新型インフルエンザリスクアセスメントについて

特に新型インフルエンザ発生後のリスクアセスメント

東北大学医学系研究科微生物学分野
押谷　仁

Pandemic Influenza Risk Management

WHO Interim Guidance

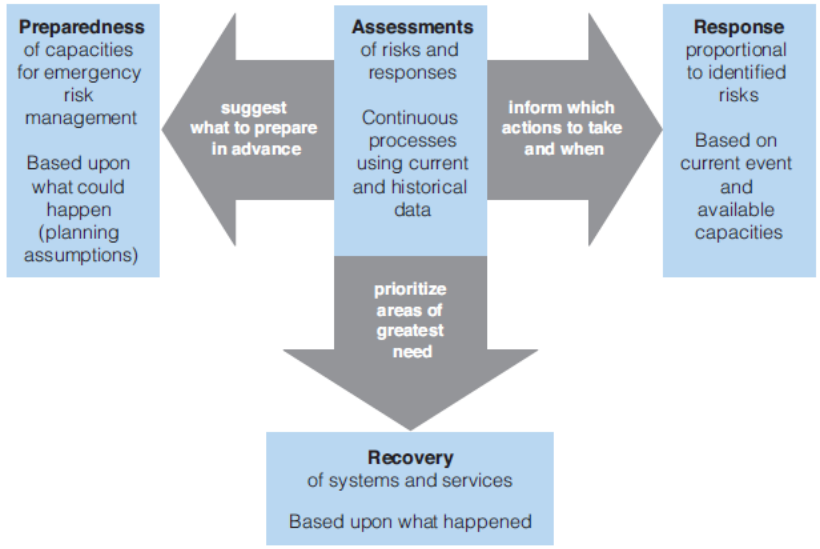
World Health Organization

2013年6月

新たなWHOのガイダンス

—2013年6月に暫定版として公表
—基本的な考え方：各国のリスクアセスメントに基づくリスクマネジメント

Figure 3. Pivotal role of risk assessment in preparedness, response and recovery actions



新型インフルエンザに関するリスクアセスメント

- パンデミック発生前のリスクアセスメント
  ―パンデミックを起こす可能性のあるウイルスについての評価
  （例）H7N9に対してWHOや感染症研究所が実施

- パンデミック発生後のリスクアセスメント
  ―パンデミックとなった、もしくはパンデミックとなる可能性の非常に高いウイルスについての評価
  ―WHOの新しいガンダンスの対象

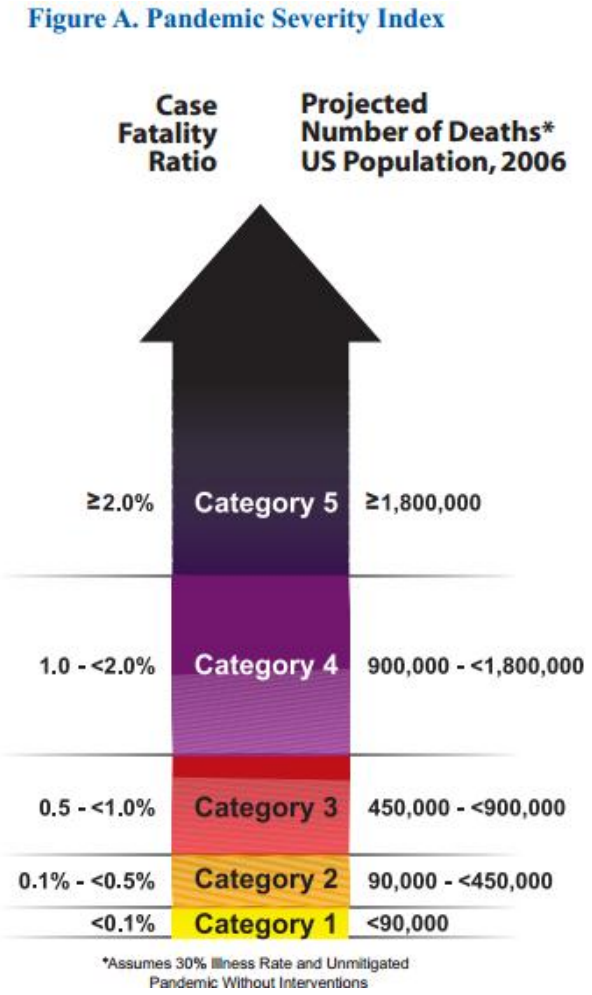
パンデミック発生後のリスクアセスメントはなぜ必要か？

- 2009年のパンデミック対応の反省
  ―適切なリスクアセスメントなしに病原性の高いパンデミックとしての対応が行われた

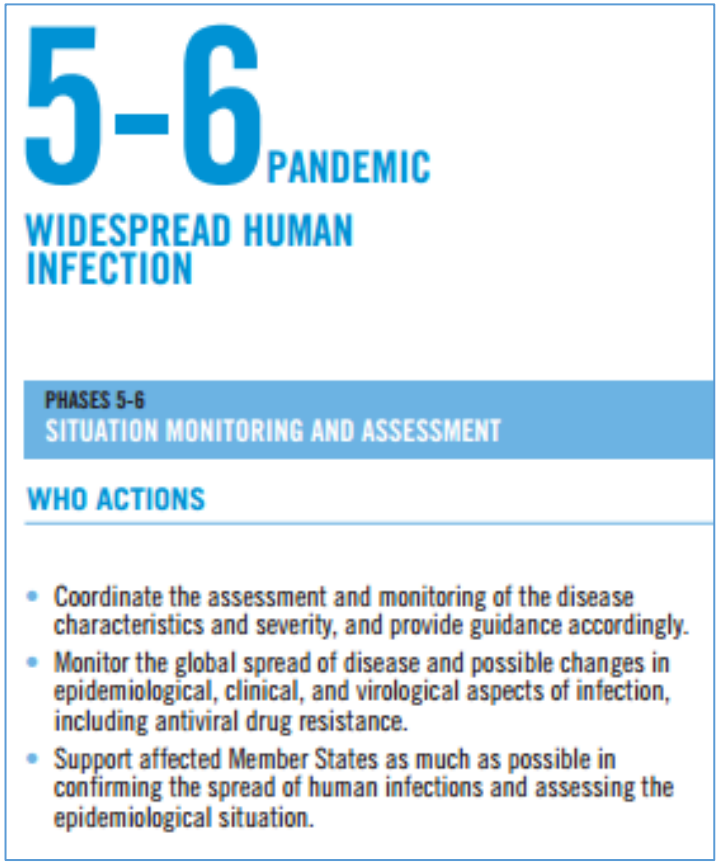
- WHOの対応
  ―2009年のパンデミック対応への批判を受け、リスクアセスメントに応じた対応を基本とすることに方針転換

- 日本政府の対応
  ―行動計画において病原性・感染力等に応じた対応が求められることを明記

2009年以前のリスクアセスメントの考え方



Community Strategy for Pandemic Influenza Mitigation in the United States (CDC, 2007)



Pandemic Influenza Preparedness and Response: A WHO Guidance Document (WHO, 2009)

Pandemic Potential of a Strain of Influenza A (H1N1): Early Findings

Christophe Fraser,[1*] Christl A. Donnelly,[1*] Simon Cauchemez,[1] William P. Hanage,[1] Maria D. Van Kerkhove,[1] T. Déirdre Hollingsworth,[1] Jamie Griffin,[1] Rebecca F. Baggaley,[1] Helen E. Jenkins,[1] Emily J. Lyons,[1] Thibaut Jombart,[1] Wes R. Hinsley,[1] Nicholas C. Grassly,[1] Francois Balloux,[1] Azra C. Ghani,[1] Neil M. Ferguson[1]†;

Andrew Rambaut,[2] Oliver G. Pybus[3];

Hugo Lopez-Gatell,[4] Celia M. Alpuche-Aranda,[5] Ietza Bojorquez Chapela,[4] Ethel Palacios Zavala[4];

Dulce Ma. Espejo Guevara[6];

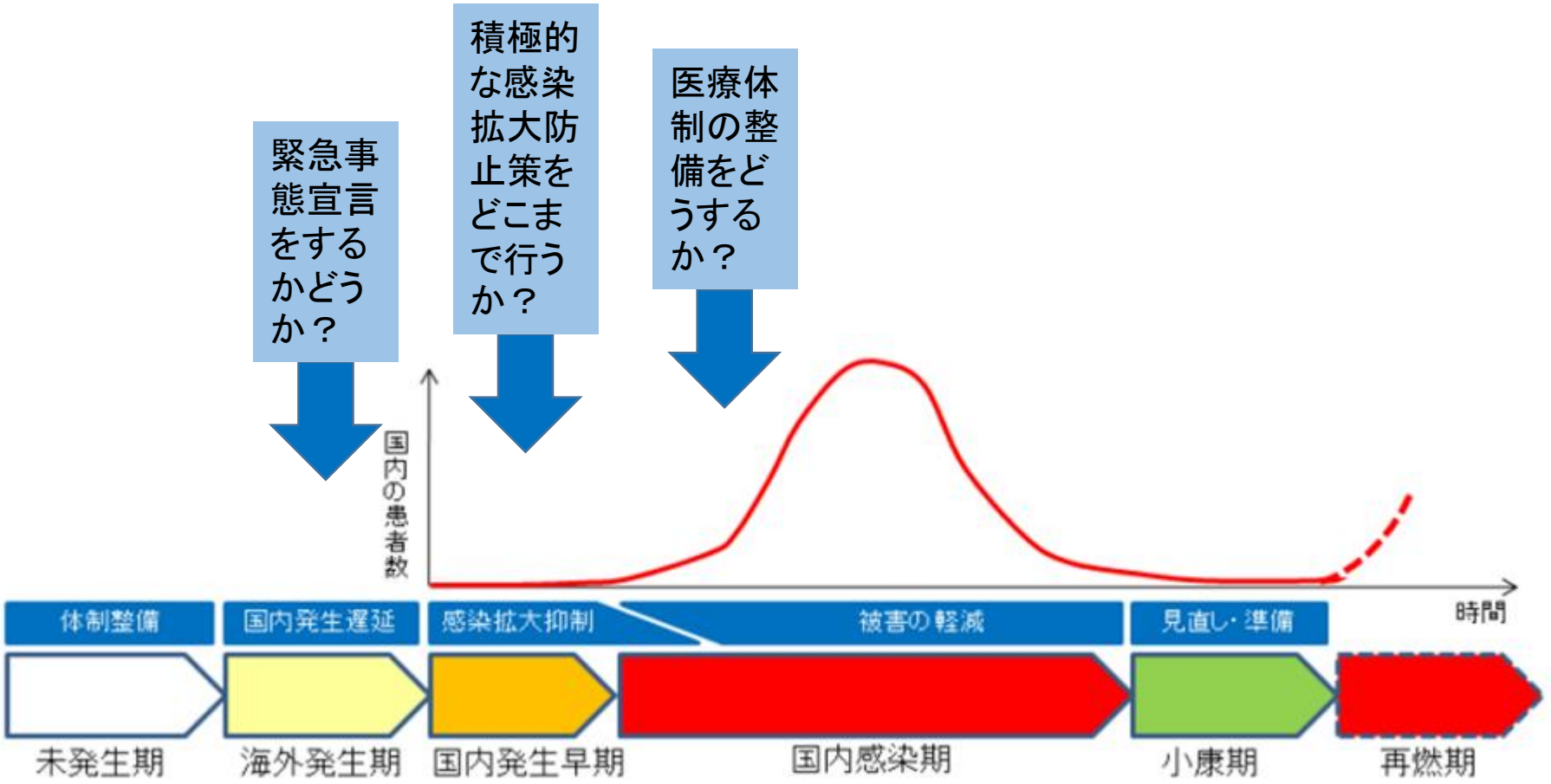
Francesco Checchi,[7] Erika Garcia,[7] Stephane Hugonnet,[7] Cathy Roth[7]

The WHO Rapid Pandemic Assessment Collaboration‡

A novel influenza A (H1N1) virus has spread rapidly across the globe. Judging its pandemic potential is difficult with limited data, but nevertheless essential to inform appropriate health responses. By analyzing the outbreak in Mexico, early data on international spread, and viral genetic diversity, we make an early assessment of transmissibility and severity. Our estimates suggest that 23,000 (range 6000 to 32,000) individuals had been infected in Mexico by late April, giving an estimated case fatality ratio (CFR) of 0.4% (range: 0.3 to 1.8%) based on confirmed and suspected deaths reported to that time. In a community outbreak in the small community of La Gloria, Veracruz, no deaths were attributed to infection, giving an upper 95% bound on CFR of 0.6%. Thus, although substantial uncertainty remains, clinical severity appears less than that seen in the 1918 influenza pandemic but comparable with that seen in the 1957 pandemic. Clinical attack rates in children in La Gloria were twice that in adults (<15 years of age: 61%; ≥15 years: 29%). Three different epidemiological analyses gave basic reproduction number (R_0) estimates in the range of 1.4 to 1.6, whereas a genetic analysis gave a central estimate of 1.2. This range of values is consistent with 14 to 73 generations of human-to-human transmission having occurred in Mexico to late April. Transmissibility is therefore substantially higher than that of seasonal flu, and comparable with lower estimates of R_0 obtained from previous influenza pandemics.

Science (Published online on May 11, 2009)

対策の意思決定とリスクアセスメントの必要性



なぜ発生早期のリスクアセスメントは困難なのか？

- 重症度評価の分子（重症者・死者数）はわかっても分母（軽症者を含めた感染者の全体像）がわからない
- 疫学像・重症度は流行の進展とともに変化し得る
  - ―感染する人口の変化
  - ―ウイルスの変異の可能性

現時点で発生早期に正確なリスクアセスメントする方法論は確立していない

WHO Guidanceの中でのアセスメントの内容

3つのコンポーネントについての評価が必要

- Transmissibility(感染性)
- Seriousness of clinical illness(臨床症状の重症度）
- Impact on the health care sector(ヘルスセクターへのインパクト）

Indicator	Representative parameters
Transmissibility	**From initial investigations** • Number of symptomatic cases of influenza/influenza-like illness per week • Basic reproduction number (R0): the average number of secondary cases generated from one case at the start of the epidemic • Generation time: the mean delay between the time of infection of an index case and the times of infection of secondary cases infected by the index case • Serial interval: the average length of time between symptom onset of individual cases and the persons they infect • Secondary attack rate: the proportion of individuals exposed to a known case who become infected, e.g. in a household where a case is discovered • Clinical attack rate (CAR): the proportion of the population that is symptomatically infected in a given time period. CAR is relatively simple to measure since it does not rely on detection of asymptomatic individuals. CARs can be calculated for different age groups, different settings (e.g. school, workplace) and different risk groups (e.g. pregnant women) • Spatial distribution of cases: mapping of countries/regions in which the virus has been detected in a given time period **From later investigations** • Attack rate: the proportion of the population that become infected in a given time period (e.g. as obtained from population serologic studies) • Incidence proportion: the proportion of people who develop new disease during a specified time period • Prevalence: the proportion of people who have disease at a specific time • Mode of transmission, particularly if new modes or previously uncommon modes of transmission (e.g. faecal–oral) are important
Seriousness of disease	**From initial investigations: molecular** • Sensitivity to available antiviral medicines • Presence of genetic markers that have been associated with increased risk of severe disease • Pre-existing immunity in the population, as measured by the level of cross-reactive antibodies **From initial investigations: clinical** • Case-fatality ratio (CFR): the proportion of symptomatic cases that die. Estimations of CFR are particularly difficult at the early stages of a pandemic. Since reliable case-fatality ratios will only be available in later stages of a pandemic, other parameters that may be of use are: – the proportion of cases of pneumonia that are influenza positive from sentinel surveillance that uses a representative sampling system – the ratio of hospital admissions and deaths attributed to respiratory causes to total admissions at the sentinel site – the proportion of hospital admissions attributed to respiratory causes that require mechanical ventilation or die – the proportion of influenza admissions, intensive-care admissions and deaths with pre-existing medical conditions **From later investigations** • Number of deaths attributed to influenza • Crude disease-associated mortality rate: the number of persons in a given population who die of the illness, expressed in terms of confirmed or suspected cases • The proportional distribution of cases by clinical illness (i.e. the proportions of cases that are asymptomatic/have mild illness/severe illness/die – the "clinical severity pyramid") • The number of cases of influenza-associated pneumonia and death compared with previous seasons or pandemic events based on comparisons with historical surveillance data

Indicator	Representative parameters
Impact	**From initial investigations** • Daily hospitalization rate: the number of persons in a given population who are hospitalized each day, expressed in terms of confirmed or suspected cases • The proportion of emergency department visits attributed to pandemic influenza • The proportion of emergency department visits that require hospitalization • The proportion of hospitalized cases that require admission to an intensive-care unit or require mechanical ventilation • The proportion of all hospital beds occupied by patients with pandemic influenza • The percentage of overall laboratory capacity directed to influenza testing **Potential societal impact parameters from other sectors** • Interruption of critical infrastructure and services • Work and school absenteeism • State of tourism • Sales of core capital (privately held land, livestock) • Gross Domestic Product • Border, travel and trade actions by countries • Nature of public perception

A basket of Indicators

- 致命率など単一の指標で評価することは不可能
- 多くの得られる指標を組み合わせて評価
- 季節性インフルエンザとの比較の重要性－パンデミック発生前からデータを蓄積する必要がある

日本でのパンデミック発生後リスクアセスメントのフレームワーク作成

- 特別措置法・行動計画・ガイドラインの議論の中で「病原性・感染力」に応じた対応をすることが基本方針となってきたがその評価方法についての議論はされてこなかった

- 厚生労働科研費「新型インフルエンザ発生時の公衆衛生対策の再構築に関する研究」の研究班と感染症研究所疫学センターとの共同でリスクアセスメントのフレームワーク作成の議論を開始

日本でのパンデミック発生後リスクアセスメントの現状と課題

- 発生早期には病原性・感染性等を示す明確な指標（致命率・再生産係数）は得られないということを前提として考えるべき
  - ―多くの間接的な指標から総合的に判断せざるを得ない

- 現在考えられているサーベイランス（平時のサーベイランス＋新型インフルエンザ発生時のサーベイランス）だけではリスクアセスメントには不十分
  - ―入院サーベイランスの強化、積極的疫学調査の実施体制の強化、イベントベースサーベイランスの導入などの対応が必要

- 新型インフルエンザ発生前から季節性インフルエンザなどに対するリスクアセスメントを実施し、実施体制の強化を図っていく必要がある
  - ―平時にやっていないことは非常時にできない