The Potential for International Dissemination of Emerging Viral Pathogens

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Data source: OAG traffic analyser, Jan 2017

5.2m outbound
201 countries

IMED, Vienna, Nov 2018
Aims

• Quantify delays
• Model implications for epidemic and international spread
• Apply to emergence of human-adapted avian influenza A(H7N9)
A(H7N9) human cases, China 2013-2018

Number of cases, week$^{-1}$

Data source: WHO DON; HKCPH reports
Reporting delay: Onset $\rightarrow$ Reporting to WHO

- Delays are frequent and can be substantial
  - median 13 days, range 1 – 72
- Associated with sex, age, province, and epidemic wave
- Adjusted delays:
  - Hong Kong 9 d (Prl: 7-11)
  - Zhejiang 19 d (Prl: 16-23)
  - Jiangsu 23 d (Prl: 19-27)
  - Xinjiang 51 d (Prl: 37-69)

Data source: WHO DON
Pandemic emergence model

- Stochastic state transition and infection
- Used observed interval distributions
  - Wang 2017 Lancet ID
  - Sensitivity to $R_0$

**Best case**
- Intervals as zoonotic A(H7N9)
- Infectious when symptomatic

**Worst case**
- Shorter incubation period
- Initial nosocomial transmission
- Infectious prior to symptoms
Simulated emergence example

- Infection
- Incubating
- Infectious
- Hospitalized
- Diagnosed

Cluster identified 10 cases diagnosed

Reported
## Exportation risk Zhejiang province

<table>
<thead>
<tr>
<th>Rank</th>
<th>Destination</th>
<th>Departing Passengers, month$^{-1}$</th>
<th>Cases required to exceed importation risk of 5%</th>
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</thead>
<tbody>
<tr>
<td>1</td>
<td>China</td>
<td>1,271,083</td>
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<tr>
<td>2</td>
<td>Hong Kong</td>
<td>35,771</td>
<td>80</td>
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<tr>
<td>3</td>
<td>Taiwan</td>
<td>33,288</td>
<td>86</td>
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<td>4</td>
<td>Rep. Korea</td>
<td>21,920</td>
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<td>5</td>
<td>Thailand</td>
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<td>6</td>
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<td>13,730</td>
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<td>15</td>
<td>India</td>
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</table>

\[
\frac{X}{F} \approx \frac{I}{N}
\]

### Imports A(H7N9) 2013+

<table>
<thead>
<tr>
<th>Country</th>
<th>Cases</th>
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</thead>
<tbody>
<tr>
<td>Hong Kong</td>
<td>21</td>
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<tr>
<td>Taiwan</td>
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<tr>
<td>Canada</td>
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<td>Macao</td>
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<tr>
<td>Malaysia</td>
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</tr>
</tbody>
</table>

Data source: OAG traffic analyser; HKCHP reports

Read et al 2015 Lancet
Scenario outcomes

Identification: 15 diagnosed cases
Reporting: 15 days

Best case
- Probability epidemic size $S$ or larger
- $p(S \geq s)$

Worst case
- $R_0$
  - Hong Kong
  - Rep. Korea
  - Japan, Italy
  - France
  - Spain
  - USA

Epidemic size when reported, $S$
Conclusions

• Intuitive, but important to quantify

• Feasible for epidemic to be firmly established when first identified and reported

• Reasonable risk outbreak has reached other countries before identified and reported in origin country

• Situation much worse for mild disease / poor surveillance
  • Expect significant delay in identification
  • e.g., A(H1N1)pdm 2009

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Delays in diagnosis and reporting

Delays are a function of:

- pathogen characteristics
- healthcare provision
- governance

A(H7N9) China

Infection
Hospitalized
Reported to national body
Reported by WHO

Symptoms onset
Diagnosed
Reported to WHO
Global connectivity of China

- Highly connectivity via airline network
- Provinces with more A(H7N9) cases also have most departing passengers

Data source: OAG traffic analyser, Jan 2017