Application and efficacy of interventions for influenza transmission in seasonal epidemics and pandemics

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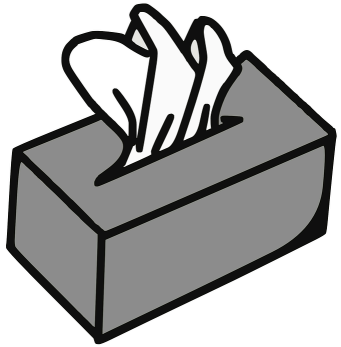
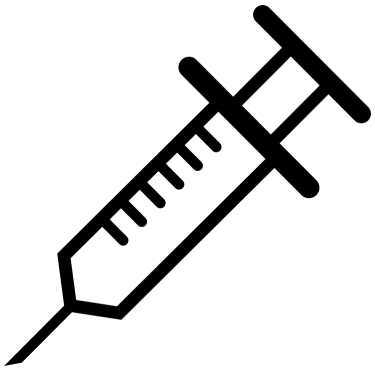
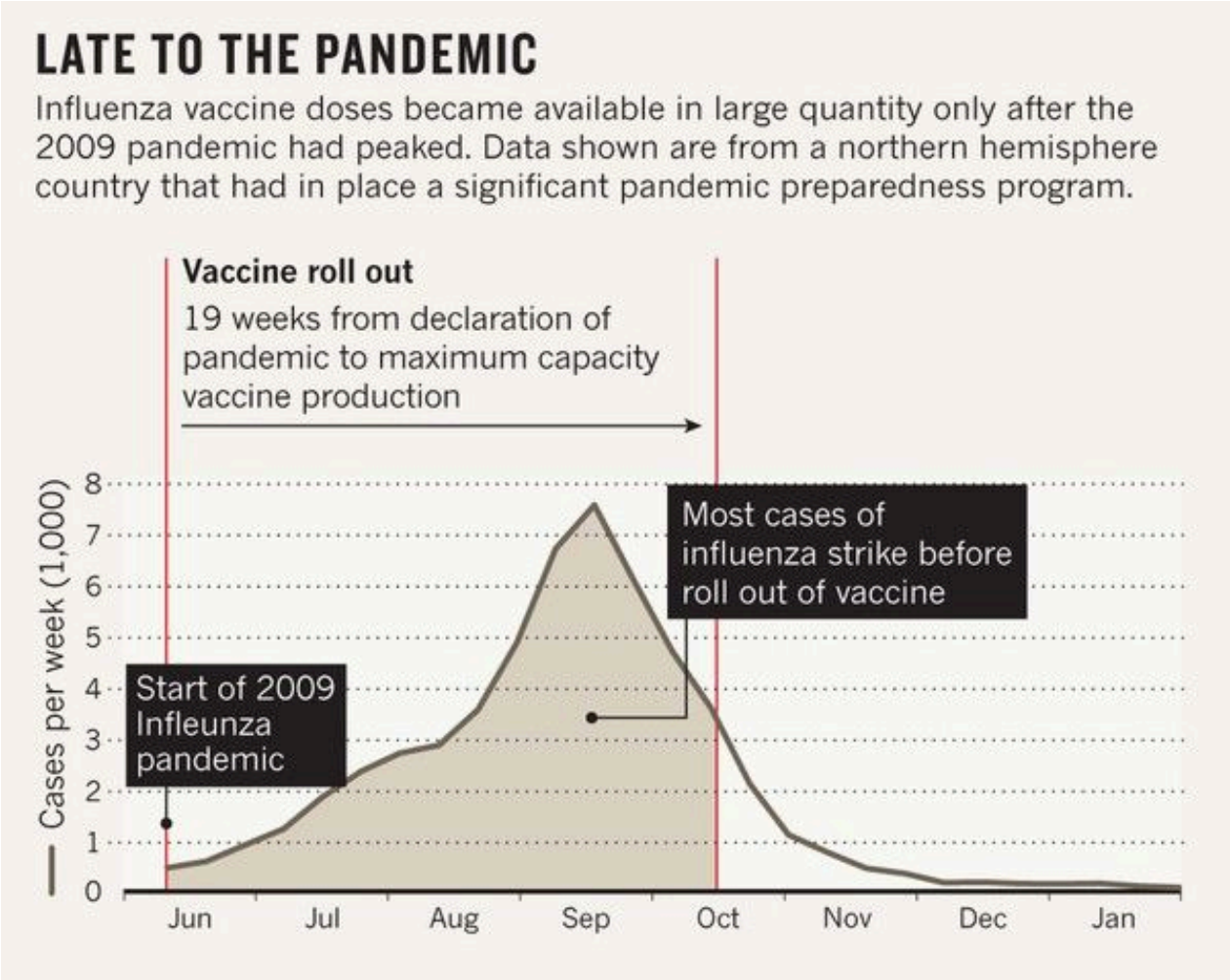
What population-based interventions can reduce the impact of pandemic and seasonal influenza?
能够在人群中实施以降低季节性和大流行流感所造成影响的干预措施有哪些？


Vaccination 疫苗接种





Stohr 2014 Nature

Vaccination in seasonal influenza
季节性流感疫苗接种

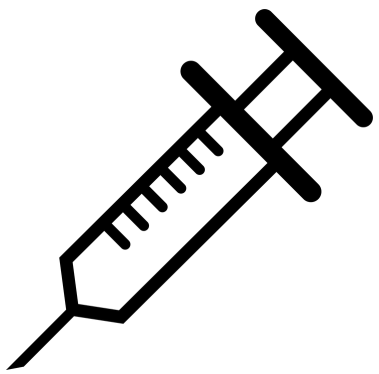
	Vaccine type	Pooled VE (%)	Pooled standard error	VE estimates (n)	p value for heterogeneity	I^2
Type B	Seasonal	54% (46–61)	0·083	36	<0·0001	61·3
H3N2	Seasonal	33% (26–39)	0·050	34	0·005	44·4
H1N1pdm09	Seasonal	61% (57–65)	0·048	29	0·783	0·0
H1N1pdm09	Monovalent	73% (61–81)	0·188	10	0·217	31·4
H1N1 (pre-2009)	Seasonal	67% (29–85)	0·397	5	0·093	57·6

Data in parentheses are 95% CIs. VE=vaccine effectiveness.

Table 2: **Pooled VE by type and subtype in studies without age restriction**

Belongia et al. 2016 Lancet Infect Dis

Breakthrough infections in vaccinees
疫苗接种失败而发生的感染



- Limited evidence on disease severity and contagiousness in breakthrough infections, in people who have received inactivated influenza vaccine

Antivirals 抗病毒药物

- Oseltamivir effective in symptomatic influenza. Observational data support effectiveness for severe influenza*
- New antivirals (e.g. Baloxavir Marboxil) encouraging†

*Dobson et al. 2015 Lancet; Kelly et al. 2015 Lancet; Malosh et al. 2018 Clin Infect Dis; Muthuri et al. 2014 Lancet Resp Med

†Hayden et al. 2018 N Engl J Med

Treatment as prevention
以治为防

- RCT of oseltamivir treatment to prevent household transmission in 1190 households in Bangladesh:
  - 23% reduction in illness in household contacts (p=0.03)
  - 16% reduction in PCR-confirmed influenza in household contacts (p=0.32)

Fry et al. 2015 Lancet Infect Dis

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Research

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Population-level effects of suppressing fever

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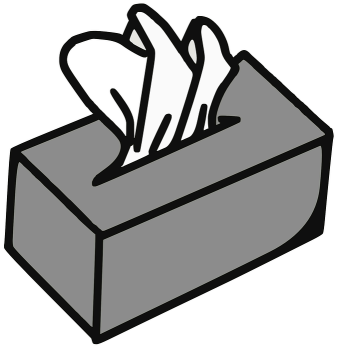
Fever is commonly attenuated with antipyretic medication as a means to treat unpleasant symptoms of infectious diseases. We highlight a potentially important negative effect of fever suppression that becomes evident at the population level: reducing fever may increase transmission of associated infections. A higher transmission rate implies that a larger proportion of the population will be infected, so widespread antipyretic drug use is likely to lead to more illness and death than would be expected in a population that was not exposed to antipyretic pharmacotherapies. We assembled the published data available for estimating the magnitudes of these individual effects for seasonal influenza. While the data are incomplete and heterogeneous, they suggest that, overall, fever suppression increases the expected number of influenza cases and deaths in the US: for pandemic influenza with reproduction number $\mathcal{R} \sim 1.8$, the estimated increase is 1% (95% CI: 0.0–2.7%), whereas for seasonal influenza with $\mathcal{R} \sim 1.2$, the estimated increase is 5% (95% CI: 0.2–12.1%).

Non-pharmaceutical interventions
非药物干预措施



US CDC guidelines*:

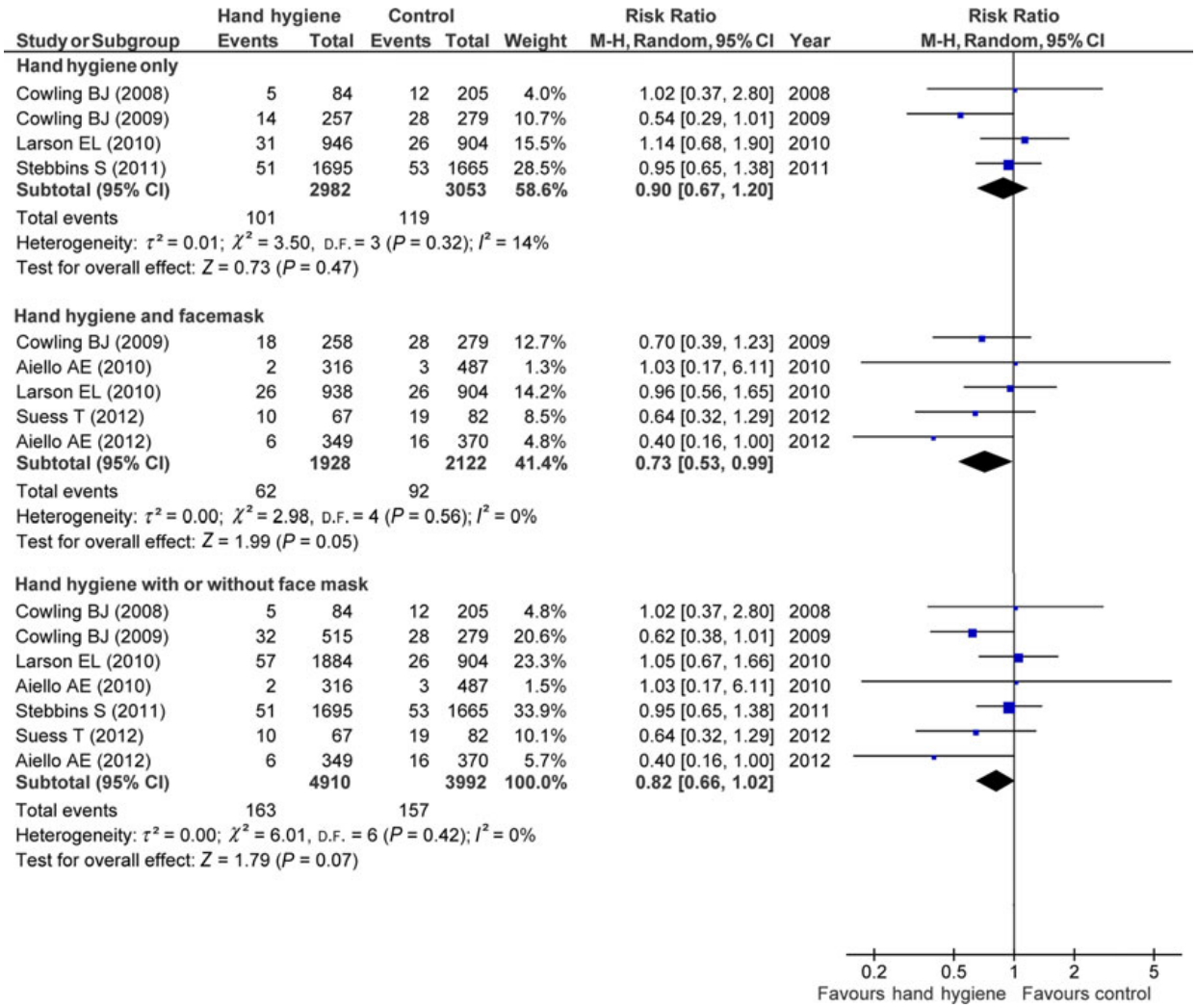
- Social distancing
- Self isolation with flu-like illness, until 24h after fever resolution
- Cough hygiene and hand hygiene
- Clean surfaces

One additional measure of interest:

- School closures

* https://www.cdc.gov/flu/consumer/prevention.htm

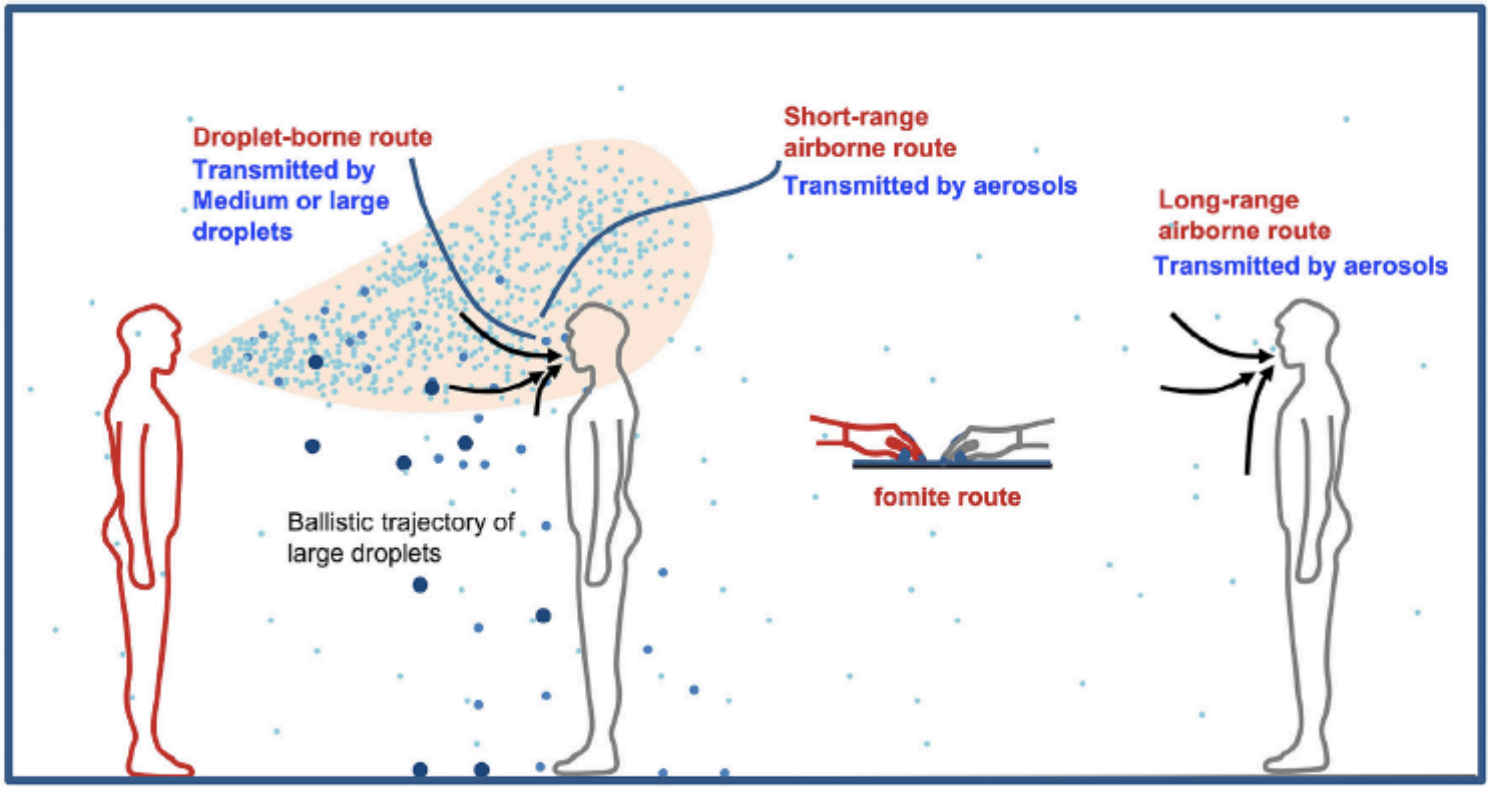
Hand hygiene and face masks



Limited benefit of hand hygiene and face masks for confirmed influenza (but may have greater effect on other respiratory pathogens)

Wong et al. 2014 Epidemiol Infect

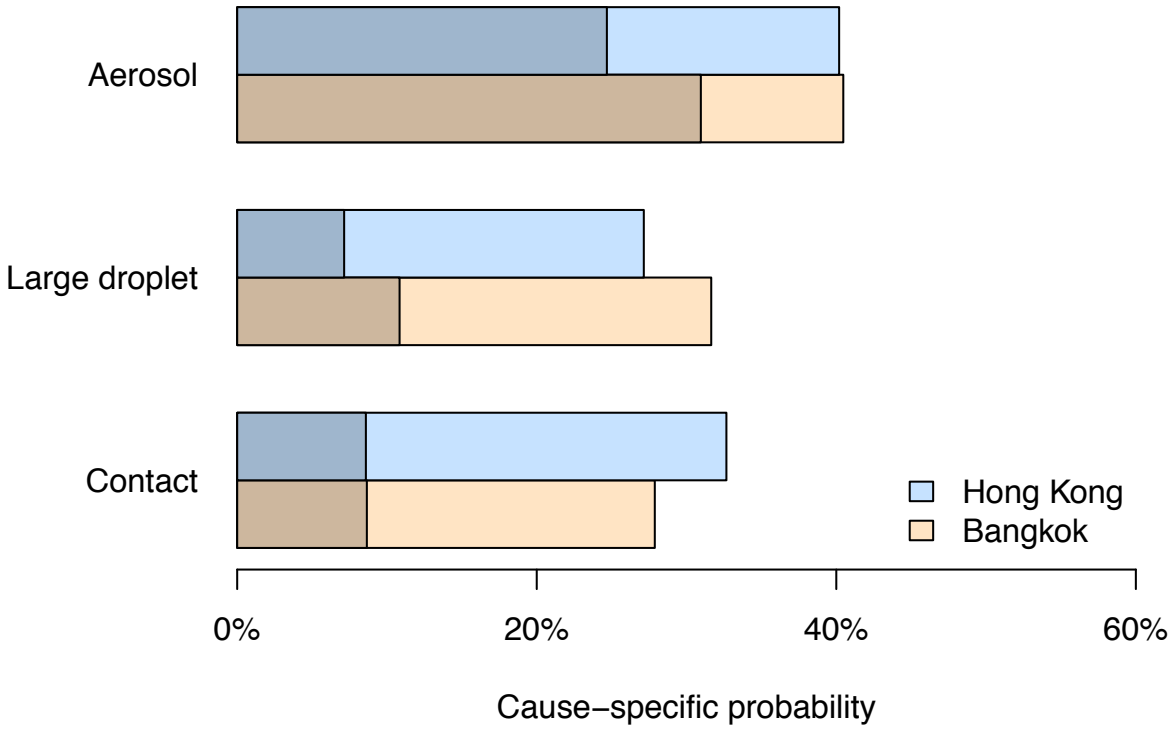
How do respiratory pathogens spread?
呼吸道病原体是如何传播的？



- Large droplets (>100 μm) : Fast deposition due to the domination of gravitational force
- Medium droplets between 5 and 100 μm
- Small droplets or droplet nuclei, or aerosols (< 5 μm): Responsible for airborne transmission

Wei et al. 2016 Am J Infect Control

Unclear importance of aerosols
气溶胶在病原体传播中的重要性尚未明确



Results of an analysis of the relative contributions of alternative modes of influenza A virus transmission in households in Hong Kong

Cowling et al. 2013 Nat Comms

Stay at home if you have a fever
出现发烧症状应该留在家里

Symptom or sign[1]	sH1N1 [n=112]	sH3N2 [n=80]	pH1N1 [n=17]	B [n=68]
Runny nose	82.1%	76.4%	64.3%	63.5%
Cough	81.3%	76.4%	85.7%	61.9%
Sore throat	65.2%	58.2%	57.1%	50.8%
Phlegm	60.7%	72.7%	50.0%	57.1%
Fever ($\geq 37.8°C$)	45.5%	41.8%	50.0%	31.7%
Headache	42.0%	49.1%	42.9%	41.3%
Muscle pain	41.1%	36.4%	35.7%	41.3%

- Prospective follow-up of household contacts of influenza cases
- Fever reported in no more than half of PCR-confirmed cases

Ip et al. 2016 Clin Infect Dis

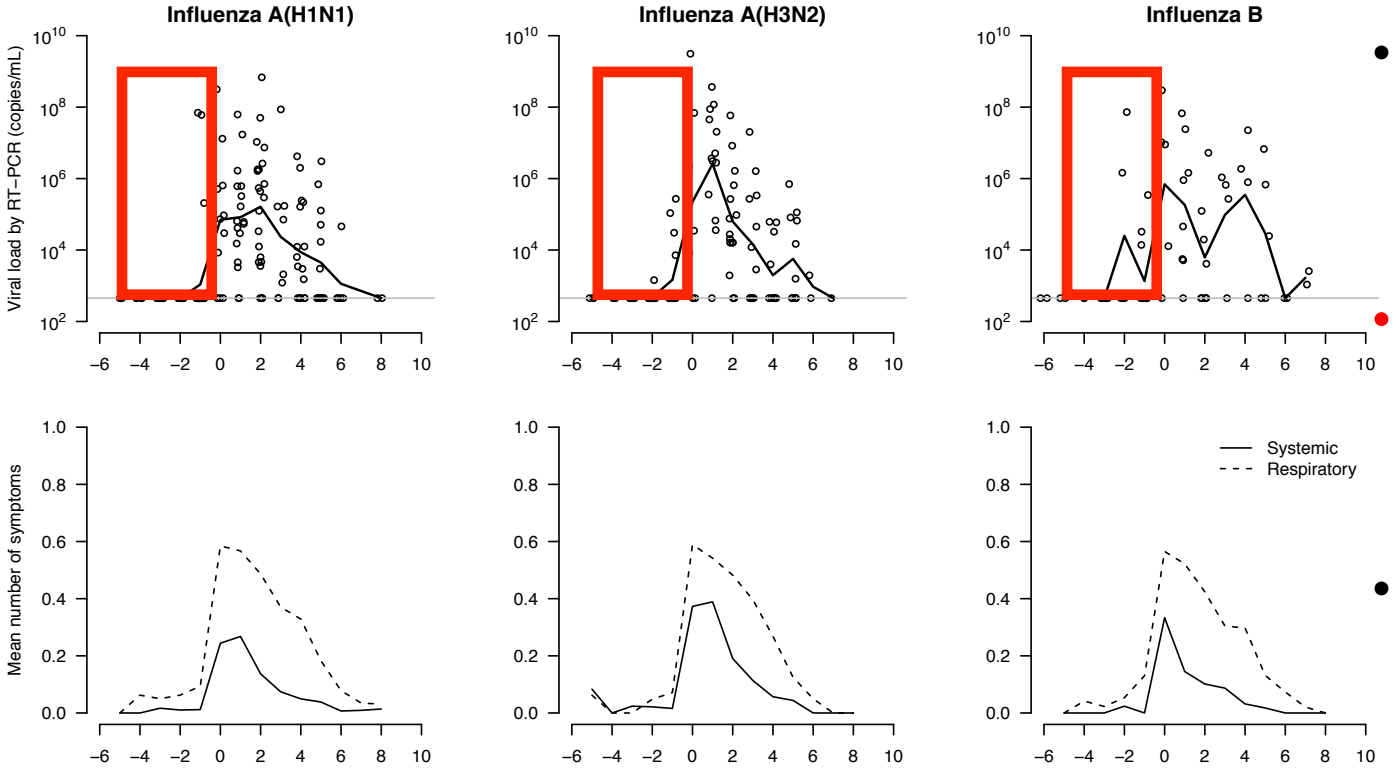
PCR-confirmed asymptomatic infections occur
存在PCR-确诊的无症状感染

Symptom or sign[1]	sH1N1 [n=112]	sH3N2 [n=80]	pH1N1 [n=17]	B [n=68]
ILI[2]	41.1%	40.0%	50.0%	30.2%
ARI	85.7%	78.2%	85.7%	69.8%
Pauci-symptomatic[3]	7.1%	12.7%	14.3%	12.7%
Asymptomatic[4]	7.1%	9.1%	0.0%	17.5%

1. Report of a symptom or sign at any time over the duration of follow up.
2. ILI is Fever ($\geq 37.8^{\circ}$C) plus cough or sore throat.
3. Pauci-symptomatic is defined as the report of at most 1 of 7 signs or symptoms on any given day.
4. Asymptomatic is defined as the report of 0 signs or symptoms over the duration of follow up.

Ip et al. 2017 Clin Infect Dis

Potential for pre-symptomatic transmission?
病原传播是否可能在症状出现前发生？



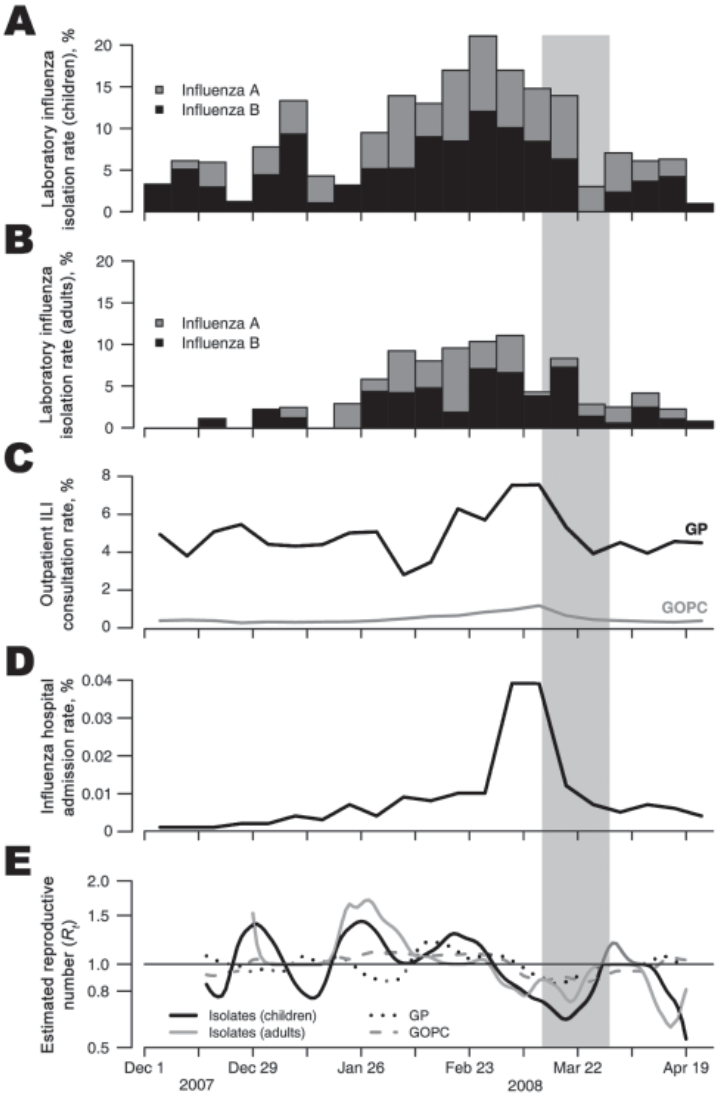
- Prospective follow-up of household contacts of influenza cases
- Evidence of pre-symptomatic virus shedding in some cases
- Asymptomatic cases also shed virus

Cowling et al. 2010 N Engl J Med; Lau et al. 2010 J Infect Dis; Ip et al. 2016 Clin Infect Dis

School closures in Hong Kong 香港学校停课

2008

- Moderate influenza season (co-circulation of H1N1, H3N2 and B) with media reports of a few pediatric deaths
- Schools were closed in 2nd week of March, 1 week earlier than scheduled Easter holiday
- Closure after the seasonal peak did not have an appreciable effect



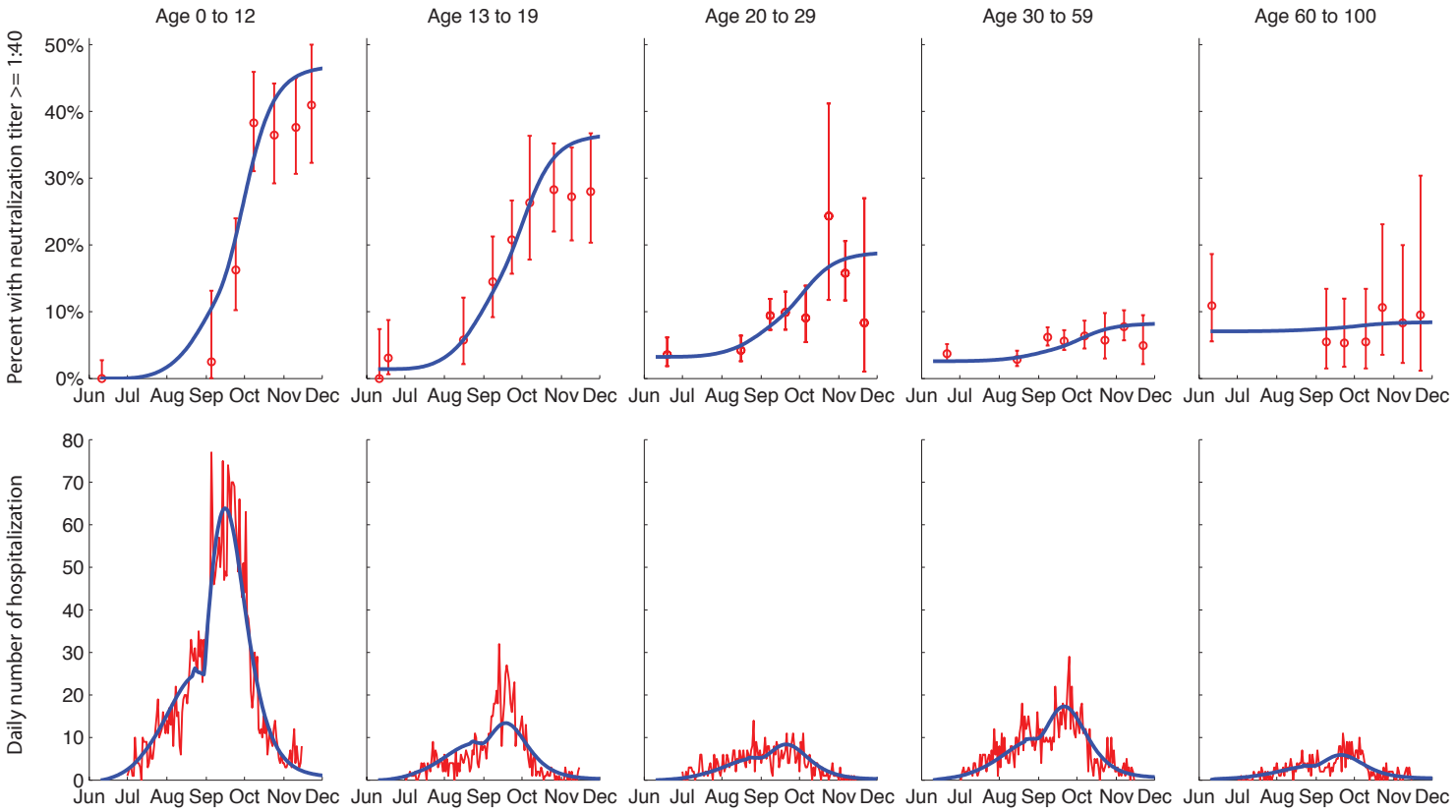
Cowling et al. 2008 Emerg Infect Dis

School closures in Hong Kong, 2009
2009年香港学校停课

- First imported case on 1 May 2009
- First documented "local" case 10 June 2009
- Schools closed on 11 June for 4 weeks until the scheduled summer break

Wu et al. 2010 Emerg Infect Dis

School closures in Hong Kong, 2009
2009年香港学校停课



- Serologic data (above) and lab-confirmed hospitalisations (below)
- School closures reduced transmission within 0-12yo by 59% (CI: 51%-70%) and within 13-19yo by 11% (CI: 2%-16%)

Wu et al. 2011 PLoS Med

Hong Kong primary schools and kindergartens to close on Thursday for early Lunar New Year holiday amid flu outbreak

City leader Carrie Lam says decision intended to 'cut off the chain of infection', but many parents upset at surprise announcement

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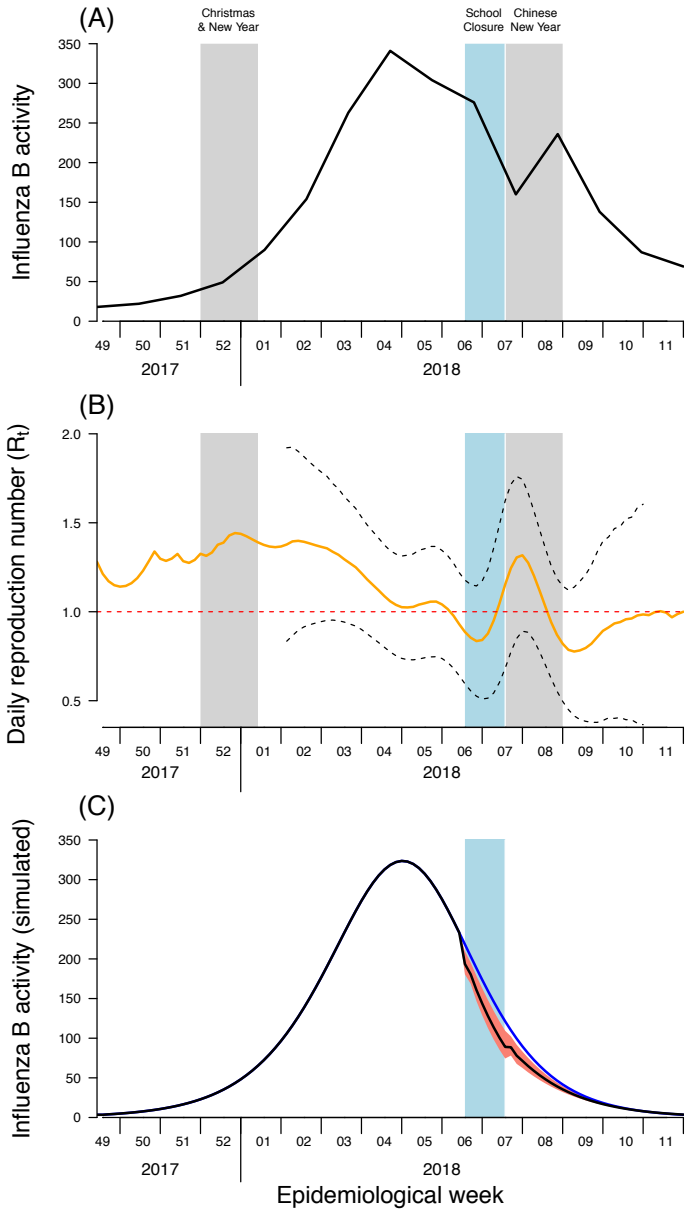
COMMENTS: 21

School closures, Hong Kong, 2018
2018年香港学校停课

- Closure from 8 February to 14 February, immediately prior to Chinese New Year holiday from 15 through 24 February
- Reduced transmission by ~16% during that week
- Reduced overall incidence of infections in the entire epidemic by ~4.2%



Ali et al. 2018 Emerg Infect Dis

Final comments – 4 of many knowledge gaps
结语 – 四个主要研究空白

- Effectiveness of non-pharmaceutical interventions
- Frequency of asymptomatic / very mild influenza virus infections, and their role in transmission
- Role of aerosols in person-to-person transmission
- Heterogeneity in influenza infectiousness / transmission (“superspreaders”?)

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