Estimating the transmissibility and severity of pandemic influenza

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Background

• Estimating the transmissibility and severity of pandemic H1N1 was a priority in the early stages of the epidemic.
• Estimates of transmissibility may aid decisions about the potential impact of control measures, and also the effectiveness of those measures already implemented.
• Estimates of severity may aid decisions about ‘how hard’ to try to control transmission.
• But there are difficulties in obtaining these estimates . . .

First wave in Hong Kong

Kindergarten and primary schools closed June 12 - early July.
Summer holidays for all schools from early July onwards.
43 secondary schools closed after 1+ case confirmed.

Changing case notification rate

• Laboratory-confirmed pandemic H1N1 was a notifiable disease throughout the first wave.
• Objective – to estimate the impact on influenza transmission of school closures and summer vacations.
• Problem – case identification rate likely changed during the switch from containment to mitigation phase.

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Modelling the impact of closures/vacations

- We used an age-structured S-I-R model to account for the non-linear transmission dynamics underlying the rising phase of the first wave of H1N1.
- We accounted in our model for the likely change in case identification rate as epidemic progressed and the public health response changed.
- We quantified transmissibility via the reproductive number R.


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$\hat{R}_1 \sim 1.7$ before June 11
$\hat{R}_1 \sim 1.5$ between June 12 and July 10
$\hat{R}_1 \sim 1.1$ after July 10

Predicted illness attack rate of 2.5% (180,000 cases) by the end of August.
Unknown proportion of population infected

- Objective – to track dynamically H1N1 transmissibility through the first wave.
- Problem – reporting delays lead to biases in estimates in recent days . . .

Methods – inferred infection networks

![Wallinga and Teunis’ infection network extended by Cauchemez to include cases not yet observed (i.e. to permit real-time analysis).](image)

Figure: Wallinga and Teunis’ infection network extended by Cauchemez to include cases not yet observed (i.e. to permit real-time analysis).

Empirical reporting delays

![Reporting delays were well-represented by a Poisson distribution (red curve).](image)

Figure: Reporting delays were well-represented by a Poisson distribution (red curve). For analysis of hospitalized confirmed cases a bivariate Poisson distribution was required for delays between onset, hospitalization and notification (not shown).

Real-time $R_t$ in Hong Kong

![Real-time $R_t$ by Cauchemez method (gray) and adjusting for reporting delays (black) using a data augmentation approach.](image)

Figure: Real-time $R_t$ by Cauchemez method (gray) and adjusting for reporting delays (black) using a data augmentation approach.
Background

Problem 1: Changing fractions of cases notified

Problem 2: Reporting delays

Problem 3: Unknown denominators

Discussion

Unknown proportion of population infected

- Objective – to estimate the proportion of the population infected during the first wave.
- Problem – no clear denominators on routine outpatient surveillance.
- Solutions – conduct population-based surveillance on infections based on serology.
Serologic surveillance

- JT Wu, BJ Cowling, JSM Peiris, Hong Kong Red Cross.
- Blood donors at 4 fixed centers across Hong Kong invited to provide sera for H1N1 antibody testing.
- ~ 750 specimens collected every week since June 12, 2009.
- Serum specimens also collected from children participating in a community study, and medical and pediatric outpatients.
- We can track the attack rate through time by studying the changes in prevalence of individuals with antibody titers \( \geq 1:40 \) (very low before first wave).
- Comparison with H1N1-associated admissions, deaths allows us to infer severity.

**First wave attack rate and severity**

**Figure:** Left: Estimated attack rate (blue). Right: Estimated severity.

- Pre-first-wave seroprevalence
- First wave attack rate
- Infection attack rate by paired-serology
- Post-first-wave seroprevalence

- Case-confirmation rate
- Case-hospitalization rate
- Case-ICU rate
- Case-fatality rate

**Comments – impact of H1N1**

- School closures and vacations were associated with substantial reductions in H1N1 transmissibility.
- Around 50% of school-age children infected in Hong Kong, but low attack rates in older adults.
- Severe illness much more common (per infection) with increasing age.

**Agreement between three sources of data**

- Blood donors (n=7391), outpatients (n=3747) and community study (n=2161)
- Around 50% of school-age children infected in Hong Kong, but low attack rates in older adults.
- Prospective cross-sectional serologic surveillance could allow timely information on transmissibility and severity, provided testing capacity exists.

**Implications for pandemic planning**

- Routine laboratory testing of a defined subset of hospitalized cases for example all patients hospitalized with severe ARI in a subset of hospitals (Lipstich et al. 2009 Lancet).