



## Potential impact of pandemic influenza interventions in New Zealand: a brief modelling study

**Background and aim**—Some simple modelling approaches have been used for examining the potential impact of pandemic influenza in New Zealand,<sup>1,2</sup> along with possible control interventions.<sup>3</sup> Since this work was undertaken, many studies have been published internationally, including detailed historical analyses of the 1918 pandemic. One of the latter suggested that social distancing interventions was of considerable value during this pandemic (i.e. a study of 43 US cities<sup>4</sup>). We aimed to utilise a more sophisticated modelling approach to examine what might be the benefit of plausible social distancing interventions as well as use of antivirals for treatment of severe cases.

**Methods**—In our analysis, the basic model components and parameters were based on the published deterministic model *InfluSim*<sup>5</sup> (version 2.1<sup>6</sup>). This model and freely available software has been used for published modelling studies (e.g. on non-pharmaceutical interventions<sup>7</sup> and studying antivirals and resistance to them<sup>8,9</sup>). The programming of *InfluSim* has also been repeatedly improved following feedback from other programmers (as the code for *InfluSim* is also open source) and as a result of its use by health sector agencies for pandemic planning.

The scenarios we examined included: partial isolation of cases only, social distancing, antiviral treatment of severe cases, and all of these three interventions together (see Appendix for further details). The population age structure used was that for the New Zealand population in December 2008.<sup>10</sup> However, due to persisting epidemiological uncertainty around key parameters, we selected values within plausible ranges for these (see Appendix), using Latin hypercube sampling. We then ran 2000 simulations of each scenario using a simulation application that was programmed in Java.

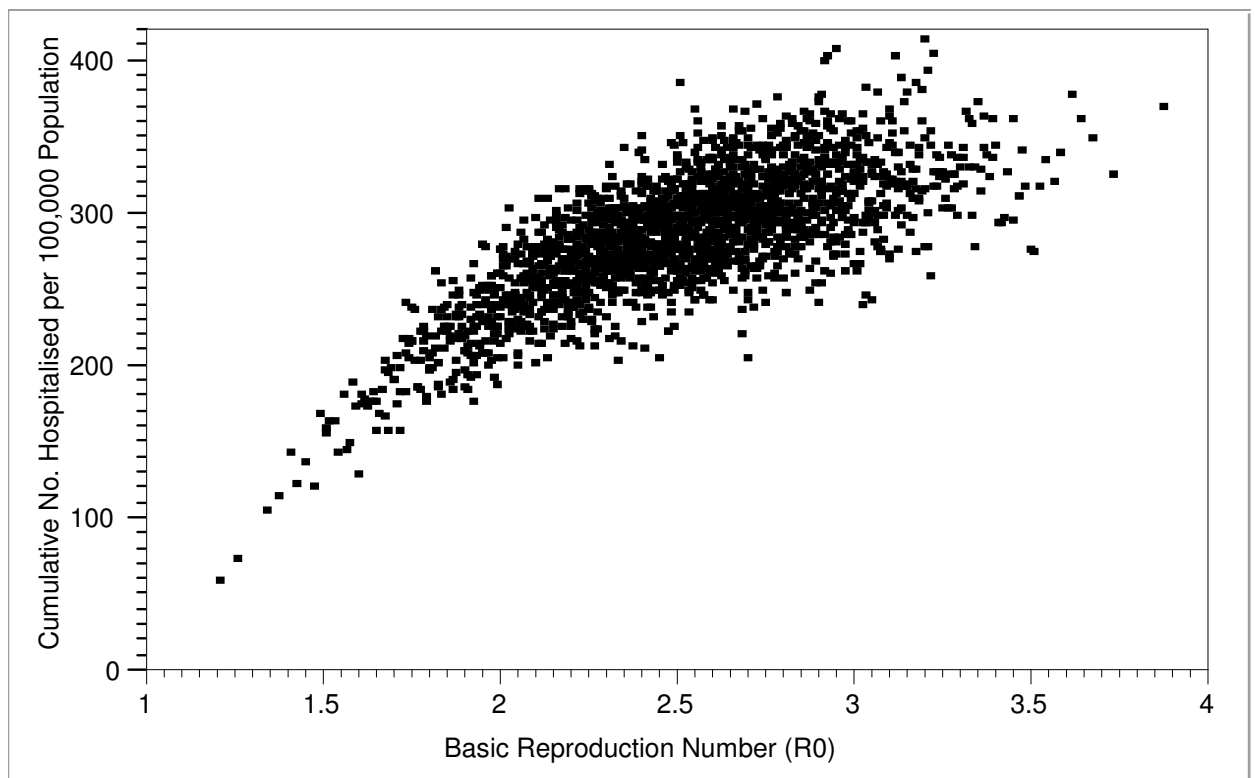
**Results and discussion**—The results in Figure 1 show the diverse range of possible outcomes in terms of cumulative number of hospitalisations per 100,000 population for different basic reproduction numbers. Figure 2 indicates that social distancing (by 5 to 25%) is generally not as effective as antiviral treatment of severe cases for reducing the hospitalisation burden. Combining all three interventions produces the maximal average benefit in terms of lower hospitalisation burdens. Figure 3 shows how the more effective intervention scenarios also reduce the peak size of the epidemic curve and delay this peak (i.e. relative to case isolation alone). Therefore the use of the multiple interventions would even out the burden on hospital beds over time and reduce the risk of this sector being overwhelmed for long periods.

Although this model uses over 1300 differential equations, this deterministic model still involves many simplifying assumptions. Similarly the parameter ranges sampled from are still subject to considerable uncertainty. Indeed, it is quite possible that social distancing levels could be even more substantial (e.g. >50% over the course of the pandemic). This could occur if pre-schools and schools were closed early and for long periods, if mass gatherings were cancelled, if more people used alternatives to public transport (e.g. walking or cycling), and if the population made greater use of

the Internet in their lives (e.g. for working from home, home schooling, shopping and leisure pursuits). Furthermore, the benefit of antiviral treatment could be substantially reduced by the emergence of viral resistance and so its value relative to social distancing is far from certain. Finally, these results could be expanded upon by undertaking more sophisticated parameter sensitivity studies (as conducted for other health sector agencies e.g. Switzerland) and considering other health outcomes (e.g. medical consultations and deaths).

In conclusion, New Zealand health authorities could consider undertaking more modelling work to better explore a wider range of possible public health and health care setting interventions (including use of pre-pandemic vaccine and the possible emergence of antiviral resistance by a new pandemic strain). In the meantime these authorities should continue to plan for the use of social distancing interventions and antivirals for treatment in the next revision of the national influenza pandemic plan.

**Figure 1. Cumulative number of hospitalisations per 100,000 population for different basic reproduction numbers in the New Zealand setting (case isolation only scenario, n=2000 simulations)\***

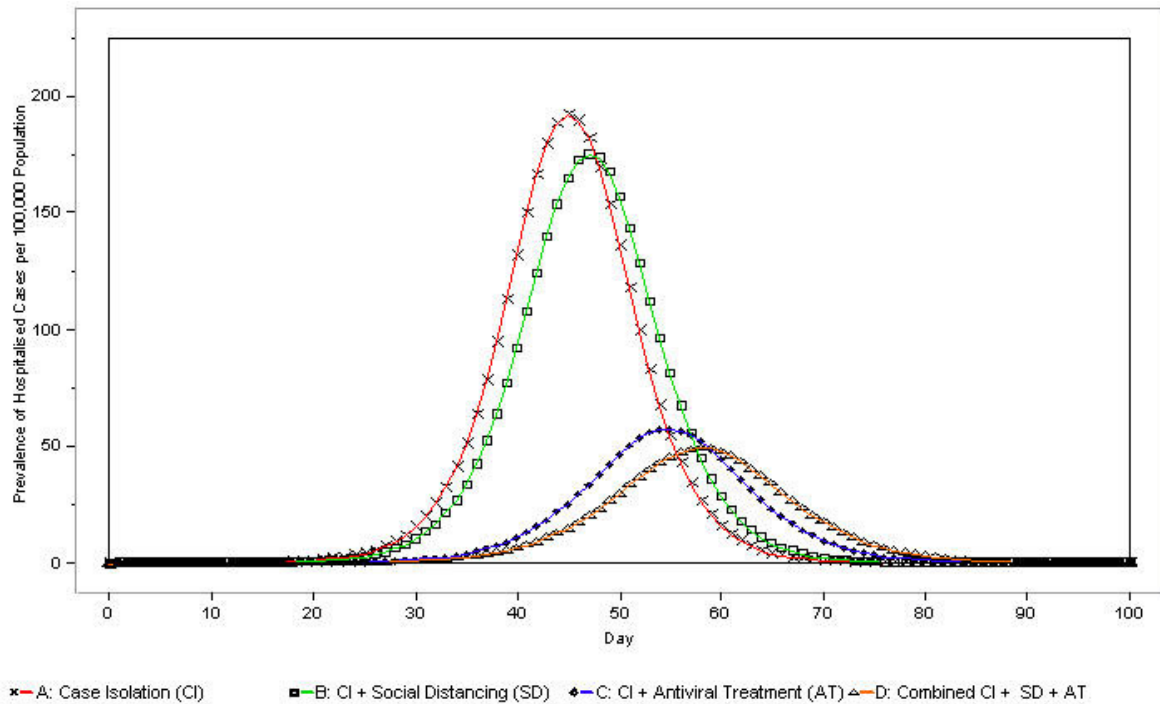


\* Note: We sampled  $R_0$  and the other parameters from a normal distribution so that 99% of sampled values are within the ranges specified in the Appendix. However, 1% of the samples lie outside these intervals and hence 1% of values are where  $R_0$  is  $< 1.5$  or  $> 3.5$ .

**Figure 2. Cumulative number of hospitalisations per 100,000 population for various scenarios in the New Zealand setting (boxes show inter-quartile range and whiskers the 95% range for 2000 simulations for each scenario)**



**Figure 3. Daily prevalence of hospitalised cases for the various scenarios in the New Zealand setting (for each individual scenario but otherwise using default settings in *InfluSim* and  $R_0=2.5$ )**



## Appendix. Key parameter ranges used in the modelling\*

| Key parameter   | Range of values used              |
|---|-----------------------------------|
| <i>Natural history of the disease</i>   |                                   |
| Basic reproduction number ( $R_0$ ) with this range reflecting most values reported for the second (most severe) wave of the 1918 influenza pandemic (and is consistent with a New Zealand estimate for this pandemic <sup>11</sup> ).  | 1.5 – 3.5                         |
| Contagiousness during the first half of the infectious period. The range used is consistent with the pattern for viral shedding reported for seasonal influenza. <sup>12</sup>  | 75% – 95%                         |
| Proportion asymptomatic (based on 95% confidence interval of the values for seasonal influenza reported in a meta-analysis <sup>12</sup> ).   | 26% – 42%                         |
| <i>Disease control interventions</i>  |                                   |
| <b>Partial isolation of cases:</b> moderately sick cases (10% isolation), severe cases at home (20% isolation), and severe cases in hospital (30% isolation). These values for partial isolation were applied in all of the scenarios used in this analysis.  | Set values only (see to the left) |
| <b>Social distancing</b> reduction i.e. the general reduction in contacts throughout the population (best guess estimate of plausible range when averaged over the full course of the pandemic).  | 5% – 25%                          |
| Reduction of contagiousness as a result of <b>antiviral treatment</b> where treatment occurs one day since symptoms develop on average and assuming no antiviral resistance. In <i>InfluSim</i> it is assumed that moderately severe cases will not be treated but that all severe cases will be treated at home or hospital with antivirals (and these severe cases comprise 50% of all symptomatic cases). The range used is an arbitrary one around the default value of 80% used in <i>InfluSim</i> . The size of the antiviral stockpile was not considered to be a limiting factor (as in all simulations the current New Zealand stockpile was sufficient for treatment only usage). | 70% – 90%                         |

\* With 99% of the Latin hypercube sampling occurring within the ranges specified and assuming a normal distribution for values within the range. All other parameter settings are as per the default settings used in *InfluSim* version 2.1.<sup>6</sup>

**Competing interests:** Dr Schwehm has had financial contracts with health agencies in various countries concerning extensions of the software *InfluSim*. Dr Wilson has had contracts with the Ministry of Health on pandemic influenza modelling. However, there was no funding for this work.

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## References:

1. Wilson N, Mansoor O, Baker M. Estimating the impact of the next influenza pandemic on population health and health sector capacity in New Zealand. *N Z Med J*. 2005;118:U1346. <http://www.nzma.org.nz/journal/118-1211/1346>
2. Wilson N, Baker M, Crampton P, et al. The potential impact of the next influenza pandemic on a national primary care medical workforce. *Hum Resour Health*. 2005;3:7.
3. Roberts MG, Baker M, Jennings LC, et al. A model for the spread and control of pandemic influenza in an isolated geographical region. *J R Soc Interface*. 2007;4:325-30.
4. Markel H, Lipman H, Navarro J, et al. Nonpharmaceutical interventions implemented by US cities during the 1918-1919 influenza pandemic. *JAMA*. 2007;298:644-54.
5. Eichner M, Schwehm M, Duerr H, et al. The influenza pandemic preparedness planning tool Influsim. *BMC Infect Dis*. 2007;7:17.
6. Department of Medical Biometry. Pandemic influenza planning tool Influsim (version 2.1). Tübingen: University of Tübingen, 2008. [http://www.uni-tuebingen.de/modeling/Mod\\_Pub\\_Software\\_InfluSim\\_en.html](http://www.uni-tuebingen.de/modeling/Mod_Pub_Software_InfluSim_en.html)
7. Duerr HP, Brockmann SO, Piechotowski I, et al. Influenza pandemic intervention planning using Influsim: pharmaceutical and non-pharmaceutical interventions. *BMC Infect Dis*. 2007;7:76.
8. Brockmann SO, Schwehm M, Duerr HP, et al. Modeling the effects of drug resistant influenza virus in a pandemic. *Virol J*. 2008;5:133.
9. Eichner M, Schwehm M, Duerr HP, et al. Antiviral prophylaxis during pandemic influenza may increase drug resistance. *BMC Infect Dis*. 2009;9:4.
10. Statistics New Zealand. National population estimates tables. Wellington: Statistics New Zealand, 2009. <http://www.stats.govt.nz/tables/nat-pop-est-tables.htm>
11. Sertsov G, Wilson N, Baker M, et al. Key transmission parameters of an institutional outbreak during the 1918 influenza pandemic estimated by mathematical modelling. *Theor Biol Med Model*. 2006;3:38.
12. Carrat F, Vergu E, Ferguson NM, et al. Time lines of infection and disease in human influenza: A review of volunteer challenge studies. *Am J Epidemiol*. 2008;167:775–85.