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Background 0 Changing fractions 0000000 Reporting delays 000000000 Unknown denominators 0000000 Discussion 00

## Estimating the transmissibility and severity of pandemic influenza

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## Acknowledgments

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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 ...

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Background

Problem 1: Changing fractions of cases notified

Problem 2: Reporting delays

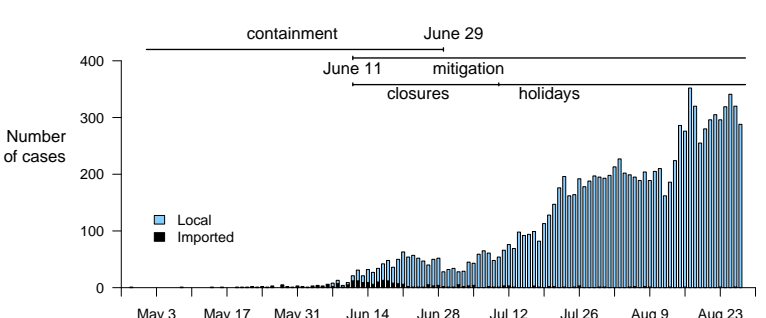
Problem 3: Unknown denominators

Discussion

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## First wave in Hong Kong



Number of cases

Local Imported

May 3 May 17 May 31 June 14 June 28 July 12 July 26 Aug 9 Aug 23

- 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.

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## Changing case notification rate

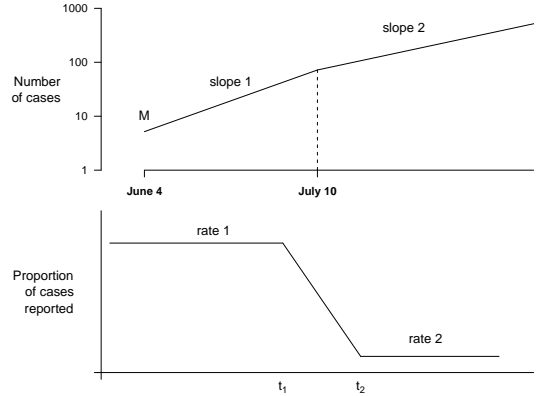
- Laboratory-confirmed pandemic H1N1 was a notifiable disease throughout the first wave.
- Objective – to estimate the impact on influenza transmission of school closures and summer vacations.
- Problem – case identification rate likely changed during the switch from containment to mitigation phase

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### Modelling the impact of closures/vacations

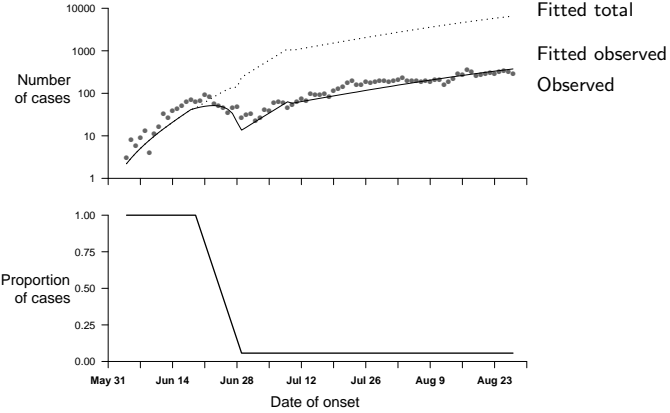
- JT Wu, BJ Cowling et al. Emerg Inf Dis 2010; 16:538-41.
- We used an age-structured S-I-R model to account for the non-linear transmission dynamics underlying the rising phase of the first wave of H1N1.
- We accounted in our model for the likely change in case identification rate as epidemic progressed and the public health response changed.
- We quantified transmissibility via the reproductive number R.

### Model schematic

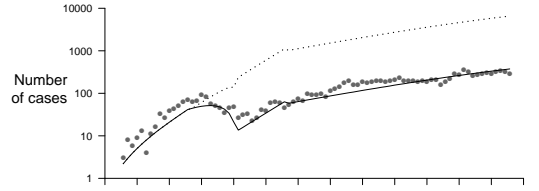


M, slope 1, slope 2, rate 1, rate 2, t<sub>1</sub> and t<sub>2</sub> estimated using MCMC.

### Fitted model



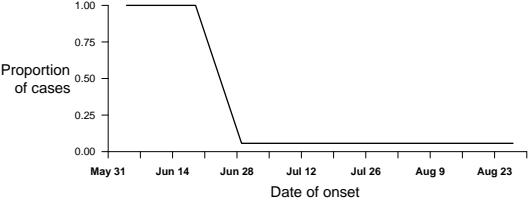
### Fitted model



- $R \sim 1.7$  before June 11
- $R \sim 1.5$  between June 12 and July 10
- $R \sim 1.1$  after July 10
- Predicted illness attack rate of 2.5% (180,000 cases) by the end of August.

### Fitted model

- We assumed 100% of cases were identified prior to mid-June.
- We estimated 5% of ill cases were identified in July-August.



- Background
- Problem 1: Changing fractions of cases notified
- Problem 2: Reporting delays
- Problem 3: Unknown denominators
- Discussion

# Unknown proportion of population infected

- BJ Cowling, MSY Lau et al. Epidemiol 2010 (in press).
- Objective – to track dynamically H1N1 transmissibility through the first wave.
- Method – use Cauchemez' et al 2006 AJE method for real-time estimation of the daily effective reproductive number  $R_t$  (extension of Wallinga & Teunis 2004 AJE).
- Problem – reporting delays lead to biases in estimates in recent days ...

# Reporting delays

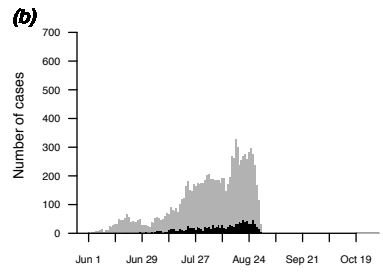


Figure: Reporting delays lead to an apparent drop-off in the epidemic over the most recent few days.

# Methods – inferred infection networks

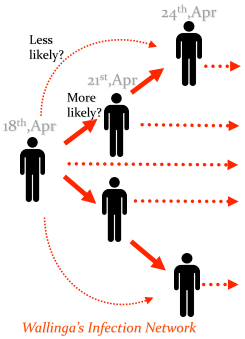


Figure: Wallinga and Teunis' infection network extended by Cauchemez to include cases not yet observed (i.e. to permit real-time analysis).

# Empirical reporting delays

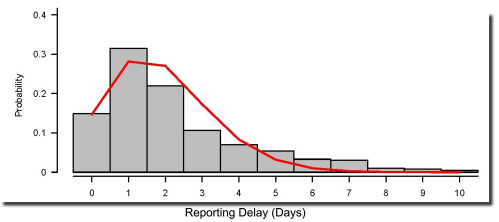


Figure: Reporting delays were well-represented by a Poisson distribution (red curve). For analysis of hospitalized confirmed cases a bivariate Poisson distribution was required for delays between onset, hospitalization and notification (not shown).

# Real-time $R_t$ in Hong Kong

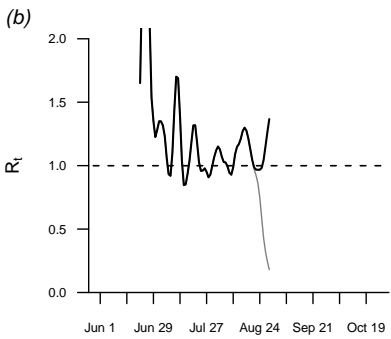
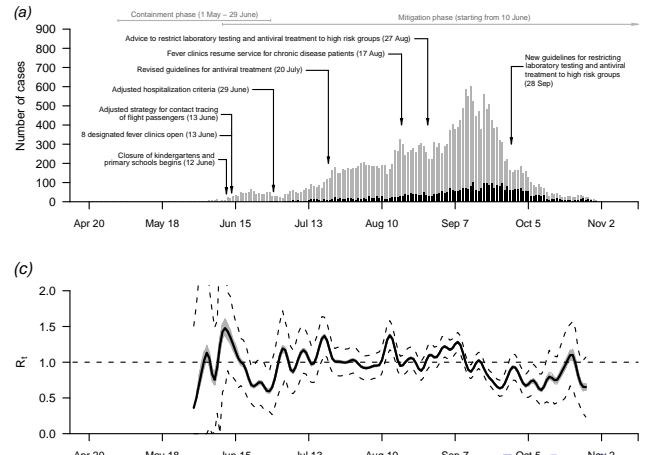


Figure: Real-time  $R_t$  by Cauchemez method (gray) and adjusting for reporting delays (black) using a data augmentation approach.

# $R_t$ based on notifications



Background ○ Changing fractions ○○○○○○ Reporting delays ○○○○○○● Unknown denominators ○○○○○○ Discussion ○○

## Rt based on hospitalizations

(a) Number of cases (Apr 20 to Nov 2). Annotations: "Competition phase (17 May - 23 June)", "Mitigation phase (starting from 10 June)", "Advice to restrict laboratory testing and antiviral treatment to high risk groups (27 Aug)", "Fewer clinics receive service for chronic disease patients (17 Aug)", "Revised guidelines for antiviral treatment (23 June)", "New guidelines for restricting laboratory testing and antiviral treatment to high risk groups (28 Sep)", "Adjusted hospitalization criteria (28 June)", "Adopted strategy to control spread of high transmission (13 June)", "Reopened lower clinics open (13 June)", "Closure of daycares and primary schools (22 June)".

(b) % hospitalized (Apr 20 to Nov 2).

(c)  $R_t$  (Apr 20 to Nov 2).

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## Real-time $R_t$ similar for both time series

(a) Number of cases (Jun 1 to Oct 19).

(b)  $R_t$  (Jun 1 to Oct 19).

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Background

Problem 1: Changing fractions of cases notified

Problem 2: Reporting delays

Problem 3: Unknown denominators

Discussion

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## Routine surveillance data in Hong Kong

Top panel: ILI Rate (per 1,000 consultations) (Apr 1 to Nov 1).

Middle panel: No. of cases with fever/respiratory symptoms at fever clinics (Apr 1 to Nov 1).

Bottom panel: Number of cases (Apr 1 to Nov 1).

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## 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.

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## 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.

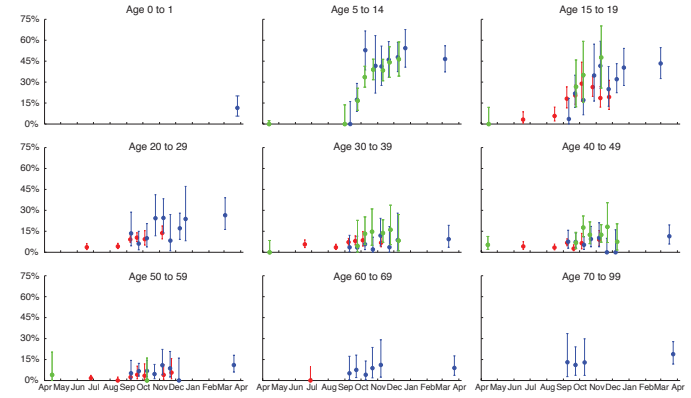
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## Serologic surveillance

- 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.

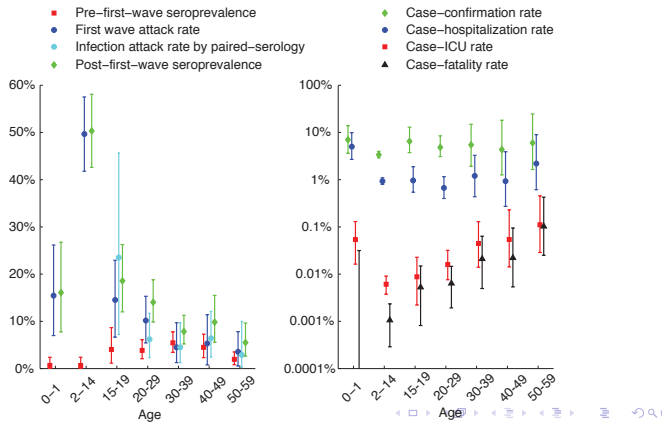
## Agreement between three sources of data

Blood donors (n=7391), outpatients (n=3747) and community study (n=2161)



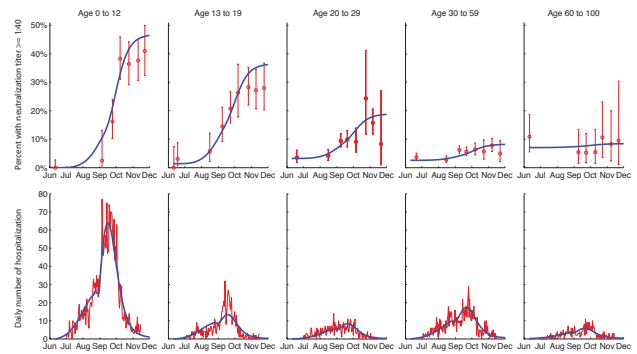
## First wave attack rate and severity

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



## Age-specific time course

Figure: Age-specific transmission model fitted to the proportion with viral neutralization titer  $\geq 1 : 40$  (above) and hospitalizations (below).



## 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.

## 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 (Lipsitch et al. 2009 Lancet).
- Prospective cross-sectional serologic surveillance could allow timely information on transmissibility and severity, provided testing capacity exists.