Pandemic Influenza:
The pharmacist as a key player in the preparedness for, and response to, a global threat

FIP MEPS
G8 – ACCESS TO MEDICINES
Thursday, 8 September 2005
09:00 – 10:00 a.m., Al Hambra 1

Dr. York F. Zöllner
Global Health Economics Manager
Solvay Pharmaceuticals GmbH
Hannover, Germany
Overview

1. Introduction
2. Pandemic phases
3. WHO checklist for influenza pandemic preparedness planning
4. ‘Supranational’ & national plans for pandemic preparedness & response
5. Conclusions
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Influenza Pandemics in the 20th Century

<table>
<thead>
<tr>
<th>Year</th>
<th>Subtype</th>
<th>Name</th>
<th>Est. n° deaths</th>
</tr>
</thead>
<tbody>
<tr>
<td>1918</td>
<td>H1N1</td>
<td>“Spanish Flu”</td>
<td>&gt; 40 million</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>(50-100 mill.?!?)</td>
</tr>
<tr>
<td>1957</td>
<td>H2N2</td>
<td>“Asian Flu”</td>
<td>&gt; 1 million</td>
</tr>
<tr>
<td>1968</td>
<td>H3N2</td>
<td>“Hong Kong Flu”</td>
<td>&gt; 1 million</td>
</tr>
</tbody>
</table>
6,000,000 DEATHS FROM INFLUENZA

This is estimate for world for past 12 weeks.

RECALLS BLACK DEATH

"Flu" five times deadlier than World War.

LONDON, Dec. 31. (Canadian Press via Reuters) — The Times' medical correspondent says that it seems reasonable to believe that about 8,000,000 persons perished from influenza pneumonia during the past 11 weeks. It has been estimated that war caused the death of 30,000,000 persons in four and a half years. Thus, the correspondent points out, influenza has proved itself five times deadlier than war.

Treasury Department
United States Public Health Service

INFLUENZA
Spread by droplets sprayed from nose and throat

Cover each COUGH and SNEEZE with handkerchief.

Spread by contact:

AVOID CROWDS.

If possible, WALK TO WORK.
Do not spit on floor or sidewalk.
Do not use common drinking cups and common towels.
Avoid excessive fatigue.
If taken ill, go to bed and send for a doctor.
The above applies also to colds, bronchitis, pneumonia, and tuberculosis.
Recent outbreaks…

…of highly pathogenic avian influenza (HPAI)

- East Asia  H5N1
- Canada      H7N3
- Netherlands H7N7
Future Pandemic

Global toll, most (!) conservative estimates:

- 233m outpatient visits
- 5.2m hospital admissions
- 7.4m deaths

Source: WHO checklist for influenza pandemic preparedness planning.
Influenza A virus reservoir
Influenza A virus
- Antigenic drift and antigenic shift -
## Confirmed human cases of Avian Influenza A(H5N1) reported to WHO

<table>
<thead>
<tr>
<th>period</th>
<th>cases</th>
<th>deaths</th>
<th>case-fatality rate</th>
</tr>
</thead>
<tbody>
<tr>
<td>26.12.03 – 10.03.04</td>
<td>35</td>
<td>24</td>
<td>69%</td>
</tr>
<tr>
<td>19.07.04. – 08.10.04</td>
<td>9</td>
<td>8</td>
<td>89%</td>
</tr>
<tr>
<td>16.12.04 – to date</td>
<td>68</td>
<td>25</td>
<td>37%</td>
</tr>
<tr>
<td><strong>total</strong></td>
<td><strong>112</strong></td>
<td><strong>57</strong></td>
<td><strong>51%</strong></td>
</tr>
</tbody>
</table>

Modeling pandemic preparedness scenarios: health economic implications of enhanced pandemic vaccine supply

Jeroen K. Medema\textsuperscript{a,}\textsuperscript{*}, York F. Zoellner\textsuperscript{b}, James Ryan\textsuperscript{c}, Abraham M. Palache\textsuperscript{a}

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Available online 9 April 2004

Abstract

Influenza pandemic planning is a complex, multifactorial process, which involves public health authorities, regulatory authorities, academia and industry. It is further complicated by the unpredictability of the time of emergence and severity of the next pandemic and the effectiveness of influenza epidemic interventions. The complexity and uncertainties surrounding pandemic preparedness have so far kept the various stakeholders from joining forces and tackling the problem from its roots. We developed a mathematical model, which shows the tangible consequences of conceptual plans by linking possible pandemic scenarios to health economic outcomes of possible intervention strategies. This model helps to structure the discussion on pandemic preparedness and facilitates the translation of pandemic planning concepts to concrete plans. The case study for which the model has been used shows the current level of global pandemic preparedness in an assumed pandemic scenario, the health economic implications of enhanced pandemic vaccine supply and the importance of cell culture-based influenza vaccine manufacturing technologies as a tool for pandemic control.

© 2004 Published by Elsevier B.V.
Strategies for containing an emerging influenza pandemic in Southeast Asia

Neil M. Ferguson¹,², Derek A.T. Cummings³, Simon Cauchemez⁴, Christophe Fraser¹, Steven Riley⁵, Aronrag Meeyai¹, Sopon Iamsirithaworn⁶ & Donald S. Burke³

Highly pathogenic H5N1 influenza A viruses are now endemic in avian populations in Southeast Asia, and human cases continue to accumulate. Although currently incapable of sustained human-to-human transmission, H5N1 represents a serious pandemic threat owing to the risk of a mutation or reassortment generating a virus with increased transmissibility. Identifying public health interventions that might be able to halt a pandemic in its earliest stages is therefore a priority. Here we use a simulation model of influenza transmission in Southeast Asia to evaluate the potential effectiveness of targeted mass prophylactic use of antiviral drugs as a containment strategy. Other interventions aimed at reducing population contact rates are also examined as reinforcements to an antiviral-based containment policy. We show that elimination of a nascent pandemic may be feasible using a combination of geographically targeted prophylaxis and social distancing measures, if the basic reproduction number of the new virus is below 1.8. We predict that a stockpile of 3 million courses of antiviral drugs should be sufficient for elimination. Policy effectiveness depends critically on how quickly clinical cases are diagnosed and the speed with which antiviral drugs can be distributed.

The continuing spread of H5N1 highly pathogenic avian influenza in wild and domestic poultry in Southeast Asia represents the most serious human pandemic influenza risk for decades⁴,⁵. Great potential benefits would be gained from any intervention able to contain the spread of a pandemic strain and eliminate it from the human population. However, the rapid rate of spread of influenza—as witnessed both in annual epidemics and past pandemics⁴,⁵—poses a significant challenge to the design of a realistic control strategy.

The basic reproduction number, \( R_0 \), quantifies the transmissibility of any pathogen, which is defined as the average number of secondary cases generated by a typical primary case in an entirely susceptible population. A disease can spread if \( R_0 > 1 \), but if \( R_0 < 1 \), chains of if applied at the source of a new pandemic, when repeated human-to-human transmission is first observed? Here we address this question, and focus on identifying the threshold level of transmissibility below which containment of any new pandemic strain might be feasible.

**Modelling pandemic spread**

We modelled pandemic spread in Southeast Asia, as this region remains the focus of the ongoing avian H5N1 epidemic and is where most human cases have occurred. Data availability led us to model Thailand rather than any perceived greater risk of emergence compared to other countries in the region; however, we believe our conclusions are also valid for other parts of Southeast Asia.
Containing Pandemic Influenza at the Source

Ira M. Longini Jr.,1* Azhar Nizam,1 Shufu Xu,1
Kumnuan Ungchusak,2 Wanna Hanshaoworakul,2
Derek A. T. Cummings,3 M. Elizabeth Halloran1

Highly pathogenic avian influenza A (subtype H5N1) is threatening to cause a human pandemic of potentially devastating proportions. We used a stochastic influenza simulation model for rural Southeast Asia to investigate the effectiveness of targeted antiviral prophylaxis, quarantine, and pre-vaccination in containing an emerging influenza strain at the source. If the basic reproductive number \( R_0 \) was below 1.60, our simulations showed that a prepared response with targeted antivirals would have a high probability of containing the disease. In that case, an antiviral agent stockpile on the order of 100,000 to 1 million courses for treatment and prophylaxis would be sufficient. If pre-vaccination occurred, then targeted antiviral prophylaxis could be effective for containing strains with an \( R_0 \) as high as 2.1. Combinations of targeted antiviral prophylaxis, pre-vaccination, and quarantine could contain strains with an \( R_0 \) as high as 2.4.

The world may be on the brink of an influenza pandemic (1–4). Avian influenza A (subtype H5N1) is causing widespread outbreaks among poultry in Southeast (SE) Asia, with sporadic transmission from birds to humans (5) and limited probable human-to-human transmission (6). Should an avian virus reassort with a human virus, such as influenza A subtype H3N2, within a dually infected human host or reassort in a nonhuman mammalian species, or if mutation of the virus occurs, the resulting new variant could be capable of sustained human-to-human transmission. The outbreak among humans would then spread worldwide via the global transportation network more rapidly than adequate supplies of vaccine matched to the new variant could be manufactured and distributed (1, 7). The pressing public health questions are whether and how we can contain the spread of an emerging strain at the source or at least slow the initial spread to give time for vaccine development. We used a discrete-time stochastic simulation model of influenza spread within a structured geographically distributed population of 500,000 people in SE Asia to compare the effectiveness of various intervention strategies against a new strain of influenza. Here we examine the effectiveness of the targeted use of influenza antiviral agents (8–12), quarantine, and pre-vaccination with a poorly matched, low-efficacy vaccine in containing the spread of the disease at the source.

We used information about rural SE Asia (13, 14) to construct the model population. Our goal was to represent the contact connectivity of a typical rural SE Asian population. The model population of 500,000 people was distributed across a space of 5625 km², yielding a density of 89/km², which is approximately the population density of rural SE Asia (13). The 500,000 people were partitioned into 36 geographic localities. This model is an extension of a model used to simulate interventions against pandemic influenza in the United States (12).

The model [see the supporting online material (SOM) for details] represents the number of close and casual contacts that a typical person makes in the course of a day. The age and household size distributions of the population are based on the Thai 2000 census (13). Many of the mixing group sizes and distributions are based on a social network study of the Nang Rong District in rural Thailand (14). We constructed the social network for contacts sufficient to transmit influenza as a large set of connected mixing groups. The close contact groups consist of households, household clusters, preschool groups, schools, and workplaces; and the casual contact groups consist of other social settings (such as markets, shops, and temples) and a single regional 40-bed hospital. All people can

(first on Science Express, 03 Aug 2005)
http://www.sciencemag.org/cgi/content/abstract/1115717
WHO statement

The World Health Organization (WHO) welcomes the pandemic influenza response modelling papers published in the journals Science and Nature this week. This is work done by expert scientists using two different sets of assumptions. The models provide additional information which will help WHO and public health officials in our Member States to improve pandemic influenza preparedness planning.

Both papers suggest that a combination of early, targeted use of antiviral medicines and social distancing (measures such as cancelling mass gatherings and closing schools) can stop a pandemic, or at least slow its spread. There would be significant practical challenges to implementing such measures, but the enormous social trauma and human suffering that an influenza pandemic could inflict creates an obligation to thoroughly explore all proposals to limit this damage.

Several countries have already purchased stockpiles of antiviral drugs and WHO has taken steps to establish an international stockpile. National and international stockpiles of antiviral drugs may be an essential component of comprehensive international pandemic preparedness, that also includes vaccine development and disease surveillance.
Drugs, Quarantine Might Stop A Pandemic Before It Starts

Thirty-six years after the last influenza pandemic, researchers wonder whether they can make these global disasters a thing of the past.

It might just work. With military-style planning, a big stash of pills, and a lot of luck, the world might be able to stop a nascent influenza pandemic dead in its tracks, two new modeling studies conclude.

The models, published online this week in *Nature* and *Science* (www.sciencemag.org/cgi/content/abstract/1115717), are the first attempts to estimate the power of the antiviral actions because until now, there’s been little if any official commitment to such a plan.

The World Health Organization (WHO), which the researchers say would have to lead the effort, is “interested,” says the agency’s pandemic chief, Margaret Chan. Rich countries are stockpiling oseltamivir to protect their own populations, but they have no plans yet for shipping it to the cradle of a pandemic. Nor are the only way to prevent disaster in the majority of countries unable to afford vaccines or drugs at all, notes Arnold Monto of the University of Michigan, Ann Arbor. Oseltamivir would make those who get the flu less infectious to others, but by far its most important task would be to prevent infection in those exposed to the virus.

Now, that idea has been put to the test. Longini and his colleagues simulated an imaginary population of 500,000 people who live, work, and move about in rural Southeast Asia. Meanwhile, Ferguson and his colleagues built a model based on the 85 million people living in Thailand and a 100-kilometer-wide border zone in neighboring countries. Both then introduced a pandemic virus and looked at how well different containment strategies performed.

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# Inter-pandemic period

<table>
<thead>
<tr>
<th>Phase</th>
<th>Characterisation</th>
<th>Public health goals</th>
</tr>
</thead>
</table>
| 1     | • No new virus subtypes detected in humans  
       • Risk of human infection considered **low** | • Strengthen pandemic preparedness |
| 2     | • No new virus subtypes detected in humans  
       • However, circulating *animal* influenza virus poses **substantial** risk of *human disease* | • Minimise risk of tx to humans  
       • Detect & report rapidly if tx occurs |
## Pandemic Alert Period

<table>
<thead>
<tr>
<th>Phase</th>
<th>Characterisation</th>
<th>Public health goals</th>
</tr>
</thead>
<tbody>
<tr>
<td>3</td>
<td>• Human infection(s) with new subtype, but <strong>no</strong> human-to-human spread</td>
<td>• Rapid characterisation of new subtype</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Early detection, notification &amp; response of additional cases</td>
</tr>
<tr>
<td>4</td>
<td>Small cluster(s) with <strong>limited</strong> human-to-human transmission (!)</td>
<td>• Contain new virus within limited foci or delay spread</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• <strong>Vaccine development</strong></td>
</tr>
<tr>
<td>5</td>
<td>Larger cluster(s); human-to-human spread still localised but <strong>increasingly transmissible</strong></td>
<td>• Maximise efforts to contain or delay spread</td>
</tr>
</tbody>
</table>
## Pandemic Period

<table>
<thead>
<tr>
<th>Phase</th>
<th>Characterisation</th>
<th>Public health goals</th>
</tr>
</thead>
<tbody>
<tr>
<td>6</td>
<td><strong>Pandemic:</strong> Increased and sustained transmission in the general population</td>
<td>Minimise <strong>impact</strong> of the pandemic</td>
</tr>
</tbody>
</table>

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* Source: WHO checklist for influenza pandemic preparedness planning
1. Preparing for an Emergency

- **Getting started**
  - importance, aim, funding, designate responsibles

- **Command and control**
  - management, decision-making, SOPs

- **Risk assessment**
  - model the impact of pandemic:
    - n° outpatient visits, hospitalisations, deaths
    - economic damage
  - without & with intervention

- **Communication**
  - public domain
  - within response team
Risk Assessment

FluAid, FluSurge

- test software (free)
- by: CDC
- aim: to assist state and local-level planners in preparing for the next influenza pandemic
- provides only a range of estimates of impact in terms of deaths, hospitalizations, and outpatients visits due to pandemic influenza

URL:
http://www2.cdc.gov/od/fluaid/
http://www.cdc.gov/flu/flusurge.htm
Population Numbers By Age Group

1. Enter State: California

<table>
<thead>
<tr>
<th>Age Group</th>
<th>0.18 yrs</th>
<th>19-64 yrs</th>
<th>65+ yrs</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>California</td>
<td>8951653</td>
<td>19744884</td>
<td>3571964</td>
<td>32268301</td>
</tr>
</tbody>
</table>

High risk percentages by age group

<table>
<thead>
<tr>
<th>Age Group</th>
<th>0.18 yrs</th>
<th>19-64 yrs</th>
<th>65+ yrs</th>
<th>Weighted Average</th>
</tr>
</thead>
<tbody>
<tr>
<td>California</td>
<td>6.4</td>
<td>14.4</td>
<td>40.0</td>
<td>15</td>
</tr>
</tbody>
</table>
1. Preparing..., cont’d

• Legal and ethical issues
  
  – Legal issues: “over-ruling”...
    • of existing pharm. legislation:
      – authorisation process
      – off-license use of drugs
    • of human rights
      – enforcement of quarantine
      – compulsory vaccination
      – use of privately owned buildings as clinics
  
  – Ethical issues: “cultural acceptability”...
    • of selected isolation
    • of targeted vaccination/treatment of pre-defined groups
2. Surveillance

- **Inter-pandemic surveillance**
  - case definitions, sampling rules
  - sentinel system
  - unexplained deaths

- **Enhanced surveillance (≥ phase 2)**
  - early warning
  - monitoring incoming travellers, people exposed to infected birds/animals, healthcare workers (HCWs)

- **Pandemic surveillance**
  - potentially *discontinue* (!) early warning systems, in order to free resources to monitor other indicators
    - hospital admissions
    - deaths in suspected/confirmed cases of pandemic infection
    - workforce absenteeism in “essential” services
    - vaccines use, effectiveness, ADRs,…
3. Case investigation and treatment

- **Diagnostic capacity**
  - Local laboratory (routine diagnosis, typing & sub-typing)
  - Reference laboratory (confirmation, determination)

- **Epidemiological investigation & contact management**
  - *exposure* (rates & source),
  - *transmission* (likelihood of human-to-human ~)

- **Clinical management**
  - Case management
    - decide on treatment centre, admission criteria, specimen collection, treatment protocols
  - Infection control in healthcare settings
    - biosafety standards/guidelines, training, equipment
4. Preventing spread of the disease in the community

• Public health measures
  – personal respiratory hygiene
  – community infection control programmes
    • routine vaccination, during events with pandemic potential, of humans with bird/animal contact
    • ensure AV supplies for early (!) treatment
  – social distancing and quarantine
  – travel and trade restrictions
4. Preventing the spread, cont’d

• Vaccine programmes
  – *Routine* vaccine programmes
    • define target coverage
    • develop strategy (incl. funding) to *reach* target
    • ensure supply
  
  – *Pandemic-strain* vaccine programmes
    • *Countries with* domestic manufacturing base:
      develop timelines for manufacture & expedited testing, licensing, distribution

    • *Countries without* domestic manufacturing base:
      develop contingency plans for procuring vaccine
Solvay Pharmaceuticals will supply Norway with special vaccines in the event of an influenza pandemic

February 17, 2005 at 8:30 AM (Brussels Time)

SOLVAY PHARMACEUTICALS today announce that they have signed an agreement with the Norwegian authorities whereby Solvay Pharmaceuticals will supply influenza vaccines to Norway in the case of a pandemic. Thanks to the development of a new technology involving cell culture, Solvay Pharmaceuticals expects to have much greater flexibility for delivering special influenza vaccines in the event of a pandemic.

The agreement with Norway is the first of its kind for Solvay Pharmaceuticals; more are expected to follow. The agreement represents a type of insurance for which a yearly premium is paid. Should the World Health Association determine that a pandemic is occurring, they will supply the seed virus and we will make a special influenza vaccine against that particular viral strain. The agreement with Norway is for 4 million doses of this special vaccine.

An influenza pandemic occurs when a new influenza virus appears against which the human population has no immunity, resulting in several simultaneous epidemics worldwide with large numbers of infected people and deaths.

The World Health Organization (WHO) and influenza experts worldwide are concerned that the appearance and widespread distribution of an avian influenza virus, influenza A(H5N1), has the potential to ignite a pandemic. Given this current threat, the WHO has urged all countries to develop or update their influenza pandemic preparedness plans for responding to the widespread socioeconomic disruptions that would result.

Solvay Pharmaceuticals, one of the leading producers of influenza vaccines in Europe, is engaged in negotiations with other European authorities about the supply of vaccines in the case of a pandemic. The company has developed an innovative method to produce vaccines and has obtained marketing approval from the Dutch regulatory authorities for this cell culture technology. At its site in Weesp, The Netherlands, Solvay Pharmaceuticals has built a new manufacturing plant.

Sjir Kok, Manager of the Business Group Influenza at Solvay Pharmaceuticals, said: "We are very pleased with the agreement between Solvay and Norway. At the moment this new cell
Pandemic-strain vaccine programmes, cont’d

• **establish priority list, e.g.**
  1. bird cullers; veterinarians, farmers
  2. healthcare workers
  3. workers in other essential services

• **decide on payment**
  • in priority groups
  • in non-priority groups

• **decide on safe storage, distribution & administration**
  • cold chain, theft prevention
  • location of mass immunisation clinics
  • record-keeping of administered vaccine (esp. two-dose programme!)
5. Maintaining essential services

• Health services
  – Health service facilities
    • primary, secondary & tertiary referral patterns
    • emergency admissions, intensive care
    • alternative sites (schools, gyms, nursing homes, tents)
  – Health service personnel
    • staff matrix (N x level)
    • further recruitment (volunteer organisations, …)
    • psychological support for HCW
  – Health service supplies
    • stockpiling capacities (incl. protective equipment)
    • antibiotics suitable to treat complications
  – Excess mortality
    • max. disposal capacity of corpses using “culturally appropriate methods”
5. Maintaining..., cont’d

- Other essential services
  - Police
  - Fire fighters
  - Armed Forces
  - Gov’t officials, esp. crisis management
  - Utility workers (water, gas, electricity, communication systems)
  - Funeral/Mortuary services
  - Transportation of goods, food, medical supplies
6. Research and evaluation

• Research during phase 2 and beyond
  – Outbreak with widespread animal/bird cases, but limited human cases:
    • determine risk factors
  – Outbreak with widespread human cases
    • collect impact measures

• From research to action
  – Ensure evaluation of response measures after 1st wave
  – Ensure all results are made public
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Prevention and control of influenza pandemics and annual epidemics

URGES member states:

• (1) [...] to establish and implement strategies to increase vaccination coverage of all people at high risk, including the elderly and people with underlying disease, with the goal of attaining vaccination coverage of the elderly population of at least **50% by 2006** and **75% by 2010**;

• (2) [...] to assess the disease **burden and economic impact** of annual influenza epidemics as a basis for framing and implementing influenza prevention policies… .

“Member States agreed to make additional efforts to improve uptake on their territory in accordance with their own recommendations and to achieve the WHO target of 75% in high risk groups before 2010. It was also noted that the changing demographic profile of the EU population would result in increasing number of elderly people falling within the current target groups.”

“At-risk” population, EU-25

65+ : 75.4 million
0-4 : 23.2 million
5-49, medical conditions : 36.8 million
health care workers : 4.6 million
50-64 : 83.4 million

EU-25 total : 223.4 million

49.1% at risk
EU-25 population at risk

Cyprus 41.6%

EU-25 avrg: 49.1%

UK 56.4%

annual vaccination coverage: 13.8% !

Source: Medema JK et al. 2005, forthcoming
"Bottleneck":

Current vaccines:

1 dose (trivalent) = 1 embryonated chicken egg!
Culture Substrates for Vaccine production

Embryonated chicken eggs

Cell culture (mammalian)

OR

MDCK cells

Vero cells
• Access:
  http://www.hhs.gov/nvpo/pandemicplan/

• Issued by:
  Dept. of Health & Human Services
  (26 Aug 2004)

• Status:
  Draft under consultation
1. Vaccines — Preparedness measures

- increase proportion of public sector purchase
- assure year-round supply of eggs
- **expansion** of production capacity and **diversification** of influenza manufacturing technology, in particular: **cell culture**
- rapidly develop, evaluate, and license vaccines against pandemic strain; produce them in sufficient quantity to protect the population (monovalent vaccine option)
USA, cont’d

2. Vaccines — Distribution & Prioritisation

• targeted priority groups
  – with occupational risk of infection or transmission:
    • healthcare workers
  – who provide essential public services
    • public health
    • safety
• population at increased risk
• strain’s risk pattern to be assessed as pandemic unfolds!
3. Military Pharmacists

- Strategic National Stockpile (SNS)
  
  http://www.bt.cdc.gov/stockpile/index.asp

  “CDC's Strategic National Stockpile (SNS) has large quantities of medicine and medical supplies to protect the American public if there is a public health emergency (terrorist attack, flu outbreak, earthquake) severe enough to cause local supplies to run out. Once Federal and local authorities agree that the SNS is needed, medicines will be delivered to any state in the U.S. within 12 hours. Each state has plans to receive and distribute SNS medicine and medical supplies to local communities as quickly as possible.”
National Stockpile
Table 1. Estimated excess U.S. health care burden from an influenza pandemic

<table>
<thead>
<tr>
<th></th>
<th>Annual influenza</th>
<th>Pandemic Estimates</th>
</tr>
</thead>
<tbody>
<tr>
<td>Deaths</td>
<td>20,000-40,000</td>
<td>89,000 - 207,000</td>
</tr>
<tr>
<td>Hospitalizations</td>
<td>114,000</td>
<td>314,000 - 733,000</td>
</tr>
<tr>
<td>Outpatient visits</td>
<td>~5,000,000-10,000,000</td>
<td>18,000,000- 42,000,000</td>
</tr>
</tbody>
</table>

Germany

- **Access:**
  
  http://www.rki.de/cln_006/nn_387378/DE/Content/InfAZ/I/Influenza/Influenzapandemieplan.html

- **Issuer:**
  
  Robert-Koch-Institut (RKI)

- **Status:**
  
  Final version, July 2005
Germany, cont.

• some AV stockpiling, AV “pool” discussed
• only for treatment, not prophylaxis
• underlying principles of vacc. prioritisation outlined, but no decision made
• pharmacists to *promote routine vacc.* in order for manufacturers to increase & diversify production capacities

Pandemieplan – Apotheker sind einbeyogen. PZ 30 (2005)
United Kingdom

- **Access:**
  www.dh.gov.uk/PolicyAndGuidance/EmergencyPlanning/PandemicFlu/fs/en

- **Issuer:**
  Department of Health

- **Status:**
  Final plan, March 2005
Immunisation policy

- Regularly review influenza immunisation policy
- Maintain pneumococcal immunisation programme
- Develop policy for immunising poultry workers in the event of an avian influenza outbreak
- Consider maintaining a small stockpile of the annual influenza vaccine for use should an outbreak of highly pathogenic avian influenza occur in poultry in the UK
- Establish policy options for pandemic immunisation
- Estimate vaccine needs
- Plan for pandemic vaccine purchase and supply
- Plan for pandemic vaccine distribution and administration
- Plan for monitoring uptake and possible adverse reactions

Antiviral strategy

- Agree options for use of antivirals
- Estimate antiviral needs
- Establish arrangements for antiviral supply, distribution and administration
- Plan monitoring of effectiveness
United Kingdom, cont’d

17. The table below summarises the estimated additional burden on health service activity based on a 25% clinical attack rate and overall case fatality rate over a pandemic period (figures rounded):

<table>
<thead>
<tr>
<th>Population</th>
<th>People Ill</th>
<th>GP Consultations</th>
<th>Minimum total additional hospitalisations</th>
<th>Excess deaths</th>
</tr>
</thead>
<tbody>
<tr>
<td>1000</td>
<td>250</td>
<td>50</td>
<td>2</td>
<td>1</td>
</tr>
<tr>
<td>100,000</td>
<td>25,000</td>
<td>5000</td>
<td>150</td>
<td>100</td>
</tr>
<tr>
<td>1,000,000</td>
<td>250,000</td>
<td>50,000</td>
<td>1500</td>
<td>1000</td>
</tr>
<tr>
<td>England 49,138,831*</td>
<td>12.1m</td>
<td>2.4m</td>
<td>65,900</td>
<td>44,400</td>
</tr>
<tr>
<td>UK*</td>
<td>13m</td>
<td>2.9m</td>
<td>79,600</td>
<td>53,700</td>
</tr>
</tbody>
</table>

*2001 Census

0.37%
• **Access:**

• **Issuer:**
  Ministry of Health and Solidarity

• **Status:**
  Final plan, May 2005
France, cont’d

*Priority* target population: 3,645,000

of which:  
- HCW and relatives 1.3m  
- security and rescue staff 600,000  
- essential public services 45,000  
- transport & communication 1.2m  
- industry 500,000
Pharmacists / Military Pharmacists

Defense
- preserve strategic military function (deterrence, communication)
- use specific military knowledge
  - continuity of gov’t action
  - overall security
  - assist general population

Army activity
- Restrict access to sites of medical intervention, alert services and crisis management

Pharmaceutical Committee to sit with industry and resolve research, development, authorisation, delivery and stocking issues
Canada

- **Access**
  www.phac-aspc.gc.ca/cpip-pclcpi/index.html

- **Issuer**
  Public Health Agency of Canada

- **Status**
  Final plan, Sept 2004
Canada, cont’d

Vaccine Programs Checklist (3.3.1.2.)

- Enhance annual influenza vaccination coverage rates in “high-risk” groups
- Increase annual vaccination rates among healthcare & essential services workers
- Develop contingency plans for storage, distribution and admin. of vaccine
Canada, cont’d

Table 1
Estimated number of cases by outcome

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Attack Rate 15%</th>
<th></th>
<th>Attack Rate 35%</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Mean number</td>
<td>5th Percentile</td>
<td>95th Percentile</td>
<td>Mean number</td>
</tr>
<tr>
<td>Death</td>
<td>17,768</td>
<td>10,544</td>
<td>24,954</td>
<td>41,459</td>
</tr>
<tr>
<td>Hospitalization</td>
<td>46,639</td>
<td>34,042</td>
<td>59,166</td>
<td>108,824</td>
</tr>
<tr>
<td>Outpatient Care</td>
<td>2,086,327</td>
<td>2,027,496</td>
<td>2,145,282</td>
<td>4,868,097</td>
</tr>
<tr>
<td>Ill, no formal care</td>
<td>2,394,443</td>
<td>2,335,458</td>
<td>2,455,967</td>
<td>5,587,035</td>
</tr>
<tr>
<td>TOTAL</td>
<td>4,545,177</td>
<td>4,407,545</td>
<td>4,685,464</td>
<td>10,605,415</td>
</tr>
</tbody>
</table>
Overview

1. Introduction
2. Pandemic phases
3. WHO checklist for influenza pandemic preparedness planning
4. ‘Supranational’ & national plans for pandemic preparedness & response
5. Conclusions
Conclusions

- Military-style implementation of pandemic plan is a must
- Antivirals can help bridging the time gap until pandemic vaccine becomes available; use ‘post-infection’ rather than prophylactic
- Social distancing indispensable to counteract further spread
- Maintenance of public order, safe-guarding of pharmaceuticals & vaccine supply, prioritisation
- Vital to increase inter-pandemic routine vacc. coverage
- Investment in tissue-culture technologies is key
- Advance purchasing agreements may be an option for some countries
- Stockpiling of H5N1 vaccine is recommended