Epidemiology and Infection

Pandemic Risk Assessment Model (PRAM): A Mathematical Modeling Approach to Pandemic Influenza Planning

D. C. Dover, E. M. Kirwin, N. Hernandez Ceron, K. A. Nelson

**Supplementary Material**

|  |  |  |  |
| --- | --- | --- | --- |
| **Parameter** | **Transitions Affected** | **Form / Value [CI or range]** | **Source** |
| Severity  | (5) 🡪 (6)(5) 🡪 (7)(8) 🡪 (10)(9) 🡪 (10)(10) 🡪 (11)(10) 🡪 (12) | Default 1.0Severity acts as an odds ratio adjusting the medically attended, hospitalization and death transition parameters. The value is set to 1.0 for H1N1 as the reference pandemic. | Default, User selected |
| Transmissibility  | (1) 🡪 (5)(2) 🡪 (5) (3) 🡪 (5)(4) 🡪 (5) | Default 2.5%representing the probability of becoming Exposed given contact with an Infectious individual.Transmissibility affects the Force of Infection. based on 14 day follow-up and a 30.2% attack rate reported. | [57], User selected |
| Vaccination Rate  | (1) 🡪 (3) | Vaccination Capacity of 60,000 per day, if vaccine remains at time *t*. 0, otherwiseValue was obtained as the daily average number of doses delivered from the week with the most doses delivered during H1N1 in Alberta. | Alberta Health |
| Vaccination Policy  | (1) 🡪 (3) | 1, if vaccination age group *a* and risk group *r* at time *t*0, otherwise | User selected |
| Vaccine Effectiveness*VE* | (3) 🡪 (4)(3) 🡪 (12) | 0.70 [range 0.60-0.93]which represents a 70% vaccine effectiveness. This level was assumed to reflect other Canadian models, and is also supported by also a meta-analysis of monovalent pandemic H1N1 vaccine effectiveness. | [18] [27][58], User selected |
| Force of Infection  | (1) 🡪 (5)(2) 🡪 (5) (3) 🡪 (5)(4) 🡪 (5) |  where *agepop[a]* is the population in age group *a* |  |
| Contact Matrix*contact[a,a’]* | (1) 🡪 (5)(2) 🡪 (5)(3) 🡪 (5)(4) 🡪 (5) | This contact matrix is derived as the symmetrical version of the Finnish contact matrix in [12] adjusted to the listed age groups. Contact matrices are available for several other countries, three of which have demographic structures similar to Canada (Finland, Belgium and Great Britain) [12] but of the countries available, the Finnish population density was by most similar to Canada’s , and was therefore selected as the contact matrix used in PRAM. | [49] |
| Isolation / Contact Reduction*b* | (1) 🡪 (5)(2) 🡪 (5) (3) 🡪 (5)(4) 🡪 (5) | Default 1.0Values between 0 and 1 represent the proportion of contacts maintained during isolation | Default |
| Proportion Exposed Medically Attended  | (5) 🡪 (6)(5) 🡪 (7) |   | -- |
| Seeking Medical Attention  | (5) 🡪 (6)(5) 🡪 (7) | 0.0321 Value fitted simultaneously with the proportion hospitalized and proportion dying, to model the total Medically Attended during H1N1 in Alberta. |  |
| Odds Ratio for High Risk persons seeking Medical Attention  | (5) 🡪 (6)(5) 🡪 (7) | 8.38 [CI 3.69-1900]Which results in high risk individuals being 8.38 times more likely than low risk individuals to seek medical attention.Value reported in Sikora as the hazard ratio for those with underlying medical conditions to show symptoms in secondary cases within households.  | [51] |
| Antiviral Release Policy  | (6) 🡪 (8)(6) 🡪 (9) | 1, if *t* ≥ release time for risk group *r*0, otherwise | User selected |
| Hospitalization Probability  | (8) 🡪 (10)(8) 🡪 (12)(9) 🡪 (10)(9) 🡪 (12) |  |  |
| Requiring Hospitalization | (8) 🡪 (10)(8) 🡪 (12)(9) 🡪 (10)(9) 🡪 (12) | 0.0026Value fitted simultaneously with the proportion medically attended and proportion dying, to model the total Medically Attended during H1N1 in Alberta. | Second variable calibrated to total hospitalized during H1N1 |
| Odds Ratio for High Risk persons requiring Hospitalization | (8) 🡪 (10)(8) 🡪 (12)(9) 🡪 (10)(9) 🡪 (12) | 6.83 [CI 5.63, 8.33]Which results in high risk individuals being 6.83 times more likely than low risk individuals to require hospitalization.Value was the odds ratio obtained from a population based logistic regression analysis of hospitalization as the outcome on the cohort of medically attended individuals not receiving antivirals, controlling for risk group. 95,236 observations with 599 hospitalizations. Internal Alberta Health analysis linking hospitalization (the outcome) to hospital and emergency department data (comorbidities). | Alberta Health |
| Antiviral Effectiveness*AVE* | (8) 🡪 (10)(8) 🡪 (12) | 0.60 [range 0.50-0.70]Which represents a 60% antiviral effectiveness. This is an assumed, composite measure of both the antiviral efficacy, likelihood of prescription collection and adherence. Conceptually, this figure is the clinical efficacy of the antiviral, adjusted for deficits in uptake and adherence in the eligible group. Users should note that the baseline value is sourced from another modeling study. | [4], User Selected |
| Death Probability  | (10) 🡪 (11)(10) 🡪 (12) |  | -- |
| Death  | (10) 🡪 (11)(10) 🡪 (12) | 0.0260Value fitted simultaneously with the proportion medically attended and proportion hospitalized, to model the total Medically Attended during H1N1 in Alberta. | Third variable calibrated to total deaths during H1N1 |
| Odds Ratio for High Risk persons Dying |  | 2.30 [CI 0.87 – 6.05]Which results in high risk individuals being 2.30 times more likely than low risk individuals to die.Value was the odds ratio obtained from a logistic regression analysis of death as the outcome on the cohort of hospitalized cases, controlling for risk group. There were 18 deaths in 599 hospitalizations.  | Alberta Health |
| Mean time to antibody response, inverse of   | (3) 🡪 (12) | 1/10resulting in a mean time to antibody response following vaccination of 10 days | [18] , citing model fit from [27] |
| Latent Period, inverse of   | (5) 🡪 (6)(5) 🡪 (7) | 1 / 2.1resulting in a mean latent period of 2.1 days | [30], which calibrated between [59] and [60] |
| Mean time to treatment, inverse of  | (6) 🡪 (8)(6) 🡪 (9) | 1/2treatment guidelines recommend start of antivirals within 48 hours when used | Alberta Health |
| Treatment Duration, inverse of  | (8) 🡪 (10)(8) 🡪 (12)(9) 🡪 (10)(9) 🡪 (12) | 1/3.9Figures from three studies on viral shedding in quarantined populations during pdm(h1n1)2009 were used in a meta-analysis to determine the total duration infectious for those medically attended. The mean value from the meta-analysis was 5.87 (CI 5.68-6.06).. Because two days were spent infectious prior to treatment, only 3.9 infectious days remained for this transition. | [64-66] |
| Length of Stay, inverse of  | (10) 🡪 (11)(10) 🡪 (12) | 1/3.4Figures from two studies on viral shedding in quarantined populations during pdm(h1n1)2009 were used in a meta-analysis to determine the total duration infectious for those medically attended. The mean value from the meta-analysis was 9.27 (CI 8.85 -9.68). Because two days were spent infectious prior to treatment, and 3.9 days were spent in the treatment compartment, only 3.4 infectious days remained for this transition. | [67-70] |
| Mean time to Recovery, inverse of   | (7) 🡪 (12) | 1/4.8Figures from two community studies for viral shedding of pdm(h1n1)2009 and duration of illness were used in a meta-analysis to determine the value for the mean time to recovery. While the mean value from the viral shedding data [52-63] is 6.38 (CI 5.72-7.04), both studies state that viable virus ceased to be detected after 5 days. This is consistent with the highly cited Carrat [61] study, which gives a value of 4.8. The 4.8 value is used for our study. | [61] |

The time transitions, effectiveness, severity and transmissibility parameters are all given to 2 decimal places and taken from the literature, with the exceptions of severity and transmissibility (user selected), and the odds ratios (calculated internally). However, the fitted transition probabilities for seeking medical attention, being hospitalized and dying are smaller in magnitude and extremely influential on model, so they are given with more accuracy in the table above.

**A note on treatment durations.**

Three key pathways for the compartments contribute to the force of infection.

1. No medical treatment, recover.

(5) 🡪 (7) 🡪 (12)

1. Medically attended, may get AV, recover.

(5) 🡪 (6) 🡪 (8/9) 🡪 (12)

Medically attended, may get AV, hospitalized, and die or recover.

(5) 🡪 (6) 🡪 (8/9) 🡪 (10) 🡪 (11/12)

Because the latent compartment doesn’t contribute to the force of infection, the duration infectious for each pathway is:

1. 4.8
2. 2 + 3.9 = 5.9
3. 2 + 3.9 + 3.4 = 9.3

The delay of two days is selected for the average time to recognise symptoms, be medically attended (and eligible for antiviral treatment). The 3.9 value reflects the balance of time to recover for those who were Medically Attended and recover. The 4.3 value reflects the balance of time to death or recovery for those who were medically attended went on to be hospitalized.

Although it is likely, for example, that an individual treated with antivirals would be hospitalized prior to the 3.9 day duration in their compartment, only the sum of the duration times for each infectious pathway will influence the force of infection in the model. This is because infectiousness does not change based on compartment or vary over time. By simplifying the duration parameters, we are able to draw from more data sources in our meta-analysis.

**Estimated Transmissibility and Severity Parameter Values for Historic Pandemics**

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
|  | Analytic R0 (Excludes interventions) | Estimated R0 (includes interventions) | Severity Parameter Value | Transmissibility Parameter Value |
| pdm(H1N1)09 | 1.42 | 1.31 | 1.00 | 0.025 |
| 1957 | 1.69 | 1.55 | 1.75 | 0.030 |
| 1918 | 2.08 | 1.83 | 7.25 | 0.035 |

The values for R0 given above are taken from the analytic calculation described in appendix 2. The model also offers an approximation of R0 which gives the ratio of the exposed to the total population. The analytic calculation assumes no antivirals and immunizations are distributed, while the approximation of R0 is based on the inclusion of these interventions. The ranges given in the table above correspond to those specified in a systemic review [71].