Truth, double truth and statistics

Robert Booy\textsuperscript{A,C} and Dominic E. Dwyer\textsuperscript{B}
\textsuperscript{A}National Centre for Immunisation Research and Surveillance of Vaccine Preventable Diseases, The Children’s Hospital at Westmead
\textsuperscript{B}Institute of Clinical Pathology and Medical Research, Westmead Hospital
\textsuperscript{C}Corresponding author. Email: RobertB2@chw.edu.au

After every influenza pandemic (including the Russian of the 1890s and the Spanish influenza of 1918–1919), learned commentaries have reflected on the clinical presentation of the disease, noting that the great majority of cases were very mild, so mild that they corresponded much more to the symptoms of an upper respiratory tract infection than to an influenza-like illness with fever and prostration.\textsuperscript{1} This seems to fly in the face of modern pronouncements such as that by Glass in 2004 that pandemic flu was more than a ‘perceived threat’ but rather a ‘real killer’.\textsuperscript{2}

The 2009 H1N1 pandemic appeared to start suddenly in Mexico; scores of deaths of healthy younger adults were reported over several weeks. The world’s attention, however, turned to North America when two related cases due to the new ‘swine flu’ virus (as it was initially known) were reported from California. Within 10 days, hundreds of confirmed cases were reported from the United States of America (USA), with only one corresponding death. It became apparent very quickly that the Mexican epidemic must have been in progress for at least 2 months to produce enough cases so that so many severe sequelae could have occurred. Herein lies the double truth: that most cases of pandemic (H1N1) 2009 influenza worldwide have been mild but some have been severe. Data from the Australian and New Zealand intensive care research project demonstrated far higher rates of adult admission for viral pneumonitis requiring ventilation, and in some cases, extra-corporeal membrane oxygenation, than previously;\textsuperscript{3,4} paediatric admission rates were double those for the worst previous influenza season of this decade which occurred in 2007. Serological testing of the community will help determine the final attack rate of the first wave of this pandemic (H1N1) 2009 influenza.\textsuperscript{5}

The response from public health in New South Wales (NSW) – and in Australia – was prompt and generally effective. On 28 April 2009 we moved from the ALERT phase to the DELAY phase, which involved preventing or delaying entry of the virus into Australia. On 22 May the phase level was raised to CONTAIN, as it was clear there were local outbreaks. Measures taken included high quality laboratory testing of suspected cases, contact tracing, treatment with antivirals for proven and suspected cases, school closures, isolation and strong public health messages around respiratory etiquette, social distancing, use of masks and hand washing. The World Health Organization (WHO) declared on 11 June that the world had a pandemic on the basis of community spread in at least one other country in a different WHO region to where the epidemic began.\textsuperscript{6} In NSW the peak incidence of disease occurred during different weeks of June and July in different parts of NSW, and across Australia there was about a 7 week gap between the peaks in the different states and territories, demonstrating the value of reporting clinical and virological surveillance regionally. Mistakes may well have been made, but that is to be expected, and can be used to inform subsequent policy and practice. The initial response seemed to some to be intense and was based on pandemic planning for the worst case scenario of a virus causing a high case fatality rate. As the nature of the illness was expressed public health policy and practice evolved, and in June the PROTECT phase was implemented and focused on shielding the vulnerable and reducing community testing and school closures.

The media gave considerable attention to the unfolding situation. In the main they behaved as responsible ciphers, spreading the message regarding respiratory etiquette and attention to hygiene. As seen with any emerging virus, some of the popular media focused on the experience of some severe and exceptional cases and situations. Substantial attention was focused on a cruise ship that docked in Sydney with a potentially infected (and infectious) child onboard.

The 1918 Spanish pandemic did not reach Australia until January 1919, first reported in Melbourne on 9 January (presumably because naval quarantine was breached) and reaching NSW overland by 21 January. The Australian states had already agreed that once a case of influenza was diagnosed in a state all traffic with that state would be suspended until the infection had clearly already spread. As a consequence, the Premiers of Western Australia and Tasmania were marooned for a time in Melbourne during the outbreak.\textsuperscript{7} In those days there were no antibiotics, antivirals, intensive care units of any substance or influenza vaccines, and the public health approaches were less sophisticated. Even so, analysis of actions taken in US cities during the Spanish pandemic demonstrated that co-ordinated, non-pharmacological interventions can substantially reduce the incidence of the disease and associated mortality.\textsuperscript{8}
Given the current era of mass travel, and knowledge about how influenza is transmitted, traditional border control measures (such as airport screening, on-site sample collection and laboratory testing) are not a beneficial use of scarce resources. It is likely that other measures taken to delay the spread of pandemic (H1N1) 2009 influenza forecasted the peak in the number of cases and limited the overall size of the epidemic in NSW. Research to confirm this is keenly awaited.

Vaccination of adults and of children aged older than 9 years, concentrating on vulnerable populations, began at the end of September using multi-dose vials. Multi-dose vials have been widely used for influenza and other vaccination programs in the USA and elsewhere.9,10 The ensuing debate regarding the use of multi-dose vials centred on concerns that medical accidents of the past, such as in Bundaberg 80 years ago, might be repeated.11 Doctors and nurses responsible for vaccination programs are now far better trained and use protocols to minimise the risks associated with multi-dose vials. To further reduce the risk each multi-dose vial is restricted for use on one day only. Over 5 million doses were distributed by early December, although the actual number of doses administered is certainly less due to inevitable wastage associated with multi-dose vials.

In retrospect, given that the vaccine was not, and almost certainly could not, be available until the first wave of the pandemic was over, and also that there was likely to be some months before the second wave of cases occurred, there was perhaps more time than anticipated to both prepare the medical and general community. There may have therefore been time to produce large quantities of vaccine in single, as well as multi-dose vials. The time and cost required to produce the vaccine in the single-dose presentation may have been offset by improved professional support, public confidence and vaccine uptake. Now that a safe and effective vaccine is widely available, the herd immunity required to prevent the next wave of infections can be effective only if vaccines become vaccinations.

Acknowledgments
Thank you to Dr G Khandaker for helpful discussions.

References