Surveillance of pandemic and seasonal influenza in Hong Kong

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Public health surveillance . . .

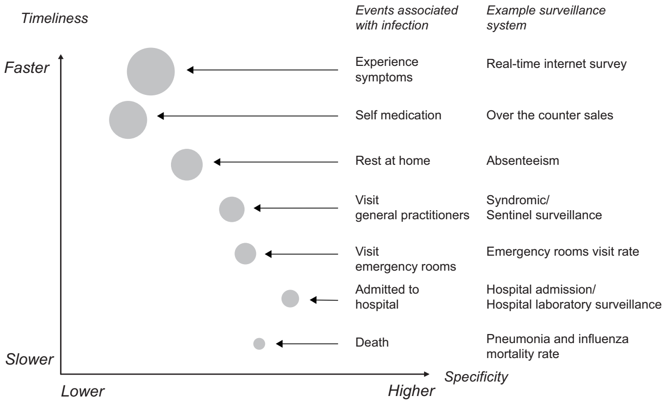
- "... is the ongoing systematic collection, analysis, interpretation and dissemination of health data." (Thacker et al. 1983 [1])
- The goal is not merely to collect data for analysis, but to guide public health policy and action.

Routine uses of surveillance data

We will monitor influenza incidence:

- To follow long-term trends and patterns (situational awareness).
- To detect sudden changes in disease occurrence (e.g. epidemics, outbreaks) and distribution.
- To identify changes in agents and host factors or health care practices, or intervention effects.
- To facilitate forecasting of future burden.

The clinical iceberg of influenza infection



- Only a small proportion of infections are severe.
- Milder influenza-like illness can have many viral or non-viral causes.

Indicators of influenza activity in Hong Kong

- Laboratory detections (mainly on specimens collected from inpatients).
- Outpatient sentinel surveillance of proportion of consultations with fever plus cough or sore throat.
- Hospital admissions/discharges with diagnosis codes.
- Deaths from specific causes.
- Currently investigating the use of school absenteeism data and inpatient rapid diagnostic test data.

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A profile of the online dissemination of national influenza surveillance data

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- Reviewed influenza surveillance systems in different countries in terms of the data disseminated via the internet
- Study conducted in February 2009 (before pandemic)

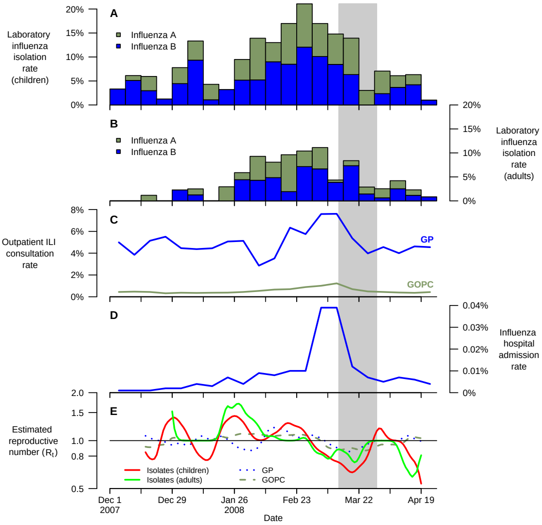
Systems reporting data in 70 countries

Table 1: Characteristics of influenza surveillance systems used in different countries

Surveillance Methods	Number (%)	of countries (n = 70)
Community consultation rates of influenza-like illness	62	(89%)
Virological data by viral culture/RT-PCR and/or HI assays	31	(44%)
Number of institutional Outbreaks	9	(13%)
Hospital admission rates	7	(10%)
Mortality (Pneumonia and influenza) rates	7	(10%)
Emergency room visits due to influenza-like illness	5	(7%)
School/Workplace absenteeism rates	5	(7%)
Real-time internet survey	4	(6%)
Antiviral resistant strain surveillance	4	(6%)
Quick immunological assays data	1	(1%)
Over the counter sales	1	(1%)
Others	7	(10%)

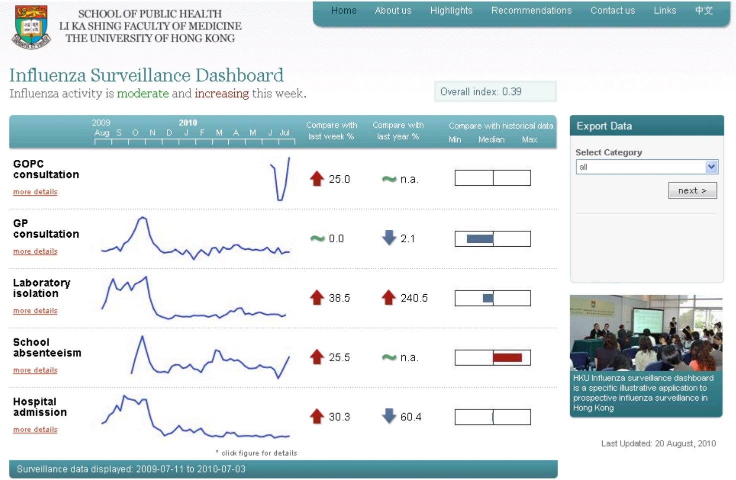
- Most common system is outpatient sentinel surveillance

School closures in 2008, Hong Kong



- Cowling BJ et al. Emerg Inf Dis 2008; 14:1660-2.
- Schools closed for two weeks in March 2008 following 3 pediatric deaths.
- Estimated the daily effective reproductive number through the epidemic.
- Closures too late to have any substantial impact on the winter influenza season.

Dissemination – HKU surveillance dashboard



http://sph.hku.hk/dashboard [usename=guest password=welcome2009] *paper under review*

Situational awareness during a pandemic

- How to maintain situational awareness of disease activity during an emerging pandemic?
  - Need early evaluation of transmissibility and severity of the new virus.
  - Need to decide on necessity/timing of various control measures.
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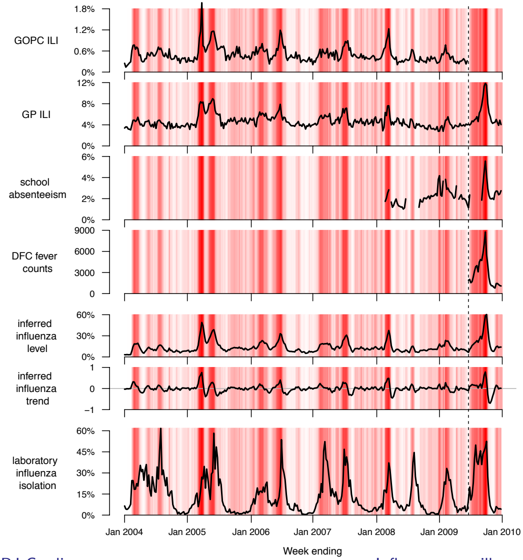
- Sources of information on disease activity
  - surveillance systems in place before the pandemic (e.g. sentinel ILI surveillance) – but how to interpret data if health-seeking behavior changes?
  - new surveillance systems (e.g. UK pandemic flu hotline, visits to flu clinics) – with no historical data for reference?

Integrating information from multiple streams



- Multivariate model fitted to multiple streams of influenza surveillance data, red bars indicate periods of high or increasing activity.
- Absenteeism data currently collected electronically from 62 participating schools.
- Visits to Designated Flu Clinics only reported during the pandemic.

2009 pandemic response in Hong Kong

- ‘Containment’ phase (from May 1)
  - Entry screening at airports, ports, border crossings.
  - Isolation of sick in hospital.
  - Contact tracing.
  - Prophylaxis and quarantine of close contacts in hospital, hotel, holiday camps.
  - “Directly observed antiviral chemoprophylaxis” rather than quarantine after May 21.

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  - “Directly observed antiviral chemoprophylaxis” rather than quarantine after May 21.
- Aim to delay local transmission for as long as possible:
  - could be reduced transmissibility during summer vacations and in late summer through autumn,
  - vaccine anticipated late 2009.

Mitigation phase

- 'Mitigation' phase to relieve disease burden and mortality primarily based on non-pharmaceutical interventions.
- Would be triggered after first case not associated with imported infection (reported on June 10).
  - Public health campaigns (improve hygiene etc.)
  - Immediate proactive kindergarten/primary school closures (children aged ≤ 12) for at least 2 weeks (starting June 12).
  - Reactive closure of secondary schools with 1+ confirmed case.
  - Medical resource mobilization.
  - Open 8 designated fever clinics (June 13).
  - Antiviral treatment of confirmed cases.

pH1N1 timeline in Hong Kong

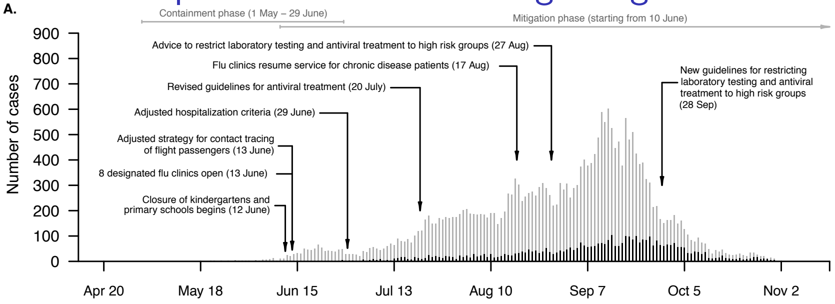
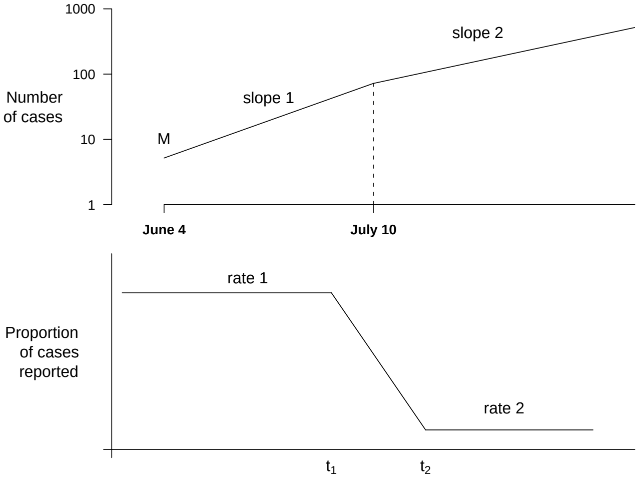


Figure: Number of lab-confirmed cases (gray) and hospitalizations (black) by day of illness onset, Hong Kong (Cowling et al. 2010 Epidemiol). Kindergarten and primary schools closed June 12 – early July; summer holidays for all schools from early July onwards. 43 secondary schools closed after 1+ case confirmed.

Estimating the impact of closures/vacations

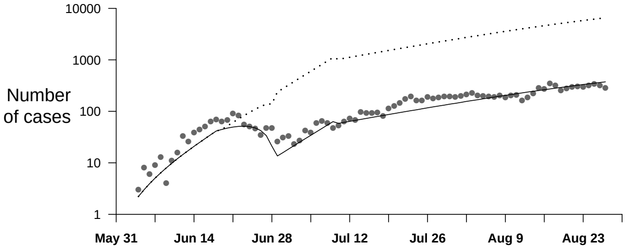
- Wu JT, Cowling BJ et al. Emerg Infect Dis 2010; 16:538-41.
- We used a mathematical model of the underlying transmission dynamics to infer the effectiveness of school closures in reducing transmission. transmission dynamics underlying the rising phase of the first wave of H1N1.
- We accounted in our 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_1 and t_2 estimated using MCMC.

Reduced transmissibility during closures and vacation



- Substantial reduction in case identification rate after mid-June.
- $R \sim 1.7$ before June 11
- $R \sim 1.5$ between June 12 and July 10
- $R \sim 1.1$ after July 10.

Serologic surveillance

- It can be difficult to estimate infection attack rates from illness-based surveillance (e.g. outpatient sentinel surveillance)
- Serologic data can be a valuable component of pandemic influenza surveillance:
  - To measure the infection attack rate over time.
  - To characterize severity on a per-infection basis.
  - To inform vaccine allocation.

Two possible approaches:

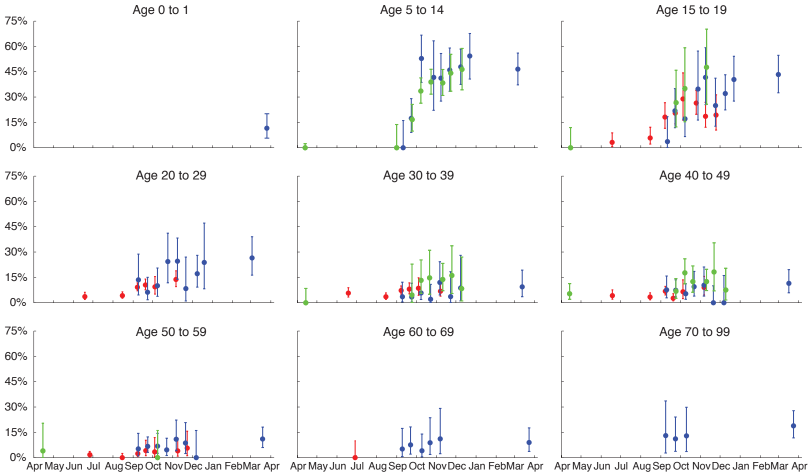
1. Establish a cohort of initially uninfected individuals, and take sera at intervals (e.g. before and after first wave) comparing paired antibody titers to infer infection rates over time (Riley, Cowling et al. 2011 PLoS Med (in press)).
2. Collect sera on a cross-sectional basis from the same population over time (e.g. blood donors) and compare seroprevalence over time to infer infection rates.
   - Both of the above require a serologic laboratory test, plus a third study which follows confirmed cases over time to estimate antibody titers over time since infection (note that serologic assays can differ between laboratories).

Hong Kong 'Red Cross study' – Objectives

- To track age-specific pH1N1 seroprevalence over the course of the first wave in Hong Kong
  - A serial cross-sectional approach: Blood donors and hospital outpatients were sampled on a daily basis for the presence of pH1N1 antibody. Compared with longitudinal serologic data from an existing cohort (Apr and Sep-Oct 2009).
- To estimate age-specific rates of pH1N1-related hospitalization, ICU admission, death during the first wave.
  - Combining surveillance data from the Hong Kong Hospital Authority with our serologic data – routine laboratory testing of all admissions throughout the first wave.
- Wu et al. 2010 CID.

Agreement between three sources of data

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

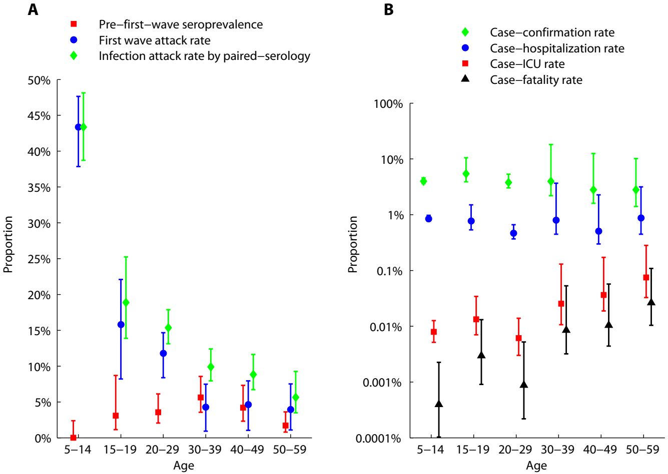


Use of the data in real-time (September 2009)

- Consulted by HK Food and Health Bureau with vaccination policy in mind (3m doses ordered and anticipated late December or early January).
- Excerpt of 3-page memo from Joe Wu and Ben Cowling:
- "Attributing the seropositivity difference between June and August to the local epidemic, we estimate that 1.5% of 16-60yo were infected by the pandemic virus in June and July. This infection attack rate estimate is consistent with the estimate we obtained earlier [in Wu et al 2010 EID]."
- "...Under these assumptions [of an age-structured mathematical model], the seropositivity rates of < 16 and 16-60 year-olds will be 45% and 19% in mid-December. With such seropositivity rates among school-aged children at the time of vaccination, vaccinating school-aged children will likely have little impact on reducing transmission unless the reproductive number increases substantially in January due to strong seasonal forcing."

Final first wave attack rate and severity

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

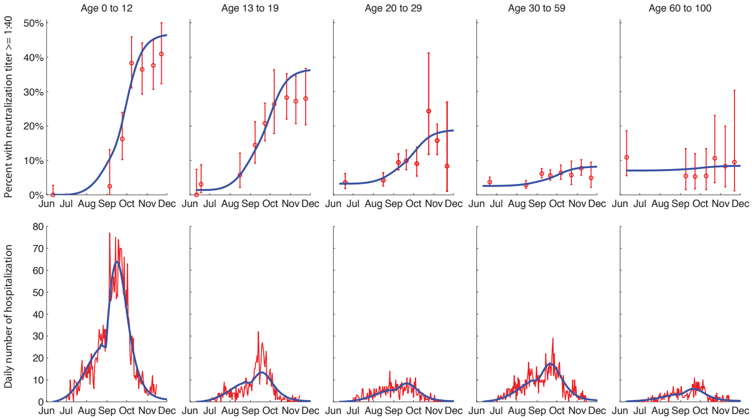


Latest results – fitted transmission model

- Stored $> 30,000$ sera from June 2009 to June 2010.
- Laboratory results on $> 16,000$ sera collected in 2009 now available (current funding only permits testing of specimens collected in 2009).
- Fitted age-structured transmission model to seroprevalence and pH1N1-associated hospitalization time series, allowing for POLYMOD-like mixing between age groups with additional parameters for relative susceptibility by age.

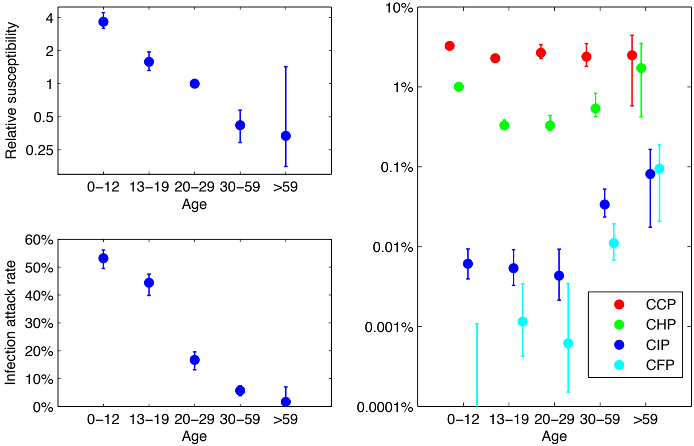
2009 H1N1 in Hong Kong – age-specific time course

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



Updated estimates

Figure: Relative susceptibility (top-left), infection attack rates (bottom-left) and updated severity estimates (right).

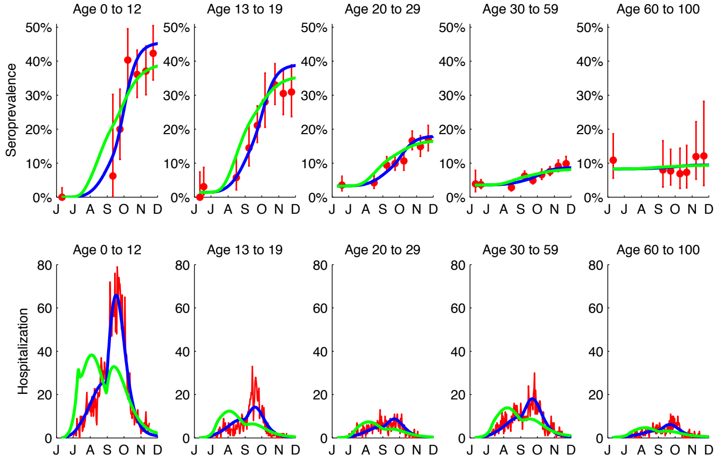


Fitted transmission model

- School closures/summer vacation reduced within-age-group transmission:
  - Reduced transmission within 0-12yo by 59% (95% CI: 51%-70%)
  - Reduced transmission within 13-19yo by 11% (95% CI: 2%-16%)
- Can also estimate what might have happened if schools had not been closed . . .

Revisiting school closures

Figure: Green line indicates the predicted first wave if kindergartens and primary schools had not been closed in June-July.



Background

Seasonal influenza

Pandemic influenza

Serologic surveillance

Discussion

Comments – Serologic surveillance

- Serologic surveillance study enabled us to infer transmission dynamics and infection attack rates of pH1N1 in Hong Kong.
  - Largest study to date valuable for real-time situational awareness in combination with other sources of surveillance data.

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- Serologic surveillance study enabled us to infer transmission dynamics and infection attack rates of pH1N1 in Hong Kong.
  - Largest study to date valuable for real-time situational awareness in combination with other sources of surveillance data.
  - High cumulative incidence of infection in children, low in older adults
  - Combining accurate data on infections, hospitalizations, and deaths we were able to estimate the age-specific severity profile of pH1N1 on a per-infection basis.

Limitations – Serologic surveillance

- Serologic surveillance study could suffer from selection bias
  - agreement in seropositive rates between (healthy) blood donors and (less healthy) outpatients gives some confidence in extrapolation of infection attack rates to the population. Results comparable to a separate longitudinal serologic study of 469 households.
- Only accounted for severity in terms of acute pH1N1-associated admissions, may have underestimated true burden if some events occurred after cessation of detectable viral shedding or tests were not performed.

Further work

- Serologic surveillance for seasonal influenza or other respiratory viruses? (too expensive for routine surveillance but potential for research purposes)
- Use of serologic surveillance data for vaccine strain selection?
- Inferring incidence rates from outpatient sentinel data or other surveillance data streams.
- Integration of multiple sources of data and use of multiple (e.g. syndromic) streams of information from the same source.

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