostic screening, meaning that it was possible to determine the proportion of ILI caused by pandemic (H1N1) 2009 during each epidemic phase; the influenza-attributable proportion peaked at around 60%.²⁶
- As Victoria's hospital surveillance mechanisms were unable to report real-time case load, three parameters were identified that could be reported daily for Victorian pandemic response planning: emergency department presentations compared with usual demand, hospitalisation for confirmed pandemic (H1N1) 2009 infection and transfer to an intensive care unit.²⁷ Having this information allowed ongoing assessment of overall hospital capacity at the moderate–severe end of the spectrum and informed requirements for surge capacity.²⁷

In New South Wales:

- A study of absenteeism among New South Wales school teachers confirmed higher-than-seasonal leave requirements that were not influenced by receipt of the 2009 seasonal trivalent influenza vaccine. These leave requirements were most likely a reflection of the higher illness attack rates among children (to whom teachers were occupationally exposed) and the relatively poor cross-protection from the seasonal vaccine.²⁸
- An existing recurrent population health survey was modified to assess the incidence of ILI in the community during the pandemic.²⁹ The survey estimated that one-quarter of Australians experienced ILI during the pandemic period, but most reported a mild, short-lived illness. The study identified youth, smoking and obesity as risk factors for symptomatic illness. Again, little protection was offered by the 2009 seasonal trivalent influenza vaccine.²⁹
- The Canning Division of General Practice in New South Wales implemented an automated data extraction system to gather data on trends in ILI presentations within their electronic records.³⁰ The New South Wales Department of Health compared these data with ILI presentations to emergency departments as well as emergency department records that had been captured through the Public Health Real-time Emergency Department Surveillance System.³⁰ This comparison revealed very similar proportions of syndromic presentations to general practitioners and emergency departments over time, each pre-empting presumptive diagnoses of ILI in the emergency department setting.³⁰
- Trends in all cause mortality in New South Wales over the 2009 influenza season showed an overall decline in death rates among all age groups compared with baseline, most notably among the elderly, reflecting the shift in age distribution of disease due to the pandemic strain compared with seasonal viruses.³¹

Overseas, during the 2009 pandemic, centralised online systems were established in the United Kingdom that were rapid and allowed efficient observation of the state of the pandemic in that country. In particular, during the pandemic, the Health Protection Agency implemented an online database to facilitate collection of information regarding the ‘first few hundred’ cases (FF100).³² Over a 6-week period, details of 392 confirmed infections were recorded, allowing near real-time assessment of clinical features, including the age distribution and clinical severity of cases. While most episodes were mild, several hospitalisations were captured, including some requiring critical care support.³²

The British National Pandemic Flu Service (NPFS), a telephone and internet-based service that determined eligibility for antiviral treatment on the basis of a clinical algorithm, captured ongoing information regarding ILI incidence.³³ A subset of users was requested to undergo confirmatory diagnostic testing, allowing real-time assessment of the H1N1 false-positive ILI rate.³³ These data were collated with a long-standing general practice surveillance system³⁴ to allow estimation of an overall attack rate as a denominator on which to base calculation of case fatality.³³

Using these real-time resources together with other data, the United Kingdom was able to evaluate clinical severity during the 2009 pandemic. These data showed increased clinical severity during the pandemic’s second wave, as a consequence of hospitalisations, intensive care unit admissions and deaths.³⁵

1.5 Age-specific incidence of disease

Globally, many of the initial reports of pandemic (H1N1) 2009 noted the involvement of children in the early transmission events, particularly in schools.^{16, 36}

In the United States, measurements of cross-reactive antibody across age distributions indicated that children and younger adults were most likely to be vulnerable to the novel strain.³⁷ A study using Australian Red Cross blood donors was consistent with these findings for people over the age of 16 (being the minimum age of donor consent) but could make no evaluation for younger people.³⁷ Further studies showed that pre-school and school-age children did not have cross-reactive antibody to the pandemic strain,^{38, 39, 40, 41} but that increased age corresponded to an increasing proportion who were seropositive, probably due to their own exposure to 1918-like viruses many decades earlier.⁴²

Although community-based surveillance and serosurvey data indicated higher overall attack rates in children, a children’s hospital in Sydney reported information that showed its overall hospitalisation and complication rates for pandemic (H1N1) 2009 were similar to those observed for seasonal influenza during peak years of activity over the preceding decade.⁴³ A similar correlation was observed at an Italian tertiary hospital between the clinical severity of H3N2 and pandemic (H1N1) 2009 influenza.⁴⁴

1.6 Population-specific risk factors

1.6.1 Indigenous status

Indigenous Australians were far more likely than the average Australian to experience serious health outcomes during the 2009 pandemic; with an increased relative risk (RR) of hospitalisation, intensive care unit admission and death of 6.6, 6.2 and 5.2, respectively.⁴⁵ This increased risk appeared largely linked to underlying health issues

within the Indigenous population, and did vary around the country; in Western Australia, a three-fold increased incidence of hospitalisation was observed among this group⁴⁶. In the Northern Territory, 54% of reported influenza cases involved individuals of Indigenous status (>3-fold higher notifications), who had a 12-fold higher age-adjusted risk of hospitalisation.⁴⁷ Similarly, in Canada, First Nations peoples were markedly overrepresented among hospital and intensive care unit admissions.⁴⁸

1.6.2 Chronic disease

Although hospital rates for pandemic (H1N1) 2009 were highest among children, a global review of risk factors for severe outcomes showed an increase with age, as well as associations with asthma, pregnancy and obesity. That review found obesity was associated with a notably increased risk of intensive care unit admission and death (RR 36.3).⁴⁹ Locally, a New South Wales study of ILI presentations in the community also identified obesity as a risk factor for mild disease.²⁹ However, a New South Wales hospital-based study found an increased requirement for ventilator support among obese inpatients, but did not observe an association between obesity and admission.⁵⁰

Underlying cardiorespiratory disease, immunosuppression and smoking were also observed as risk factors for pandemic (H1N1) 2009 admission in New South Wales hospitals.⁵⁰

1.6.3 Pregnancy

Seroprevalence studies showed that pregnant women were exposed to pandemic (H1N1) 2009 at the same rates as adults of similar ages, confirming pregnancy itself was the risk factor for a severe clinical outcome.⁵¹ This susceptibility was attributed to alterations in immunoregulation experienced during pregnancy.⁵²

Globally, the median relative risk for hospitalisation among pregnant women across 10 countries was estimated at 6.8.⁴⁹ For pregnant women in Australia during the 2009 pandemic, relative risks of hospitalisation, intensive care unit admission and death were 5.2, 6.5 and 1.4, respectively.⁴⁵ Case reports from Victoria showed half of the pregnant women who were hospitalised had no additional comorbidities.⁵³

1.6.4 Socioeconomic determinants

It is difficult to show whether observations of a correlation between socioeconomic status and areas of differential disease activity are due to chance, or represent a genuine causal relationship.⁵⁴ Residents of Western Sydney and those living in the northern and western suburbs of Greater Melbourne, both encompassing areas of relative disadvantage, experienced higher rates of emergency department presentations and paediatric admissions.^{55,26} A United States-based online survey conducted during the 2009 pandemic noted that there was a strong correlation between socioeconomically disadvantaged minorities' relative lack of access to sick leave entitlements in the workplace, their reliance on public transport and their residence in larger households.⁵⁶

1.7 Timing of pandemic relative to season and other respiratory pathogens

Although respiratory viruses are observed to be seasonal, seasons are influenced by temperature, humidity, changes in host susceptibility, human behaviour and co-circulating

viruses; the impacts of such factors are dependent on the timeframe and geographical region affected.⁵⁷

For example, during the 2009 influenza season, regional fluctuation in influenza activity in Queensland was associated more with variations in climate than with socioeconomic factors.⁹ The H1N1 pandemic in Europe showed differential timing and experiences across countries, but modelling suggests this related to the timing of the school calendar, as well as travel and transport links.⁵⁸ A further modelling study suggests school holidays helped stop the first wave of the British epidemic.¹¹

Within a given season, there is some interplay between the respiratory pathogens, which can have implications for the overall burden of disease. In the wake of the 2009 influenza pandemic, both France and Hong Kong observed a delay in the respiratory syncytial virus season.^{59,60} An improved understanding of the relationship between pathogens would be useful to be able to predict whether a pandemic influenza strain would be influenced by, or influence, other respiratory viruses.

2 Principles of proposed interventions and endgames

2.1 Front-line healthcare workload and capacity

With many Australian primary and tertiary healthcare providers already operating at high capacity, the increase in workload presented by a pandemic poses a challenge to our healthcare systems.

Globally, few studies evaluated the increased workload during the 2009 pandemic. A sample of 20% of United States hospitals identified that, when compared to previous influenza seasons, the pandemic presented a substantially greater burden of treatment, with an increase in admissions of young people and a six-fold increase in diagnostic testing.⁶¹ Redeployment of staff and facilities allowed essential services and an effective response to be maintained.^{62, 63}

Within Australia, emergency departments documented a marked increase in workload during the 2009 pandemic, and identified challenges for communications, management processes and reporting, as well as the need to ensure staff safety.⁶⁴ A separate survey reported that nearly half of all Australian emergency healthcare professionals surveyed reported a period of absence from work during the pandemic, but this absenteeism did not impact staffing levels; however, 43% of those with reported respiratory illness continued to work.⁶⁵ Even in this relatively 'mild' scenario, most Australian intensive care units ran overtime shifts and one-quarter broke normal nursing ratios.²¹ An analysis of Melbourne hospital-based healthcare workers with direct contact with influenza-infected patients and hospital employees with no patient contact found that patient contact was not a risk factor for infection; this finding was attributed to successful use of personal protective measures for patient contact.⁶⁶ Employment within intensive care settings, and living with children in the home environment were, however, risk factors for infection.

2.2 Laboratory capacity

As community transmission became established, laboratory services in Australia were overwhelmed with requests for testing, which took some time to abate. In New South Wales, during peak pandemic activity, 56% of test results were positive for pandemic (H1N1) 2009.⁶⁷ A study that examined 33 suspected H1N1 patients who were admitted to intensive care facilities in New South Wales found that 29 of these people demonstrated seroconversion to the pandemic strain, but only 18 had tested positive by PCR for the virus.⁶⁸ The authors of this study cautioned against withholding antiviral therapy from severe cases on the basis of a negative molecular test.⁶⁸

2.3 Communications strategies

Challenges exist in communicating messages to the public in a way that influences behaviour during a pandemic, to reduce both individual and population risk. There are different challenges faced by healthcare professionals, who may need a clearer awareness of how they will be protected while performing their roles, as well as more effective processes to support, for example, the use of personal protective equipment in the workplace.

South Australian population-based surveys conducted before and after the 2009 epidemic found that while people became better informed about influenza, their risk perception reduced with experience of pandemic (H1N1) 2009 and this was associated with a decline in willingness to be vaccinated against the pandemic strain.⁶⁹ Surveys of the public conducted through the pandemic period also showed a decline in trust of government communications associated with interventions,⁷⁰ which was mirrored in surveys of university students.⁷¹ By the conclusion of the public survey, only half the respondents indicated they would be vaccinated at the time of the H1N1 vaccine rollout.⁷² In spite of this, an analysis of the framing of pandemic media reporting in Australia concluded it reflected the pronouncement of national and international public health agencies.⁷³

A British study looked at motivators for compliance with government recommendations during a pandemic. It found that individuals' self-efficacy, which was represented by a balance between barriers to following the recommendations (e.g. lack of childcare) and perceived availability of resources to overcome these challenges, was a stronger motivator than perceived threats.⁷⁴

Communication strategies also need to address barriers to compliance that exist on a subpopulation level. After the 2009 pandemic, Indigenous leaders called for appropriate policies that would respect Indigenous communities but also address the challenges faced by remote Indigenous populations, who face overcrowded living conditions and are poorly served by infrastructure.⁷⁵ A survey of chronic obstructive pulmonary disease patients in Australia identified that individuals at risk of severe influenza complications need appropriate messages about preventative measures, as well as directing them to early medical presentation if they do become infected.⁷⁶

Healthcare professionals also need effective communication strategies to give them confidence to continue to practice during a pandemic event. A survey conducted before the 2009 H1N1 pandemic found that nearly one-third of general practitioners and practice nurses surveyed were not confident that their knowledge and skills would allow them to cope during a pandemic event. More than half of those surveyed indicated their ability to provide care would depend on their ability to protect themselves and their families from infection.⁷⁷ Other surveys showed that more experienced medical staff as well as staff with a higher workplace risk perception were more likely than others to effectively use personal protective equipment during the 2009 pandemic.⁷⁸

2.4 Adverse/late effects of interventions

Internationally, interventions have been shown to alter the course of the pandemic (H1N1) 2009 spread. In Hong Kong, sustained school closures reduced transmission, but this was followed by a resurgence of mostly paediatric cases once classes restarted.¹² In Taiwan, where 2009 disease and vaccination activity focused on youth, substantial H1N1 activity was seen among adults and the elderly in 2010 and was associated with higher morbidity and mortality than during the 'first wave' of the pandemic.⁷⁹

2.5 Specific interventions

Evidence for specific interventions, including border control and travel restrictions, quarantine, school/childcare and workplace closure, hygiene and barrier measures, antiviral distribution, vaccination, and stockpiling of antimicrobial agents and vaccines, are discussed in separate summary papers and will not be further described here.

3 Perspectives to consider in assessing impact

3.1 Estimated health impact of 2009 pandemic

The health impact of a pandemic refers to the burden that results from both morbidity and mortality.⁸⁰ A study examined acute respiratory illness and ILI reporting rates with historical data on seasonal influenza outbreaks in 28 European countries. Of these, disease rates did not exceed seasonal expectations in 19 countries, although paediatric consultations were higher than usual during the pandemic period.⁸¹

In the United States, pandemic impact was assessed by combining data on ILI presentations with laboratory-confirmed hospitalisations and deaths, correcting for underreporting, and providing an estimate of national case numbers and clinical severity indicators.⁸² Mortality estimates were greater than assumed during the epidemic, with eight-fold higher death rates among children and five times higher death rates among adults aged 18–64 years than observed in seasonal epidemics.⁸²

3.2 Estimated economic impact of 2009 pandemic

Economic assessment of pandemic effects as well as associated interventions often have too narrow a scope and focus solely on the healthcare sector, a recent review has suggested.⁸³ Such assessments should include the full economic impact of mitigative measures such as school closure.⁸³ Macroeconomic models have treated the impact of the pandemic as a ‘shock’ on gross domestic product, allowing wider effects of the pandemic and any mitigating interventions to be taken into account.^{84, 85}

Italian estimates of the 2009 disease burden of ILI exceeded most years of seasonal activity, with school-aged children experiencing the peak incidence.⁸⁶ Although estimated costs to the healthcare sector were extreme (ranging from €1.3–2.3 billion), this figure is similar to observations of costs for peak seasonal epidemics.

3.3 Predictive models for decision support

Models have been used to predict the spread of a pandemic under different conditions as well as to evaluate potential strategies for pandemic response. A model that looked at dynamic allocation strategies for stockpiles as well as public health response capability suggested that it is more cost-effective to base decisions on the total budget allocation to a given region, rather than proportionally rationing limited supplies.⁸⁷ Few studies have considered trade-offs of geographically targeted interventions at a local level. One example, a modelling evaluation of school closure, indicates that this type of measure can be justified in particular regions depending on the availability and capacity of local medical services.⁸⁸

The cost-effectiveness of any proposed pandemic mitigation strategy is directly linked to assumptions regarding clinical severity, which drives both healthcare and societal costs.⁸⁹ In a severe 1918-like scenario, interventions of very modest efficacy (approximately 20%) may be cost-effective if they can be implemented in a timely manner to maximise their potential benefits.⁸⁹

4 Pandemic impact modelling

4.1 Overview of pandemic impact model

A model, previously developed by McVernon and McCaw, allows study of plausible pandemic influenza scenarios within the Australian context. This model takes capacity constraints into consideration and also examines the mitigating effects of several proposed interventions.⁹⁰ This model was used to explore a range of possible future pandemic scenarios, and to predict the usefulness of various antiviral prophylaxis strategies, as well as the utility of school-based measures, in mitigating key characteristics of epidemics within different subpopulations.

The model assumes definitive containment of the pandemic that would result from rollout of a strain-specific vaccine starting in week 16 (with seroconversion resulting in protection assumed from week 18). Successful interventions would be those that reduced transmissibility in a way that the epidemic is constrained prior to vaccination and the outbreak is halted. The sensitivity of model outputs to other uncertain epidemic and intervention parameters was also explored by McVernon and McCaw, who reported on interventions that were highly likely, sometimes likely or never likely to reduce overall pandemic impact, to assist decision support.

This model assumes all individuals are fully susceptible at the outset of the epidemic, and vulnerable to acquiring infection upon contact with an infectious case. Once recovered, individuals are assumed to be fully resistant to infection. The model is both defined and constrained by parameters, for which fundamental values and their distributions are identified based on the literature.

4.2 Modelling parameters that define pandemic impact

Table 1 describes parameters that make up the pandemic impact model, as well as identifying the evidence supporting them.

Table 1 Evidence supporting modelling parameters that define pandemic impact

Parameter	Description	Mean	Min	Max	Distribution	References
R_0	Basic reproduction number	–	1.2	1.5 (or 2.0)	Uniform	Fraser et al. (2009) ¹³
$1/\omega$ (1/omega)	Exposed period	1.0 day	0.5 days	2.0 days	Right-skew	Fraser et al. (2009), ¹³ Tuite et al. (2010)
$1/\gamma$ (1/gamma)	Infectious period	1.5 days	1 days	2.5 days	Right-skew	Fraser et al. (2009), ¹³ Tuite et al. (2010)
$1/\delta$ (1/delta)	Contact period	2.5 days	2.0 days	3.0 days	Right-skew	Moss et al. (2011)
κ (kappa)	Average number of contacts	30	20	40	Central	Edmunds et al. (1997, 2006) ⁹¹
η (eta)	Severe cases	–	0.1%	10%	Log-flat	Moss et al. (2011) ⁹²
e_t	Relative infectiousness of treated cases (i.e. 0–20% efficacy)	0.9	0.8	1.0	Central	Halloran et al. (2007) ⁹³
e_s	Relative susceptibility of contacts on prophylaxis (i.e. 20–80% efficacy)	0.5	0.2	0.8	Central	Halloran et al. (2007) ⁹³
e_i	Relative infectiousness of breakthrough cases (i.e. 0–20% efficacy)	0.9	0.8	1.0	Central	Halloran et al. (2007) ⁹³
α_m (alpha _m)	Proportion of mild cases that present	0.5	0.25	0.75	Central	Moss et al. (2011) ⁹²
f_{GP}	Proportion of outpatient presentations at GPs	–	0.2	0.8	Uniform	Moss et al. (2011) ⁹²
MAX_P	Maximal number of prophylaxis doses delivered per day	–	10^3	10^5	Log-flat	McVernon and McCaw (2012) ⁹⁰
MAX_T	Maximal number of treatment doses delivered per day	–	10^3	10^5	Log-flat	McVernon and McCaw (2012) ⁹⁰

Parameter	Description	Mean	Min	Max	Distribution	References
D_c	Diagnostic capacity per day	–	10^3	10^5	Log-flat	Moss et al. (2011) ⁹²
σ (sigma)	Proportion of contacts feasibly traceable	–	0.1	0.5	Uniform	Edmunds et al. (1997, 2006) ⁹¹
μ (mu)	Compliance with policy	–	0.0	1.0	Uniform	McVernon and McCaw (2012) ⁹⁰
N	Population size (people)	20×10^6	–	–	Constant	Australia's population
O	Antiviral stockpile size (doses)	8×10^6	–	–	Constant	Australia's stockpile size
HCW_{stop}	End of healthcare worker pre-exposure prophylaxis	Week 18	–	–	Constant	Deployed until vaccine availability
HCW_{usage}	Antiviral usage for healthcare workers	300 000 doses per 10 days	–	–	Constant	McVernon & McCaw OHP report (2008)
V_{start}	Start of vaccine delivery program	Week 18	–	–	Constant	Australian 2009 experience
VDR	Vaccine delivery rate (doses per week)	750×10^3	–	–	Constant	Moss et al. (2011) ⁹²
e_v	Susceptibility due to successful vaccination (i.e. vaccine efficacy = 70%)	0.3	–	–	Constant	Basta et al. (2008)

GP = general practitioner

4.2.1 Pandemic model key outputs

Key measures of impact for the simulated epidemics are:

- the total (including asymptomatic) and clinical attack rates of the epidemic
- the timing of the peak of the epidemic
- the magnitude of the clinical peak of the epidemic.

4.3 Antiviral interventions

The pandemic model was used to consider how impact varies with transmissibility for an optimistic intervention. McVernon and McCaw found that for an intervention to change materially the outcome of an epidemic, R_0 must be less than 1.5; further, for $R_0 < 1.3$ an effectively delivered intervention can be expected to materially change the outcome of the epidemic.⁹⁰

Based on this finding, McVernon and McCaw used their model to explore two broad antiviral strategies.

4.3.1 Antiviral strategies that focus on case treatment alone

McVernon and McCaw's modelling of antiviral treatment-only strategies on attack rate showed that less controllable scenarios are characterised by higher transmissibility and a shorter serial interval. Further, lower antiviral efficacy reduces intervention success. In addition, the increased ability to effectively deliver an intervention is associated with reductions in the overall attack rate.⁹⁰

Importantly, while epidemics of greater clinical severity are understandably associated with a higher disease burden, they may be more amenable to successful intervention, as a greater proportion of cases is likely to present for medical attention.⁹⁰

McVernon and McCaw report that, as would be predicted, a more rapidly growing epidemic (with a higher R_0) peaks earlier than an epidemic caused by a poorly transmissible virus. This timing is negligibly influenced by a treatment-only intervention, with delays of around 10% being the greatest that can be achieved, in slow outbreaks.⁹⁰

The peak clinical burden is primarily determined by the intrinsic epidemic growth properties and innate pathogenicity of the virus. Intervention parameters in these treatment only scenarios were found to only exert small effects on peak incidence.⁹⁰

4.3.2 Antiviral strategies that include postexposure prophylaxis of contacts in addition to case treatment

McVernon and McCaw also used their model to consider the ability of additional targeted postexposure prophylaxis of contacts to modify epidemic impact, looking at coverage between 10% and 60% of identified contacts. This scenario assumed distribution of antivirals to healthcare workers and treatment of all severe cases as part of the response.

Modelling analysis found that increases in both the proportion of contacts traced and the maximal prophylaxis delivery capacity strongly correlated with a reduced final attack rate. Drug efficacy parameters were significantly associated with reduced final size.⁹⁰

In addition, the ability to delay the intervention (longer time to peak) correlated positively with greater achievable distribution of drug to contacts. Distribution was dependent on index case visibility and treatment compliance, but also the proportion of contacts reached within delivery constraints. McVernon and McCaw noted again that more rapidly growing epidemics are more difficult to delay, and that drug effectiveness to limit infection spread is influenced by efficacy of treatment in reducing infectiousness and efficacy of prophylaxis in reducing susceptibility.⁹⁰

McVernon and McCaw's modelling analysis found that a combined intervention (treatment of cases and post-exposure prophylaxis of a limited number of contacts) may reduce the clinical epidemic peak for high clinical severity and low transmissibility parameter combinations across a reasonably broad range. Further to this, they found that epidemic growth properties and innate pathogenicity were the key determinants of peak disease burden, and that intervention parameters were weakly but significantly associated with lower clinical burden.⁹⁰

4.4 School-based measures

It is important to consider that, as noted by Glass and colleagues, community acceptability of highly disruptive interventions such as school closure may depend on the clinical severity of the pandemic.¹

The pandemic model was used to examine how an optimistic intervention varies in impact over a wide range of transmissibility assumptions. This impact was further examined by McVernon and McCaw under different scenarios: one where age-specific attack rates were flat across the age spectrum (similar to the 1968 experience, referred to as homogeneous mixing), and one where the paediatric attack rate is heightened (similar to the 1957 and 2009 experience, referred to as enhanced child mixing). It was assumed for the purpose of this analysis that school-based measures were implemented from between 0 and 4 weeks of identification of sustained community transmission, were highly effective (reducing child-to-child mixing by 50–100%) and were kept in place for between 1 and 12 weeks.⁹⁰

4.4.1 School-based measures with equivalent adult-to-child attack rates

Under this scenario, the intervention initiation timing and maintenance periods were varied, as was the reduction in child-to-child mixing. Where adult-to-child mixing and age-specific attack rates were uniform, school-based measures did not influence either the total or clinical attack rates. While the growth of the epidemic related most strongly to the overall attack rate, there is some chance that school-based interventions of longer duration and higher efficacy that are implemented during the exponential growth phase may result in some constraint. Overall, transmissibility and clinical severity were the best predictors of clinical attack rate, regardless of the school-based measures imposed.⁹⁰ However, McVernon and McCaw note that reductions in growth rate caused by the measures in some simulations were not represented in the median values presented in these data.⁹⁰

4.4.2 School-based measures with heightened paediatric attack rate

Under this scenario, McVernon and McCaw's model was used to analyse the impact of school-based measures on a pandemic where the paediatric attack rates are higher than those observed for adults. This scenario corresponds to the observed pandemics of 1957 and 2009.

Substantial delays in epidemic growth were seen in this scenario across all sets of clinical severity and transmissibility parameters. This finding reflects the effective reduction in R achieved by interrupting child-to-child mixing. The delay in time of peak may be maintained as R_0 increases, and is independent of case visibility. The duration of the measures remained a critical determinant of their success, along with intervention efficacy and timing.⁹⁰ In contrast to the case-targeted antiviral measures, the success of the intervention was not contingent on the proportion presenting for medical care (ie visibility), given the pre-emptive 'whole population' approach employed.

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