Global updates on avian influenza and tools to assess pandemic potential

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Pandemic Influenza Risk Management

- Advance planning and preparedness are critical to help mitigate the impact of a pandemic.

- After influenza A(H1N1) 2009 pandemic, WHO updated its guidance for planning and preparedness through the release of *Pandemic Influenza Risk Management* (PIRM).

- PIRM takes an emergency risk management for health approach, which aligns more closely with the disaster risk management structures already in place in many countries.

- PIRM underscores the need for appropriate and timely risk assessment for evidence-based decision-making.

- Risk assessment is critical along the continuum of pandemic influenza phases to decide, clarify and justify public health preparedness, response and recovery actions.
GLOBAL INFLUENZA PROGRAMME

PANDEMIC INFLUENZA RISK MANAGEMENT

A WHO guide to inform & harmonize national & international pandemic preparedness and response
Highlights of PIRM Framework

- Promote all-hazards approach to Emergency Risk Management for Health
- Strengthen whole of government and whole of society approach to risk management
- Emphasize risk-based approaches with high-level guidance on risk assessment
- Uncouple global phases from national actions
  - Introducing flexibility in countries for planning and response
- Incorporate new developments e.g. PIP Framework
  - To improve and strengthen the sharing of influenza viruses with human pandemic potential; and
  - To achieve more predictable, efficient and equitable access for countries in need of life-saving vaccines and medicines during future pandemics.
Guidance

- TIPRA guidance to assess pandemic potential of non-seasonal influenza viruses
- PISA guidance to support assessment of influenza severity assessment
- Protocol to investigate non-seasonal influenza and other emerging acute respiratory diseases (in clearance)
- Summary of Key Information Practical to Countries Experiencing Outbreaks of A(H5N1) and Other Subtypes of Avian Influenza
- Draft WHO guidance for Surveillance during an Influenza Pandemic
- Global Epidemiological surveillance standards for influenza
- Manual for the laboratory diagnosis and virological surveillance of influenza
Event surveillance and routine surveillance in humans and animals

- Event based surveillance: early warning
- Indicator based surveillance: routine influenza surveillance
  - Sentinel ILI and SARI surveillance to gather quality data
Looking for the unexpected and compare to the expected

- Early detection needed to adequately respond to emerging pathogens
- Routine sentinel surveillance of ILI and SARI alone will not be sufficient to pick up an emerging pathogen early, but is needed to know what is usual
- Broad based involvement
- Triggers and reporting mechanism

Novel coronavirus

SARINET 2017
Sharing of event-based information
From the local site to the international

- Notifications
- Consultations
- Reports

Verification requests

National IHR Focal Point
(One per State Party)

WHO IHR Contact Point
(One per WHO Region)

Event Information Site

SARINET 2017
WHO Event management

Epidemic Intelligence (Media, Web, networks, etc.)

Core of event management
• based on experts' view
• risk to be wrong

Initial Screening
Verification with Member States
Risk Assessment
Response Strategy and Operations

SARINET 2017
Sharing of the virus (virus information)

- Reportable under IHR all human infections with a non-seasonal influenza virus

- Global Influenza Surveillance and Response System
  - Detailed information about the virus
  - Gene sequence through GISAID
  - The virus – using the shipping fund – to CC
  - Entering the shipment in IVTM
Influenza Virus Traceability Mechanism (IVTM)

- Records the transfer and movement of PIP Biological Materials (PIP BM) within and to parties outside the WHO GISRS to increase the transparency of GISRS activities of PIP

https://extranet.who.int/ivtm/
Within the Americas Canada, Mexico and the USA have recorded 295 original viruses in IVTM. This included the documentation of Influenza A/Mexico/7218/2012 (H7N3) isolated from a human and detected in Mexico in 2012 which was recorded in IVTM by CDC Atlanta.

These 295 viruses have been shared among GISRS and non-GISRS laboratories 707 times.
Tool for Influenza Pandemic Risk Assessment (TIPRA)
Risk Assessment Continuum

Figure 1. The continuum of pandemic phases

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This continuum is according to a “global average” of cases, over time, based on continued risk assessment and consistent with the broader emergency risk management continuum.
Objectives of TIPRA

• Support a timely and updatable hazard risk assessment for influenza viruses with pandemic potential;

• Transparently document features of the viruses and the infections they cause that might pose threats to a human population;

• Identify knowledge gaps and prompt further investigations including research and surveillance;

• Facilitate information sharing between scientists, policy-makers and other stakeholders.
TIPRA does not:

- Predict which virus will cause the next pandemic
- Eliminate need for technical experts
- Quantify risk exactly or statistically, no cut-offs

Focuses on virus’s qualitative pandemic potential, as evaluated by experts, based on different virus elements that are known to affect transmissibility and spread.
TIPRA Risk Question

What is the risk of sustained human-to-human transmission of the virus?

To evaluate this risk, two components, likelihood and impact, need to be evaluated:

- Risk Question Component A: What is the likelihood of sustained human-to-human transmission of the virus?

- Risk Question Component B: What is the impact to the human population of sustained human-to-human transmission of the virus?
TIPRA Process (11 detailed steps)
9 Risk Elements

A. Properties of the virus
   - Receptor binding properties
   - Genomic characteristics
   - Transmission in animal models
   - Susceptibility to antiviral treatment

B. Attributes in the human population
   - Human infection
   - Disease severity
   - Population immunity

C. Virus ecology and epidemiology in non-human hosts
   - Geographic distribution in animals
   - Infections in animals
## Transmission in Animal Models

For the purpose of the risk assessment tool, transmission in animal models is defined as the transmission of the virus in one or more commonly used animal (mammalian) models of human transmissibility by direct contact\(^1\) and/or through respiratory droplets\(^2\) in the absence of direct contact.

<table>
<thead>
<tr>
<th>Risk Stratification</th>
<th>Range of Point Estimate</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Lower Risk</strong></td>
<td>Virus with no or rare evidence of either direct contact or respiratory droplet transmission in commonly used animal models of human transmissibility.</td>
</tr>
<tr>
<td><strong>Moderate Risk</strong></td>
<td>Virus with consistent transmission to uninfected direct contact animals co-housed with other animals inoculated by the intranasal route in addition to lack of transmission by respiratory droplets.</td>
</tr>
<tr>
<td><strong>Higher Risk</strong></td>
<td>Virus with consistent transmission in animal models by both direct contact and respiratory droplets.</td>
</tr>
</tbody>
</table>

Terms:
1. Direct contact: naive animals are housed together with the virus-infected animals, allowing free contact to each other, sharing food and water.
2. Respiratory droplet transmission: naive animals are housed closely to the virus-infected animal but without direct contact. Virus transmission can only occur via airborne respiratory droplets.
Confidence in the mean point estimates for each risk element assessed for virus X. Darker shading indicates greater confidence & bars indicate range of point estimate values scored.
Visual Output: Risk Characterized

- Virus A: Moderate risk (Impact 7, Likelihood 3)

Lower risk: Lower risk, Moderate risk, Higher risk

Likelihood: Lower risk, Moderate risk, Higher risk
Comparison with other viruses.

- A(H5N6)
- A(H7N9)
- A(H9N2)
- A(H1N1) TRIG
TIPRA Benefits

- Can be done quickly: mobilize the GISRS network experts and other focal points (OIE, FAO, Member State, Research Group).

- Provides a method for taking into account multiple risk elements and different types of information systematically.

- Enables comparison of risk characterized for different viruses or for the same virus assessed at different time points.

- Enables risk characterization despite gaps in information.

- Captures confidence in the risk characterized based on the information available at the time of assessment: transparent.
TIPRA Limitations

- **Model construction:**
  - Simplification, 9 elements only, does not detail exposure/context aspects (outside scope). Need broader risk assessment tools for full characterization, especially at country level.
  - Risk elements defined by proxy indicators & not always capturing full spectrum. Considers feasibility and timeliness of data availability.

- **Data used to characterize risk:**
  - Comprehensive virus profile relies on data to be available and shared.

- **Risk assessment process:**
  - Scoring contingent on technical experts adhering to the scoring process. To ensure adherence, need thorough discussions to review justifications and variations in scores.
  - Technical experts may not agree with risk characterization from additive model. Rationale for experts providing confidence score about the overall risk characterized.
member states

- TIPRA output: available from their investment in influenza surveillance (GISRS), research and the collaboration.
- Available to be incorporated into national risk assessments that also consider country’s context and exposures.
- National level risk assessments that incorporate all three components will better determine the timing, scale, emphasis, intensity and urgency of the actions required.
Tool for Influenza Pandemic Risk Assessment (TIPRA)

Advance planning and preparedness help mitigate the impact of future pandemics. Risk assessment is critical to decide, clarify and justify public health preparedness, response and recovery actions. The Tool for Influenza Pandemic Risk Assessment (TIPRA) is used to assess the pandemic risk of influenza viruses with pandemic potential.

The objectives of TIPRA are to:
- support a timely and updatable hazard risk assessment for influenza viruses with pandemic potential;
- transparently document features of the viruses and the infections they cause that might pose threats to a human population;
- identify knowledge gaps and prompt further investigations including research and surveillance;
- facilitate information sharing between scientists, policy-makers and other stakeholders.

Highlights
Tool for Influenza Pandemic Risk Assessment (TIPRA) 14 July 2016
Report on Meetings to Launch TIPRA 1-5 May 2016
Monitoring TIPRA Version 1

- Website:

- Plans to use it, monitor it and refine it.
  - Monitoring framework developed: based on global launch meeting in May 2016:
    - Viruses to “challenge” TIPRA to confirm its suitability
    - Already assessed: H5N6, H7N9, H9N2, precursor pandemic H1N1pdm09
Global update avian and other novel influenza sub-types

12 May 2017

GIP / WHO Geneva

World Health Organization
Influenza A(H5)
Influenza A(H5): outbreaks in animals
January 2014 to 12 May 2017

Courtesy of FAO
Influenza A(H5N8)
Influenza A(H5N8): outbreaks in animals
January to 10 May 2017

Note: In addition to the outbreaks shown on the map, the following countries were affected between 01 June 2016 and 31 December 2016: Austria, Bulgaria, China, Croatia, Denmark, Egypt, Finland, France, Germany, Greece, Hungary, India, Iran (Islamic Republic of), Ireland, Israel, Italy, Kuwait, the Netherlands,
Influenza A(H5N1)
Influenza A(H5N1): human cases

- From 2003 through 12 May 2017,
  - 859 laboratory-confirmed human cases of avian influenza A(H5N1) virus infection have been officially reported to WHO from 16 countries; of these cases, 453 have died.
  - 8 cases since May 2016 (all reported from Egypt)
  - Dramatic decline of reported human cases of A(H5N1) worldwide
Confirmed H5N1 human cases reported to WHO as of 12 May 2017

Number of Confirmed Human H5N1 Cases
by month of onset as of 2017-05-11

- Azerbaijan (8)
- Bangladesh (3)
- Djibouti (1)
- Cambodia (56)
- Canada (1)
- Indonesia (199)
- Egypt (359)
- Myanmar (1)
- Pakistan (3)
- Laos (2)
- Thailand (25)
- Turkey (12)
- Viet Nam (127)

Month of onset

Number of cases

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Areas with confirmed human cases for avian influenza A(H5N1) reported to WHO, 2003-2017*

*All dates refer to onset of illness
Data as of 12 May 2017
Source: WHO/GIP

Areas with confirmed human cases for avian influenza

The designations employed and the presentation of the material in this publication do not imply the expression of any opinion whatsoever on the part of the World Health Organization concerning the legal status of any country, territory, city or area or of its authorities, or concerning the delimitation of its frontiers or boundaries. Dotted and dashed lines on maps represent approximate border lines for which there may not yet be full agreement.

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Influenza A(H5N1) as of 12 May 2017

- M:F ratio is 0.9
  - No significant association between outcome and gender

- Median age is 19 years (range 0-81 years)
  - Cases 20 years or older are more likely to have fatal outcomes compared to cases less than 20 years of age. (OR 1.88)

- Overall case fatality ratio is 53% (453/859).

- Some family clusters but no sustained human-to-human transmission.

- The majority of cases have exposure to poultry or live poultry markets.
Influenza A(H5N6)
Influenza A(H5N6): human cases 2014 through 12 May 2017

- 16 lab-confirmed human cases of avian influenza A(H5N6) virus infection have been reported to WHO from China.
- At least 6 were severe and 6 cases were fatal
- 1 Additional avian influenza A(H5N6) case was reported in a publication. This was a mild case in a child; had been reported as an A(H5N1) virus infection. Considered a probable human case of A(H5N6) virus infection.
- Most cases had exposure to live poultry or live poultry markets prior to disease onset.
- The virus has been detected in poultry in many provinces in China.
Risk Assessment: Influenza A(H5) as of 12 May 2017

- Likelihood of additional human A(H5) cases?
  - Most human cases were exposed to A(H5) viruses through contact with infected poultry or contaminated environments, including live poultry markets. Since the viruses continue to be detected in animals and environments, further human cases can be expected.

- Likelihood of human-to-human transmission A(H5)?
  - Despite reported small clusters of A(H5) virus infections including in healthcare workers, current epidemiological and virological evidence suggests that this and other A(H5) viruses have not acquired the ability of sustained transmission among humans, thus the likelihood is low.
What is the risk of international spread of avian influenza A(H5) viruses by travelers?

- Should infected individuals from affected areas travel internationally, their infection may be detected in another country during travel or after arrival. If this were to occur, further community level spread is considered unlikely as evidence suggests these viruses have not acquired the ability to transmit easily among humans.
Influenza A(H7N9)
Influenza A(H7N9) as of 10 May 2017

Map 1. Human cases and positive findings in birds or the environment

Click to enlarge - Note: Human cases are depicted in the geographic location where they were reported; for some cases, exposure may have occurred in a different geographic location. Precise location of 23 human cases in Anhui (2), Beijing (2), Guangdong (1), Guangxi (1), Hebei (2), Hunan (1), Hubei (2), Jiangsu (1), Jiangxi (6), Sichuan (2) and Zhejiang (3) Provinces are currently not known, these cases are therefore not shown on the map.
Influenza A(H7N9) From 2013 through 16 May 2017

- 1486 lab-confirmed human cases of avian influenza A(H7N9) virus infection have been officially reported to WHO from 3 countries; of these cases, at least 373 have died.
- Two cases were reported by Canada and one case by Malaysia. However, these cases were in travellers who likely had exposure to poultry or contaminated environments in China.
- The majority of the cases seem to occur between week 51 to week 20 of the following year.
Confirmed H7N9 human cases reported to WHO as of 16 May 2017

Number of confirmed human H7N9 cases and deaths, as reported to WHO by week, as of 2017-5-15
Influenza A(H7N9) as of 12 May 2017

<table>
<thead>
<tr>
<th>IHR notifications</th>
<th>Wave 1</th>
<th>Wave 2</th>
<th>Wave 3</th>
<th>Wave 4</th>
<th>Wave 5</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cases reported</td>
<td>135</td>
<td>320</td>
<td>224</td>
<td>102</td>
<td>688</td>
</tr>
<tr>
<td>Deaths reported</td>
<td>46</td>
<td>110</td>
<td>55</td>
<td>31</td>
<td>123</td>
</tr>
<tr>
<td>CFR</td>
<td>34%</td>
<td>34%</td>
<td>25%</td>
<td>30%</td>
<td>18%</td>
</tr>
</tbody>
</table>

Deaths reported above are those reported as fatal at the time of notification to WHO and so the CFR is underestimated. Below is data from the NHFPC:

<table>
<thead>
<tr>
<th>NHFPC</th>
<th>Wave 1</th>
<th>Wave 2</th>
<th>Wave 3</th>
<th>Wave 4</th>
<th>Wave 5</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cases reported</td>
<td>136</td>
<td>304</td>
<td>219</td>
<td>99</td>
<td>681</td>
</tr>
<tr>
<td>Deaths reported</td>
<td>45</td>
<td>127</td>
<td>99</td>
<td>38</td>
<td>248</td>
</tr>
<tr>
<td>CFR</td>
<td>33%</td>
<td>42%</td>
<td>45%</td>
<td>38%</td>
<td>36%</td>
</tr>
</tbody>
</table>

SARINET 2017
Influenza A(H7N9) as of 12 May 2017

- M:F ratio is 2.3
  - No significant association between gender and outcome.
- Median age is 57 years (range 0-91 years)
  - Cases over 60 years of age are almost 3 times more likely to have fatal outcome than cases less than 60 years of age.
- Case fatality ratio is 25% (373/1486), according to IHR reports
- 64% (958/1486) of the cases were reportedly severe, critical, or fatal (at the time of reporting)
- 70% (1054/1486) of the cases have reported exposure to poultry or live poultry markets.
- 36 family clusters but no sustained human-to-human transmission.
Influenza A(H7N9) as of 12 May 2017

Confirmed Human H7N9 Cases
Distribution of Age Groups
All Regions

Number of Cases

Age Groups (years)

0-9, 10-19, 20-29, 30-39, 40-49, 50-59, 60-69, 70-79, 80-89, 90-99, 100-109
Risk Assessment
Influenza A(H7N9) as of 12 May 2017

- Likelihood that additional human cases of infection with avian influenza A(H7N9) viruses will occur?
  - Most human cases are exposed to the A(H7N9) virus through contact with infected poultry or contaminated environments, including live poultry markets. Since the virus continues to be detected in animals and environments, further human cases can be expected. Additional sporadic human cases of influenza A(H7N9) in other provinces in China that have not yet reported human cases are also expected.
Risk Assessment
Influenza A(H7N9) as of 12 May 2017

**Likelihood of human-to-human transmission of avian influenza A(H7N9) viruses?**

- Even though small clusters of cases have been reported, including those involving healthcare workers, currently available epidemiological and virological evidence suggests that this virus has not acquired the ability of sustained transmission among humans, thus the likelihood is low.
What is the risk of international spread of avian influenza A(H7N9) viruses by travelers?

- Should infected individuals from affected areas travel internationally, their infection may be detected in another country during travel or after arrival. If this were to occur, further community level spread is considered unlikely as this virus has not acquired the ability to transmit easily among humans.
Human infections with other non-seasonal influenza A viruses
### Human infection with non-seasonal avian influenza viruses from 2016 to 12 May 2017

<table>
<thead>
<tr>
<th>Subtype</th>
<th>Country reporting</th>
<th>Clinical severity</th>
<th>Exposure</th>
<th>Viruses found in animals</th>
<th>CVV</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>H9N2</strong></td>
<td>&lt;br&gt; China</td>
<td>Usually mild; one fatal case reported from China in an individual with underlying conditions</td>
<td>Live poultry, although exposure unknown in some cases</td>
<td>Endemic in poultry in many Asian countries</td>
<td>Yes &lt;br&gt; China 2016 (11) 2017 (2) &lt;br&gt; Egypt 2016 (1)</td>
</tr>
<tr>
<td><strong>H7N2</strong></td>
<td>USA</td>
<td>Mild (1)</td>
<td>Direct exposure to symptomatic cats infected with A(H7N2) viruses</td>
<td>Limited information on current prevalence in animal populations in the US</td>
<td>No</td>
</tr>
</tbody>
</table>
Human infection with non-seasonal swine origin influenza viruses from 2016 to 12 May 2017

<table>
<thead>
<tr>
<th>Subtype</th>
<th>Country reporting</th>
<th>Clinical severity</th>
<th>Exposure</th>
<th>Viruses found in animals</th>
<th>CVV</th>
</tr>
</thead>
<tbody>
<tr>
<td>H3N2v</td>
<td>USA</td>
<td>All mild</td>
<td>Swine</td>
<td>A variety of A(H3N2)virus strains are endemic in swine population in most regions of the world</td>
<td>Yes</td>
</tr>
<tr>
<td></td>
<td>Canada</td>
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<tr>
<td></td>
<td>2016 (18)</td>
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<td>2017 (1)</td>
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<tr>
<td>H1N1v</td>
<td>Italy</td>
<td>One was mild; two were severe requiring ECMO; all recovered</td>
<td>Swine</td>
<td>A variety of A(H1N1)virus strains are endemic in swine population in most regions of the world</td>
<td>Yes</td>
</tr>
<tr>
<td></td>
<td>Netherlands</td>
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<td>2016 (1)</td>
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<td>Switzerland</td>
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<tr>
<td></td>
<td>2016 (1)</td>
<td></td>
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</tr>
<tr>
<td>H1N2v</td>
<td>USA</td>
<td>Two were hospitalized; all recovered</td>
<td>Swine</td>
<td>A variety of A(H1N2)virus strains are endemic in swine population in most regions of the world</td>
<td>Yes</td>
</tr>
<tr>
<td></td>
<td>2016 (4)</td>
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Avian Influenza in the Americas - (H5-H7), 2012-2017 - Avian Outbreaks overview -


### Number of outbreaks year & country

<table>
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<tr>
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<td>Belize</td>
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<tr>
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<td>1</td>
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<td>HPAI (H5N1)</td>
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<td>Mexico</td>
<td>46</td>
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<td>HPAI (H7N3)</td>
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**Space-time distribution of avian flu outbreaks**

World Health Organization

SARINET 2017
Only data and viruses that are shared can be used to understand the global situation

- **Local data/virus for local decisions**
  - SARI/ILI surveillance for national disease burden and risk groups description
  - Viruses to see what is circulating in the country

- **Local data/viruses for the global picture**
  - Only with the sum of all the local data can the global picture be made and patterns can be identified
  - Understand which virus is circulating where, compare evolution, understand risks

- **Global picture for the local interpretation**
  - Only if we know what is happening in the world can we predict/be prepared for what is going to happen to the local situation
Acknowledgment

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