ICMS2008（国際危機管理シンポジウム）

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# Influenza Pandemic Preparedness from Global Perspective

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# Potential Impact of Next influenza Pandemic

- 30-40 % of population may develop illness
- Rapid global spread
- Large number of deaths (at least a few millions)
- Social disruption
- Huge economic loss

# Avian Influenza H5N1

- Unprecedented outbreaks since 2003
  - More than 60 countries affected
  - A total of 385human cases from 15 countries
- Potential to cause a next influenza pandemic

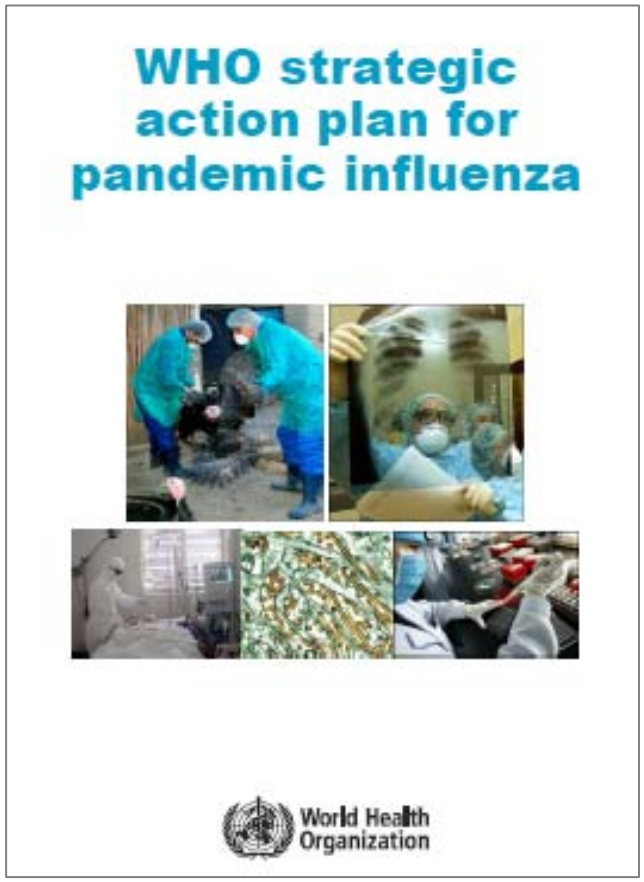
# Phases of pandemic alert in WHO global influenza preparedness plan

| | | |
|---|---|---|
| Inter-pandemic phase<br>New virus in animal, no human cases | Low risk of human cases | 1 |
| | Higher risk of human cases | 2 |
| Pandemic alert<br>New virus causes human cases | No or very little human-to-human transmission | 3 |
| | Evidence of increased human-to-human transmission | 4 |
| | Evidence of significant human-to-human transmission | 5 |
| Pandemic | Efficient and sustained human-to-human transmission | 6 |

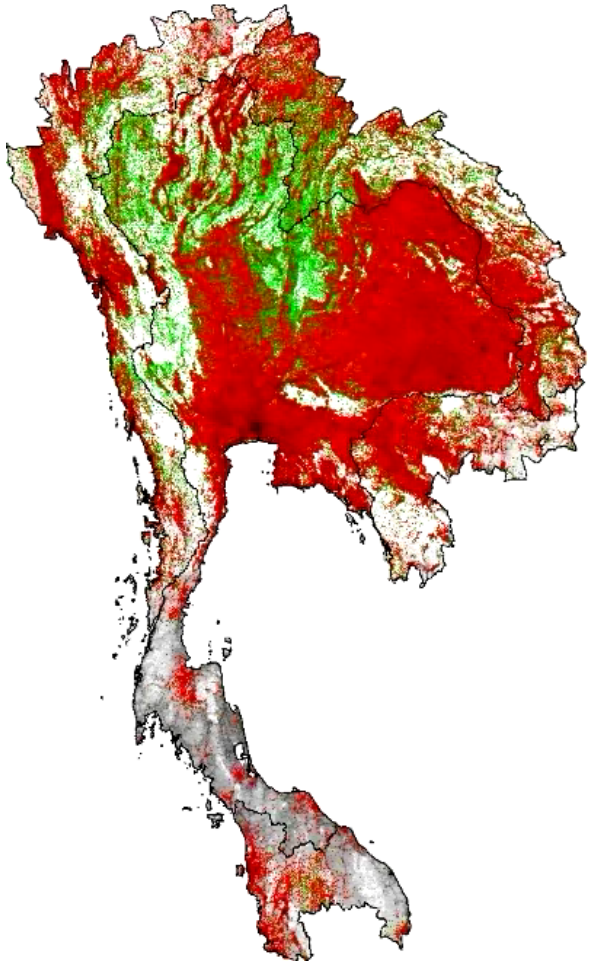
Current phase

# WHO Strategic Actions for Pandemic Influenza

1. Reduce human exposure to the H5N1 virus
2. Strengthen the early warning system
3. Intensify rapid containment operations
4. Build capacity to cope with a pandemic
5. Coordinate global scientific research and development



# Possibility of early containment of potential pandemic



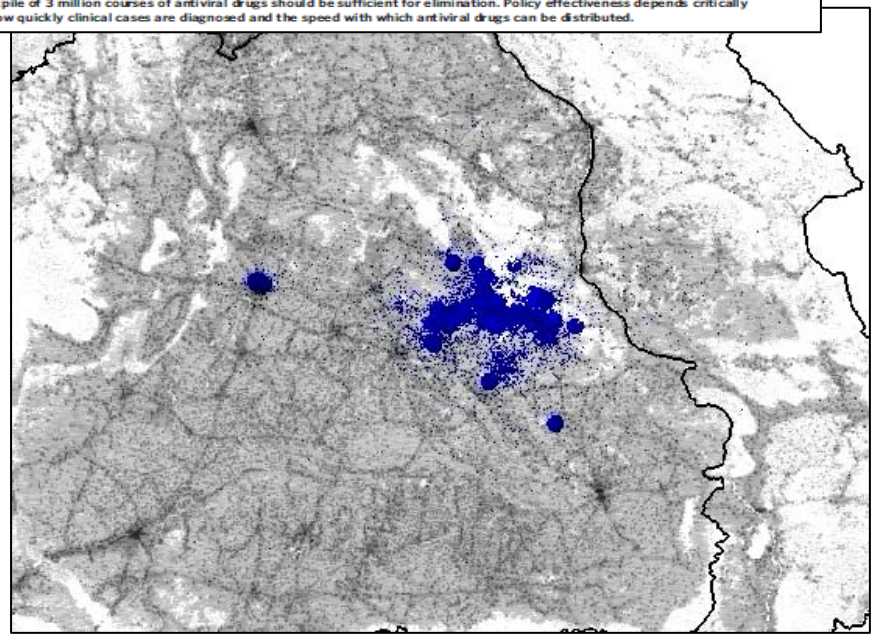
Vol 437|8 September 2005|doi:10.1038/nature04017 nature

ARTICLES

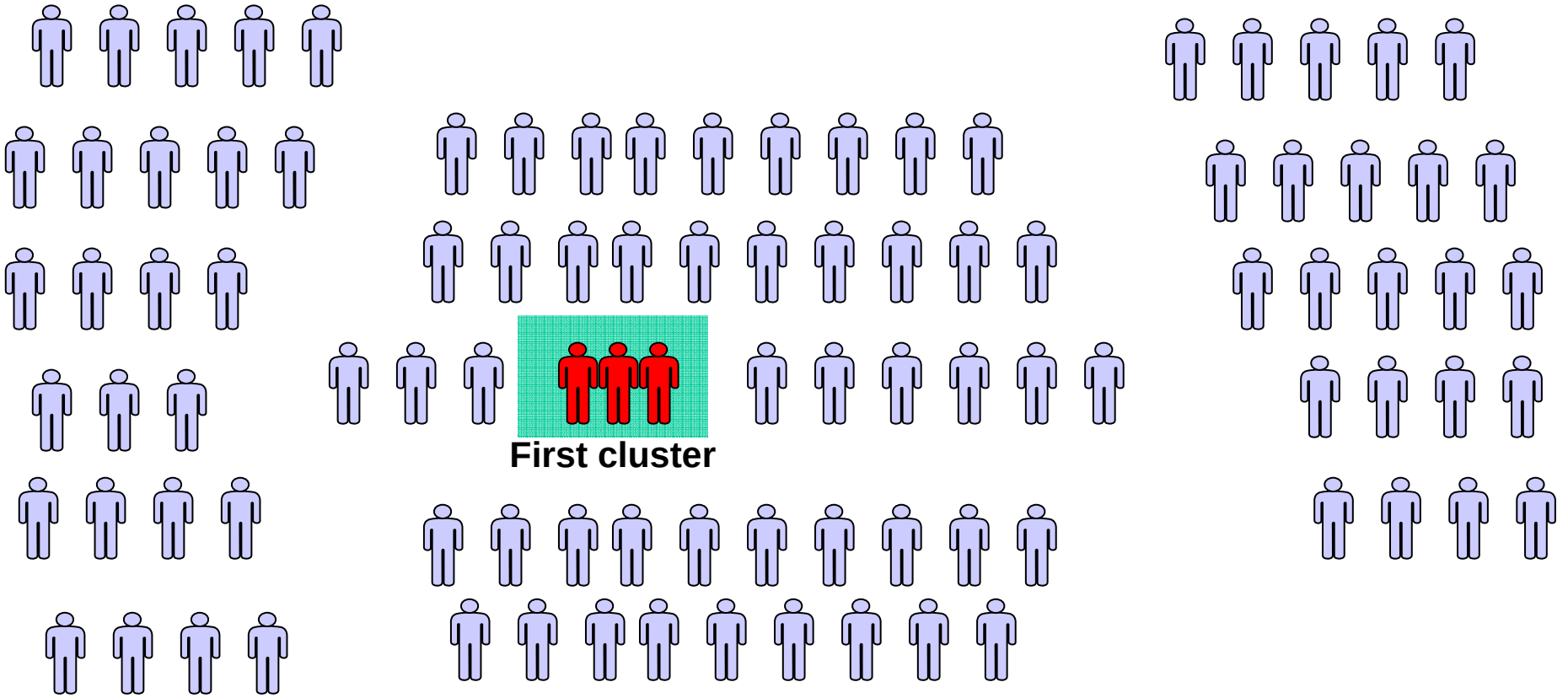
## Strategies for containing an emerging influenza pandemic in Southeast Asia

Neil M. Ferguson[1,2], Derek A.T. Cummings[3], Simon Cauchemez[4], Christophe Fraser[1], Steven Riley[5], Aronrag Meeyai[3], Sopon Iamsirithaworn[6] & Donald S. Burke[3]

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.



# Concept of Early Containment



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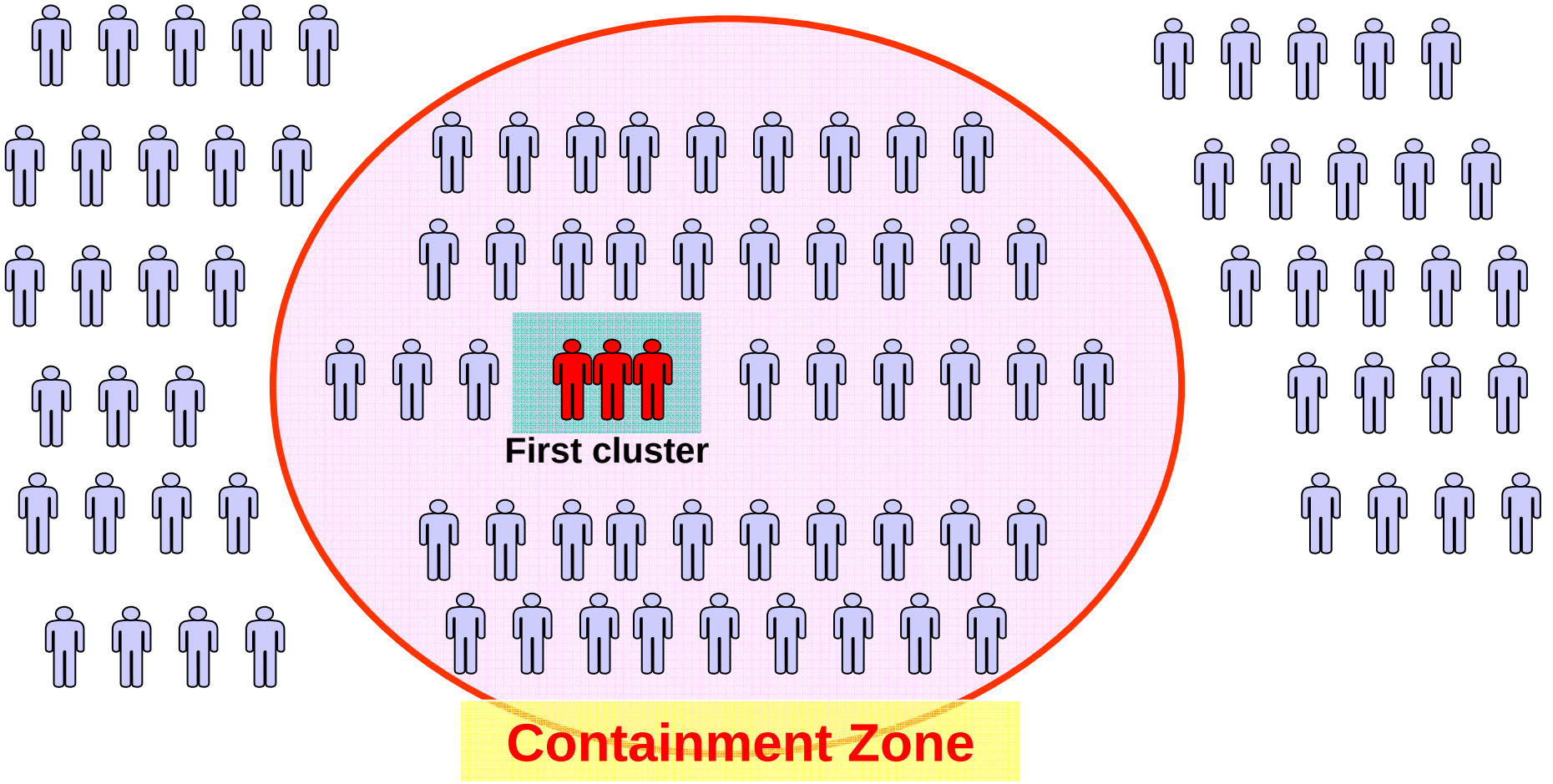

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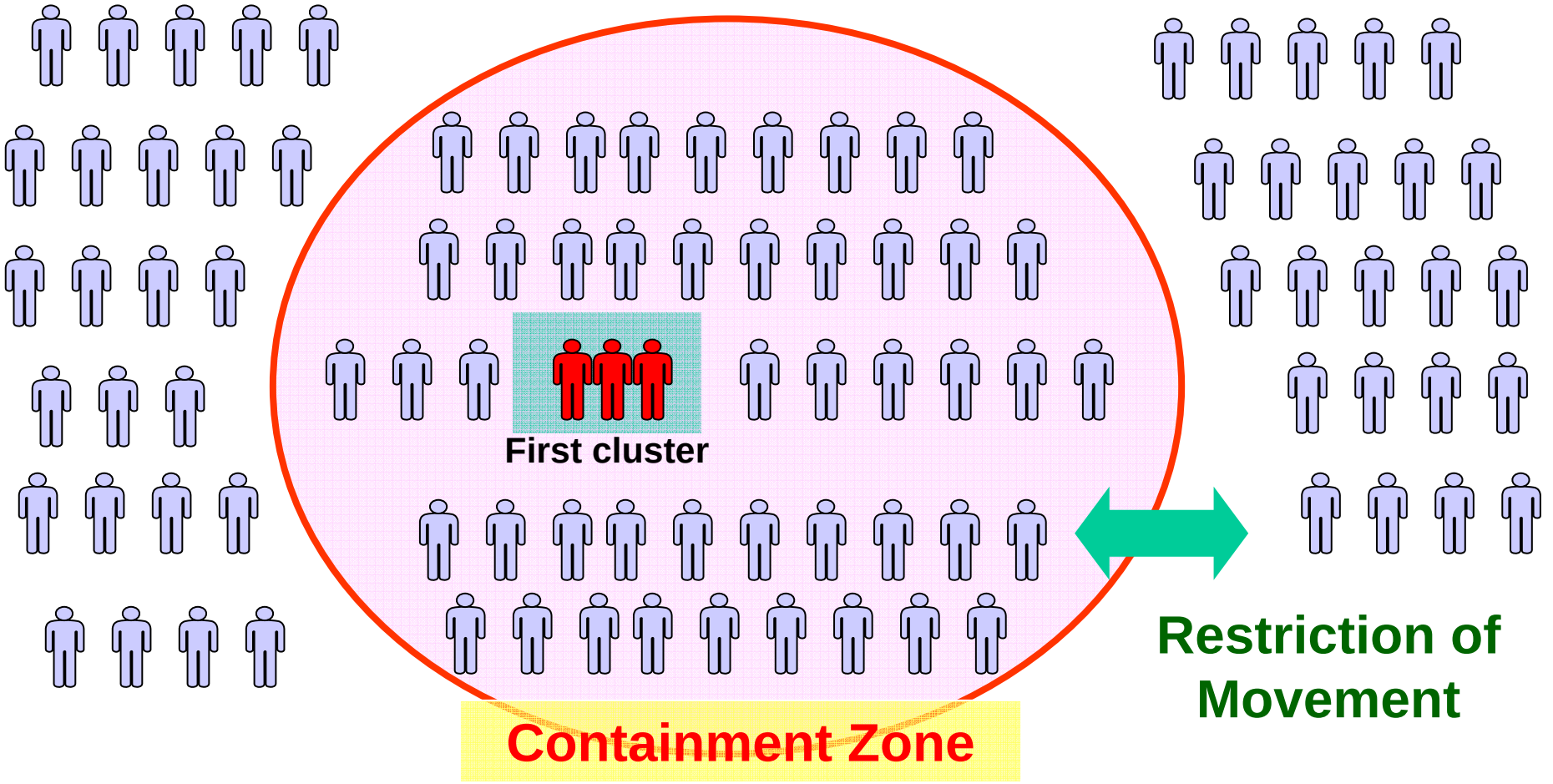

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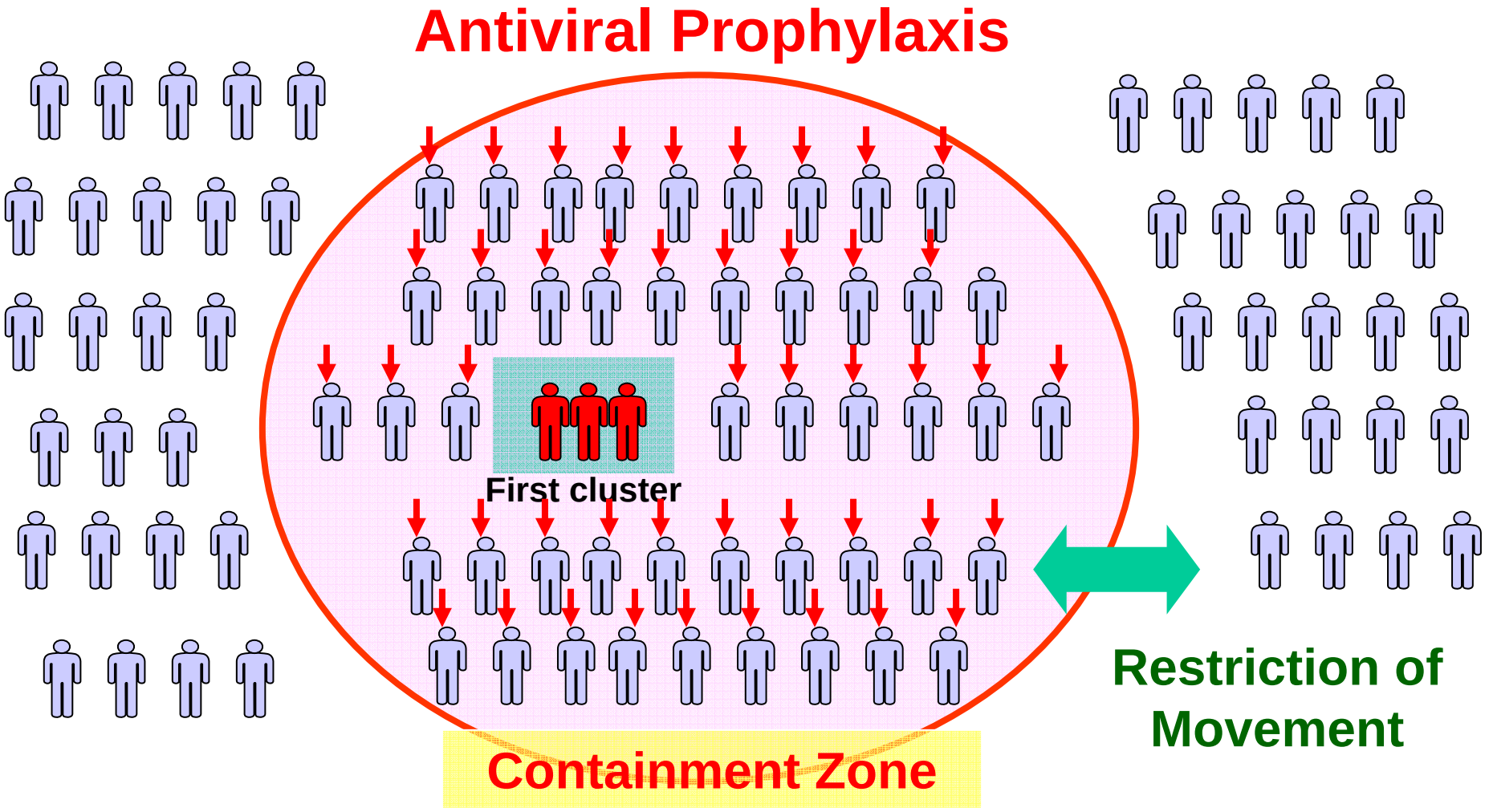

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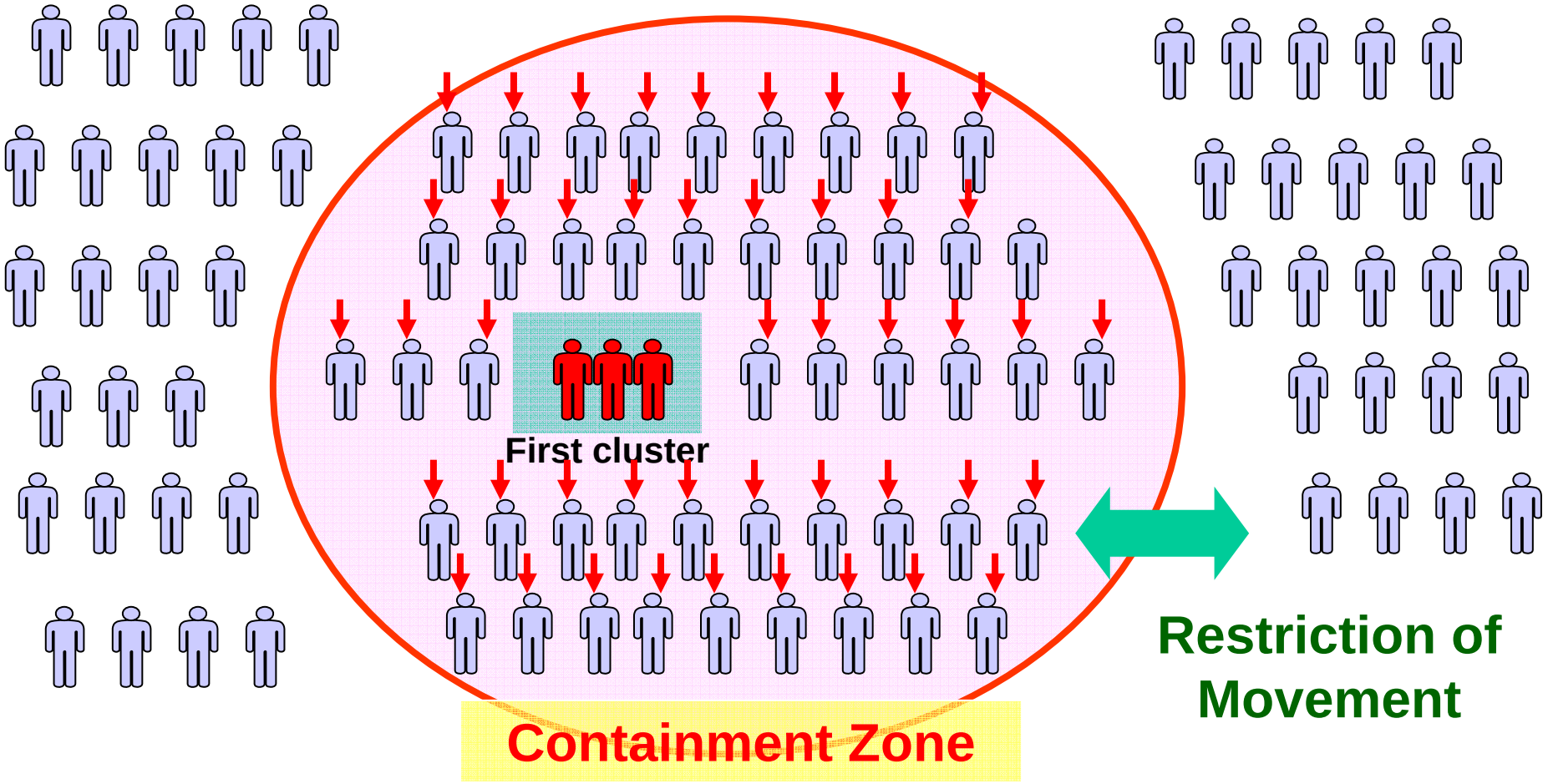
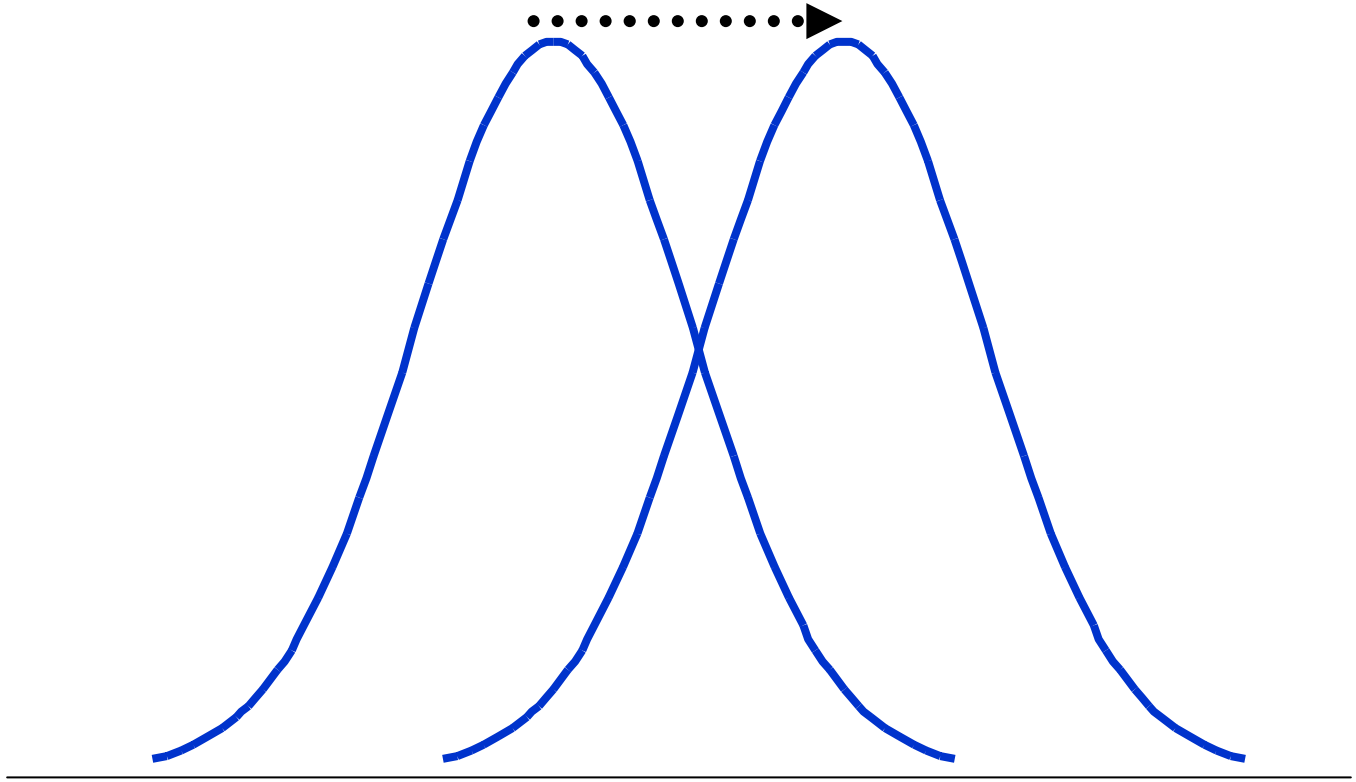


# Preconditions for early containment

- Early detection and reporting of initial sign of potential pandemic (narrow window of opportunity)
- Low population density / population movement
- Infectivity: medium - low
- Virus with pandemic potential emerges only in one or a few place

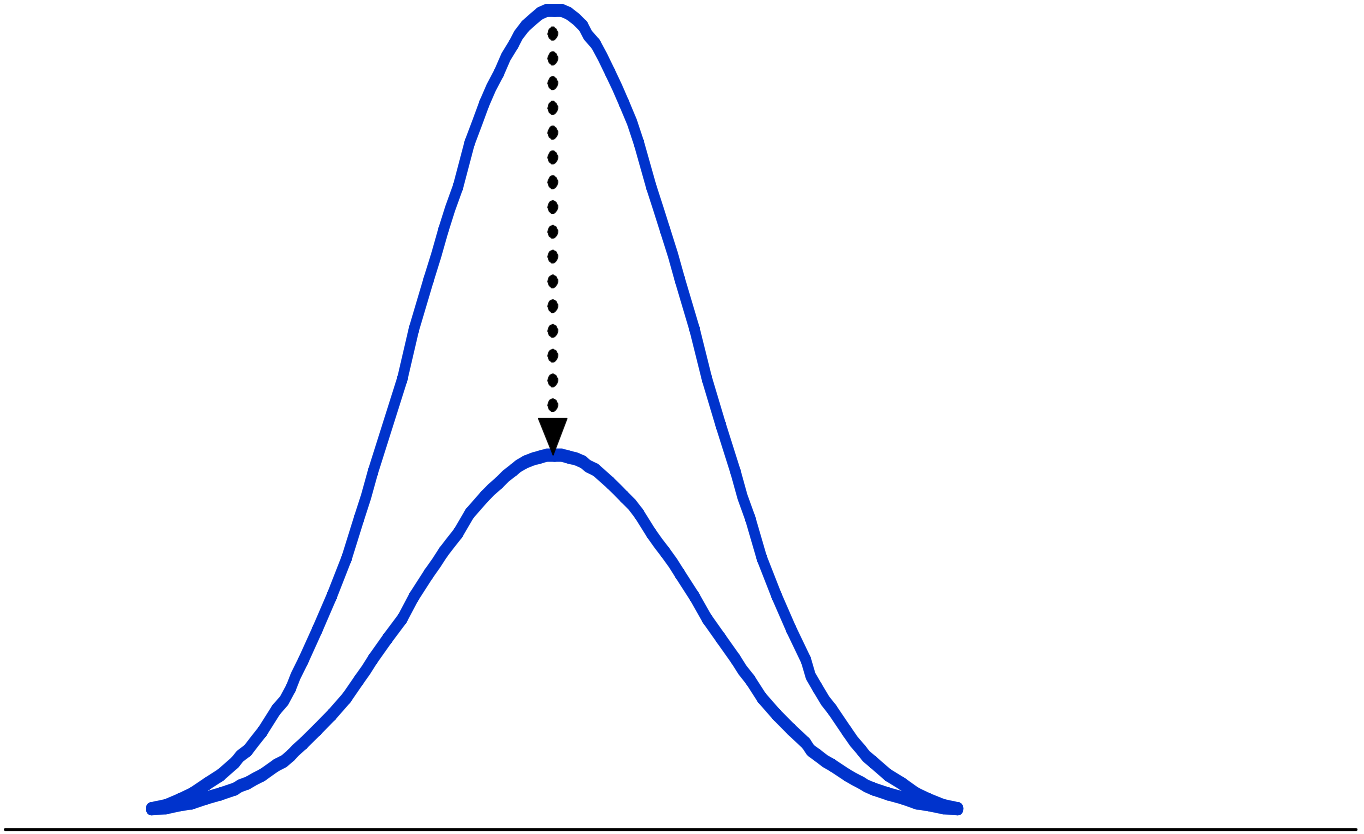
**No Guarantee for Success**

# Mitigating Strategy



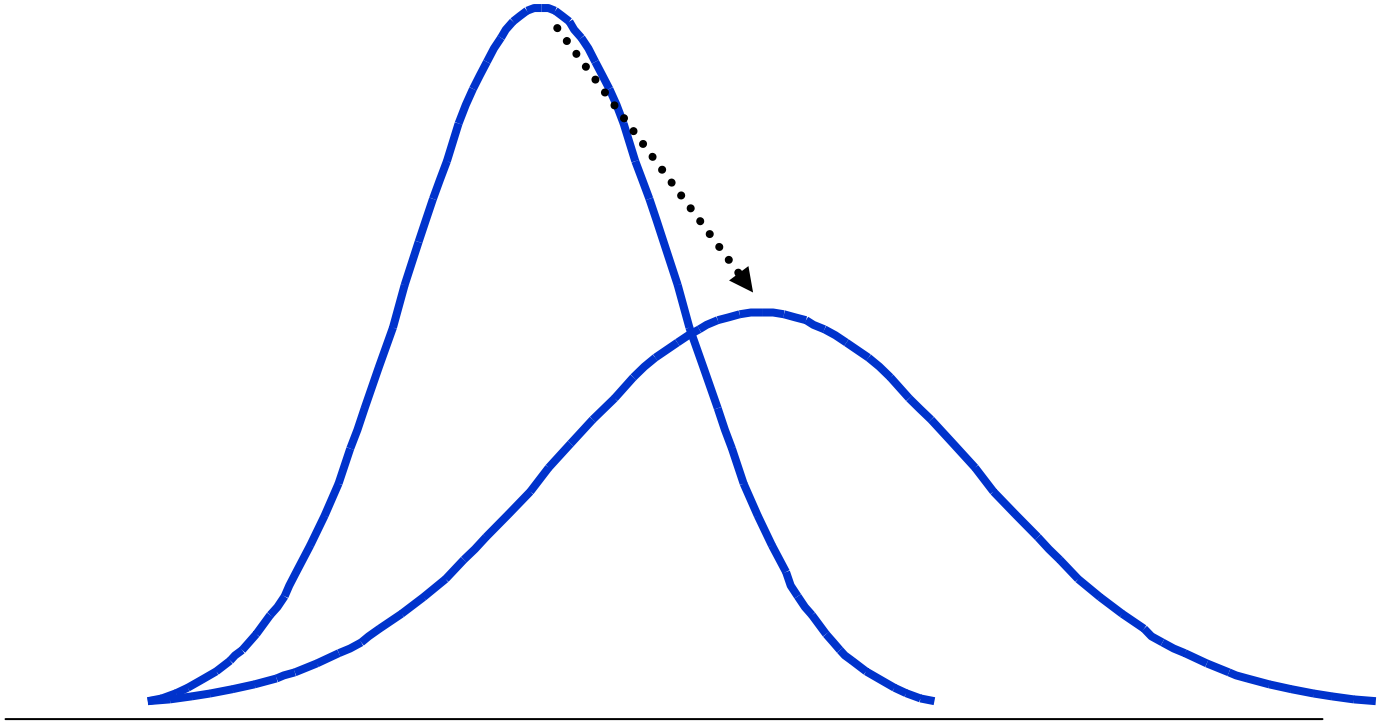
**Delaying the peak: buying the time for vaccine development and preparing other interventions**

# Mitigating Strategy



**Lowering the peak: Minimizing the impact and avoid social desruption**

# Mitigating Strategy



**Flatting the peak: Avoiding social disruption even total number of cases are same**

# Mitigating Strategy: Epidemiological models

doi:10.1038/nature04795 nature

LETTERS

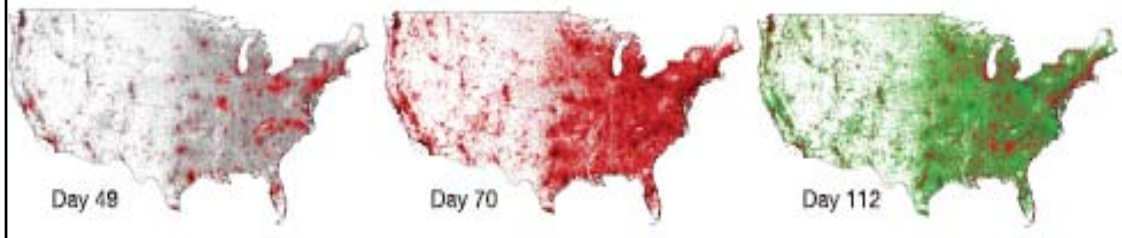
## Strategies for mitigating an influenza pandemic

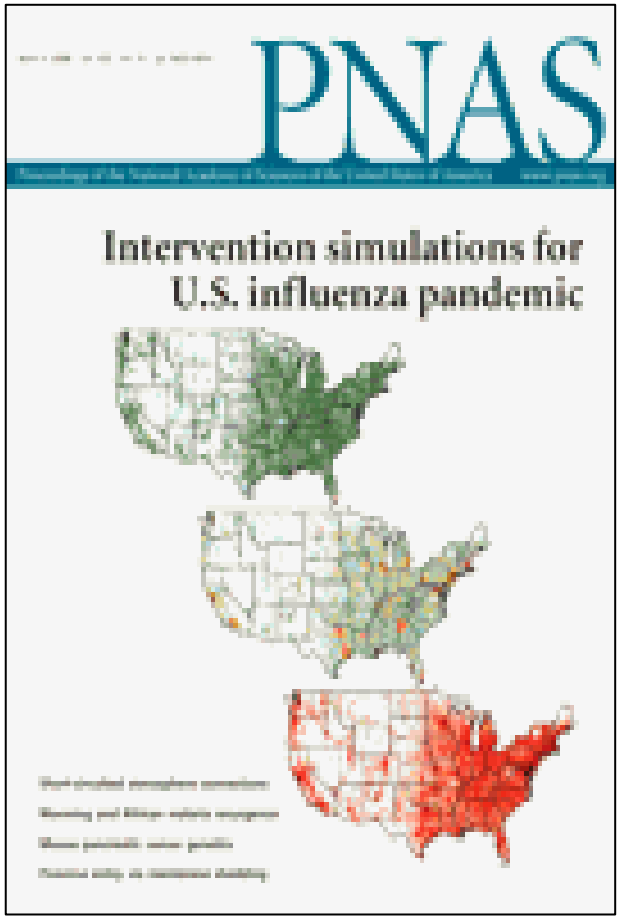
Neil M. Ferguson[1], Derek A. T. Cummings[2], Christophe Fraser[1], James C. Cajka[3], Philip C. Cooley[3] & Donald S. Burke[2]

**Development of strategies for mitigating the severity of a new influenza pandemic is now a top global public health priority. Influenza prevention and containment strategies can be considered under the broad categories of antiviral, vaccine and non-pharmaceutical (case isolation, household quarantine, school or workplace closure, restrictions on travel) measures[1]. Mathematical models are powerful tools for exploring this complex landscape of intervention strategies and quantifying the potential costs and benefits of different options[2–5]. Here we use a large-scale epidemic simulation[6] to examine intervention options should initial containment[6,7] of a novel influenza outbreak fail, using Great Britain and the United States as examples. We find that border restrictions and/or internal travel restrictions are unlikely to delay spread by more than 2–3 weeks unless more than 99% effective. School closure during the peak of a pandemic can reduce peak attack rates by up to 40%, but has little impact on overall attack rates, whereas case isolation or household quarantine could have a**

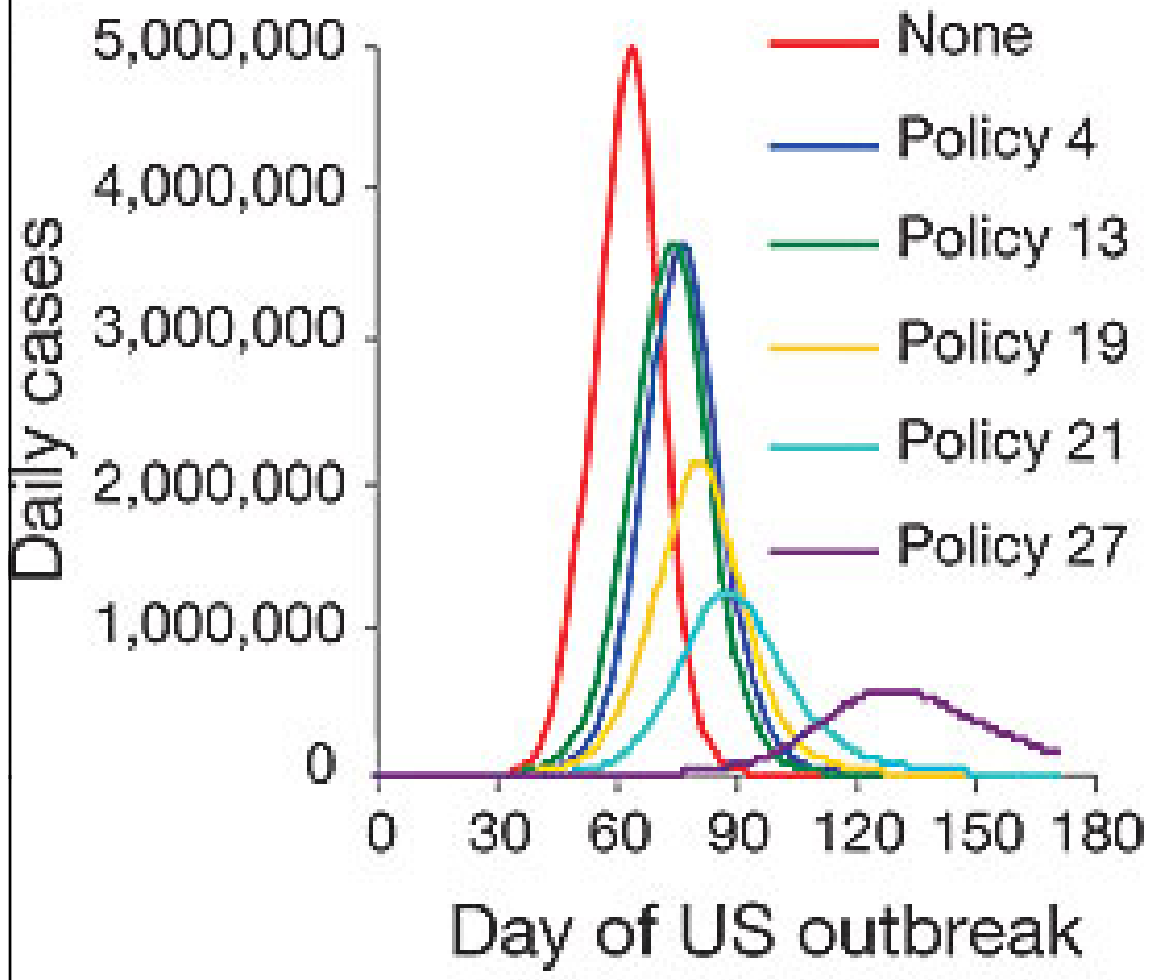
Acquiring more quantitative data on transmission in different social contexts should therefore be a priority.

We estimated the reproduction number[9] for pandemic influenza, $R_0$, to have a value of 1.7–2.0 for the first wave of the 1918 pandemic, as determined from city-level mortality data (see Supplementary Information). In 1957, epidemic growth rates were less, with UK national data giving $R_0$ values of 1.5–1.7 (see Supplementary Information). Inter-pandemic data give a value of $R_0 \approx 1.7$ (see Supplementary Information). We therefore examine values of $R_0$ in the range 1.4 to 2, particularly focusing on how conclusions differ for 'moderate' ($R_0 = 1.7$) and 'high' ($R_0 = 2.0$) transmission scenarios. Because the natural history of infection for human cases of avian H5N1 infection have to date been much more extended (and severe) than normal human influenza[10,11], we also examine sensitivity to assumptions about the duration of infectiousness. We do not assume any spontaneous change in the behaviour of uninfected individuals as the pandemic progresses, but note that behavioural changes that



# Mitigating Strategy




***Nature*** 2006;**442**(7101)**:**448-52.

Policy 4: 50% household quarantine plus reactive school closure

Policy 13 90% case treatment plus reactive school closure

Policy 19: Policy 13 + household prophylaxis

Policy 21: Policy 19 + pre-vaccination of 20% of the population

Policy 27: Policy 19 + prophylaxis of 80% of school classmates and close work colleagues + 99% effective border controls

# Possible Interventions for Mitigating Strategy

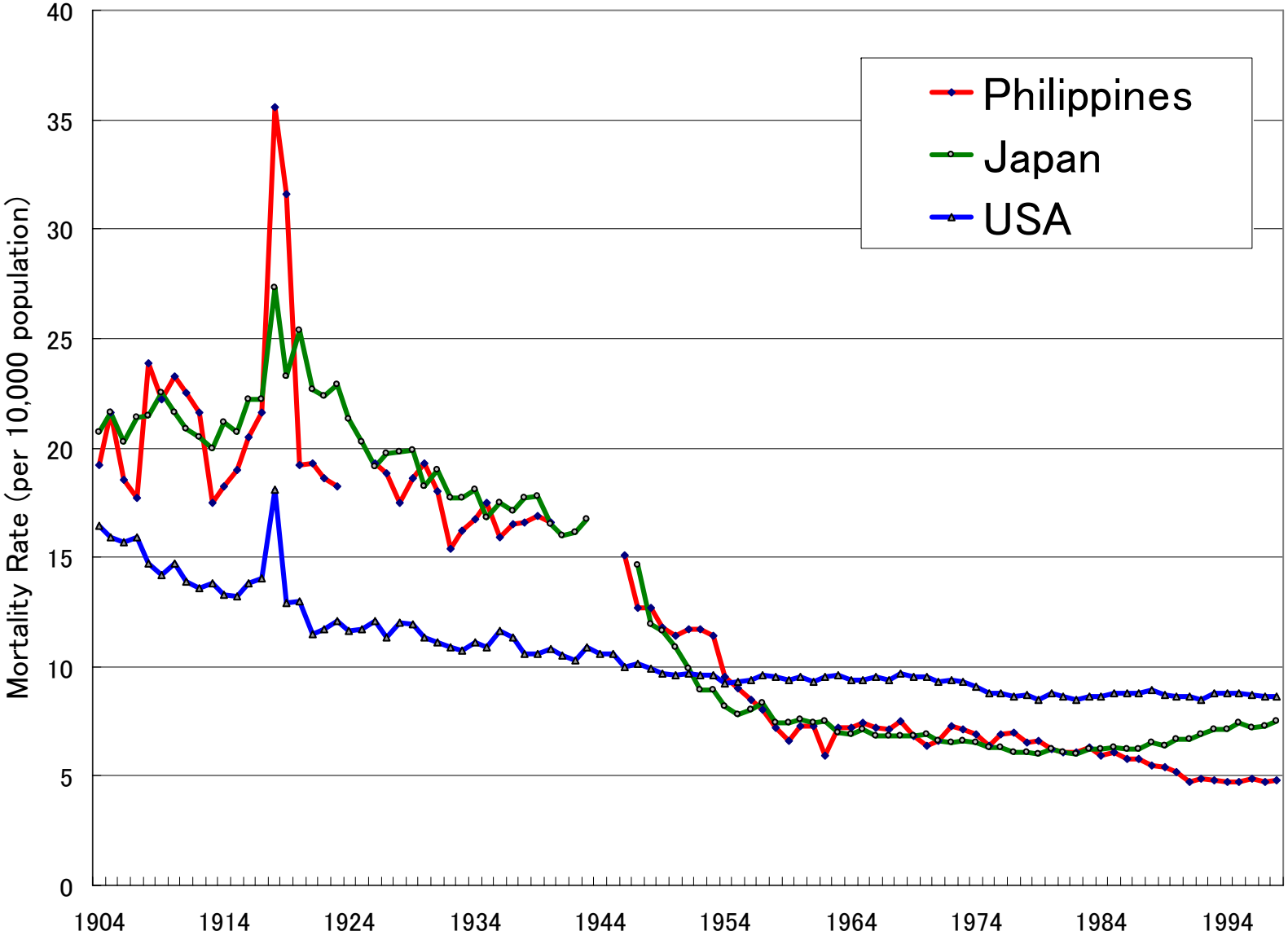
- **Home Isolation**
  - Symptomatic cases stay at home
  - Early treatment with antiviral
- **Home quarantine**
  - Close contact stay at home
  - Antiviral prophylaxis
- **Social distancing**
  - School / workplace closure
  - Restriction of mass gathering
- **Vaccine**
  - Even low efficacy vaccines may be useful

# Impact of Pandemic Influenza

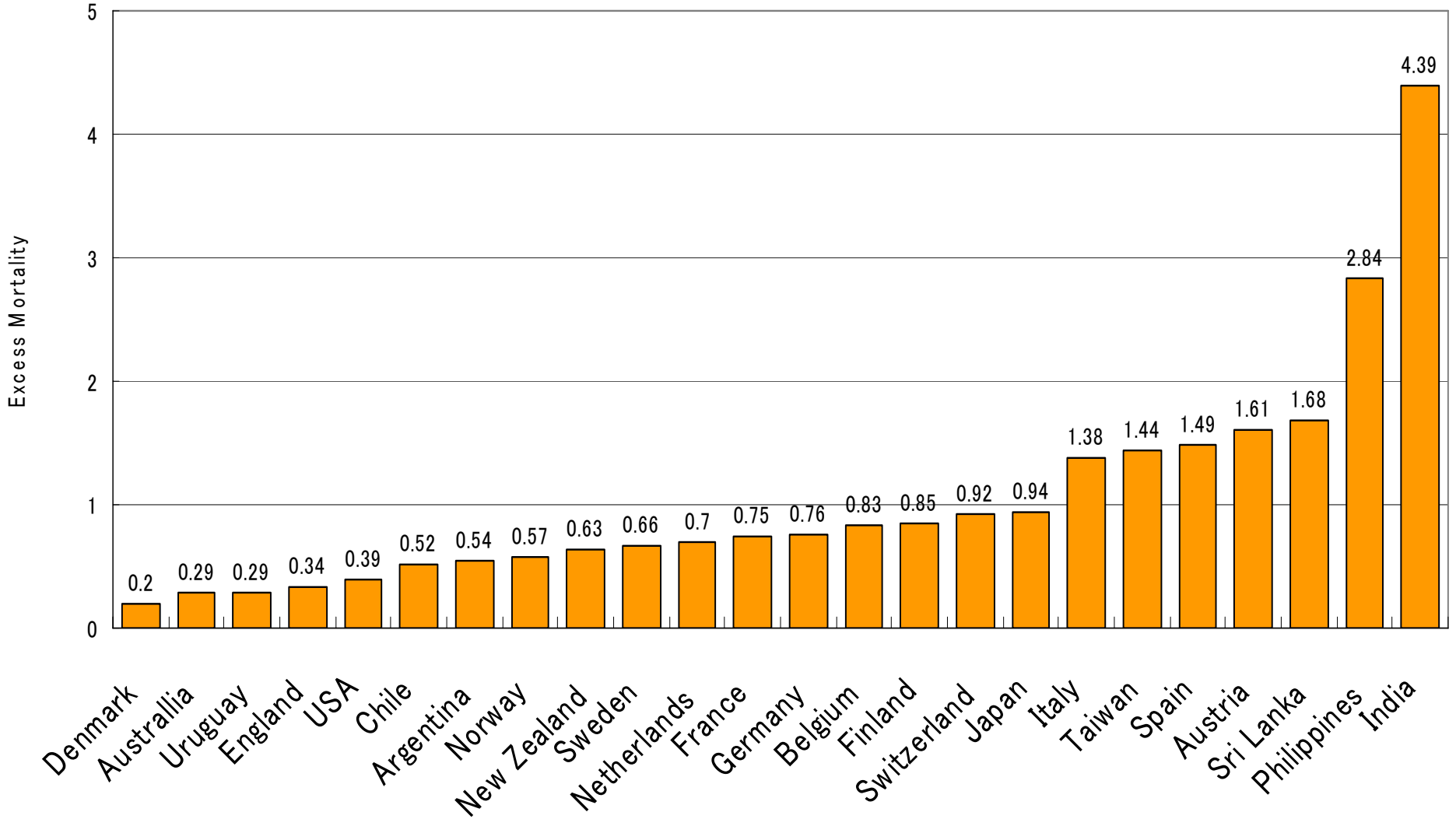
- Direct impact
  - Clinical attack rate: 30-40% of total population
  - Case fatality rate：0.5－2.0% of ill persons
- Indirect impact
  - Paralyzed health care system
  - Social disruption
  - Economic loss

# Impact of Pandemic Influenza

- Global Population:6.5 billion
- Number of cases: 2-2.6 billion
- Number of deaths:
  - Case fatality rate 0.5%: 10-13 million
  - Case fatality rate 2.0%: 40-52 million


Mortality Rate (per 10,000 population)
40
35
30
25
20
15
10
5
0
1904
1914
1924
1934
1944
1954
1964
1974
1984
1994
Philippines
Japan
USA

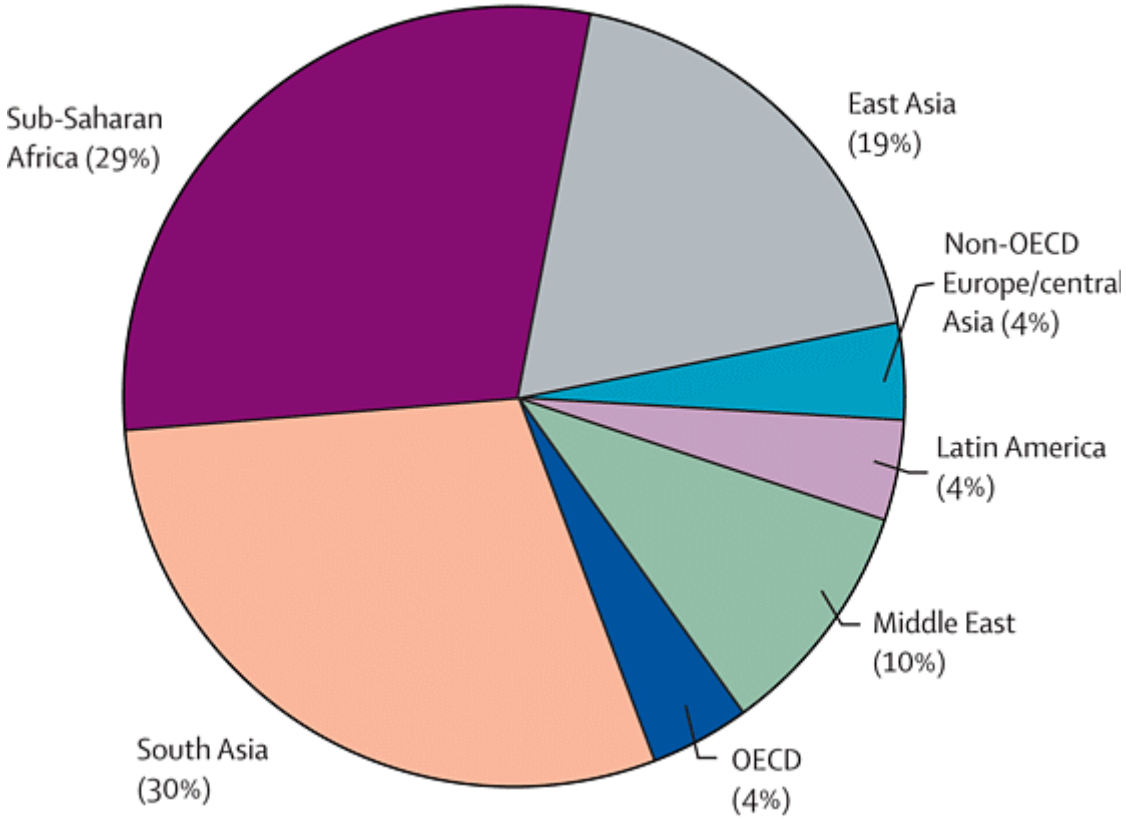
# Excess Mortality During 1918-20




Murray CLJ et al. Lancet 2006 ; 368: 2211-18

# Estimated deaths in the next influenza pandemic

- Global estimate: 62 million deaths
- 96 % of deaths would occur in developing countries




*Christopher J L Murray et al.* ***Lancet*** **2006; 368: 2211–18**

# Possible Intervention for Pandemic Influenza

## Pharmaceutical Interventions

- Vaccine
- Antivals

## Non-pharmaceutical Interventions

- **Social Distancing**
  - School / workplace closure
  - Restriction of social gathering
- **Border Control**
  - Screening
  - Travel restriction
- **Personal Protection**
  - Cough etiquette
  - Hand hygiene
  - Masks

# Cost of Antivirals

- **One treatment course (2 tablets per day X 5 days = 10 tablets)**
- **At least 15 US$**

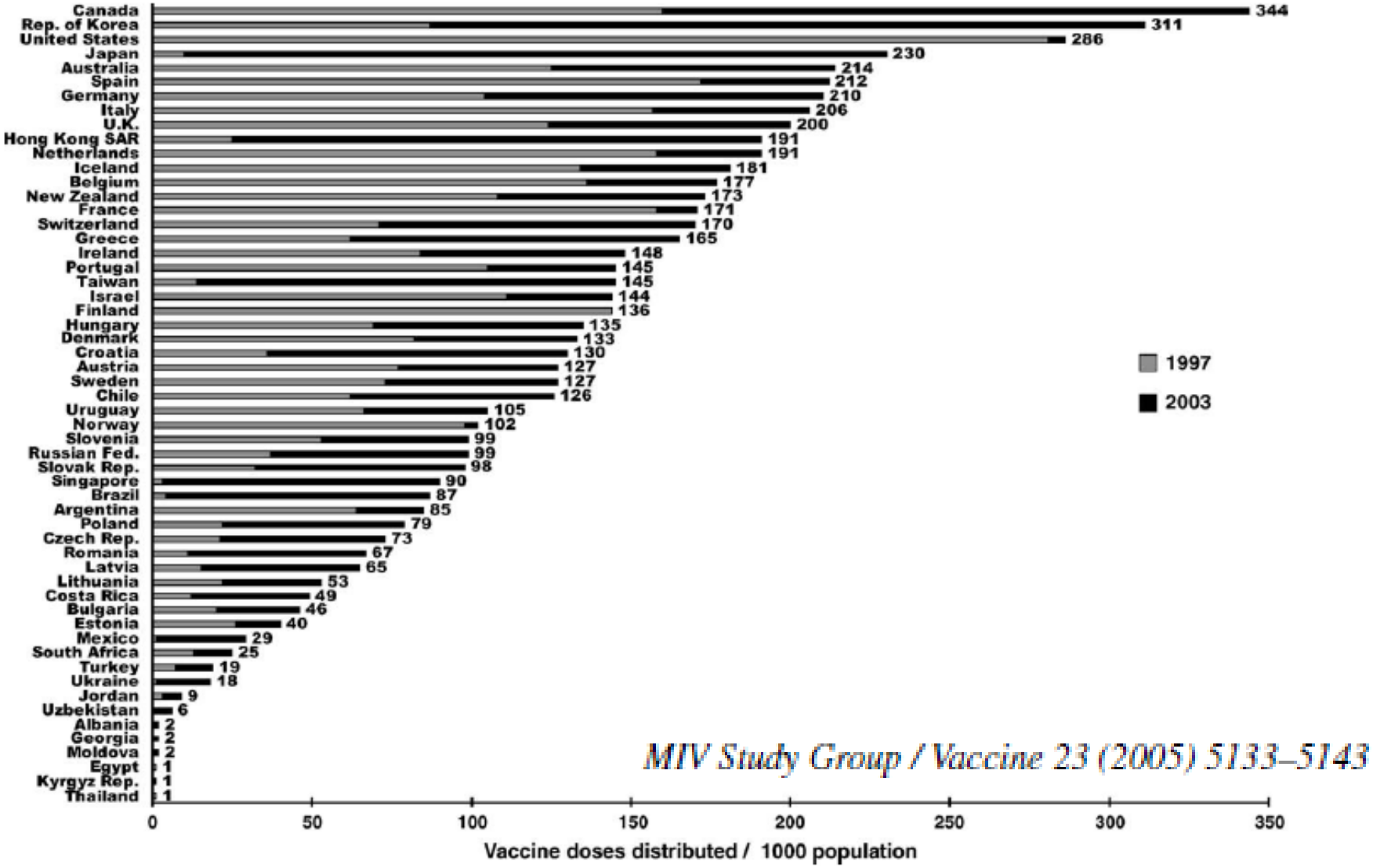
# Cost of purchasing oseltamivir to cover 25% population

| Category of country | Average GDP per capita | Annual health expenditure, per capita | Cost of purchasing oseltamivir stockpiles (% annual health expenditure) |
|---|---|---|---|
| High income | 30,168 | 3,376 | 0.11 |
| Upper middle income | 4,310 | 280 | 1.34 |
| Lower middle income | 1,364 | 77 | 4.87 |
| Low income | 753 | 29 | 12.93 |

# Current situation of global influenza vaccine supply

- Estimated vaccine production capacity: 350 million doses / year
- Concentrated in 9 industrialized countries
  - Australia, Canada, France, Germany, Italy, Japan, the Netherlands, the UK and USA

# Influenza vaccine distribution in 56 countries in 1997 and 2003



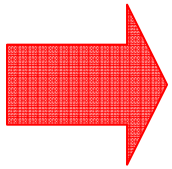

*MIV Study Group / Vaccine 23 (2005) 5133–5143*

# Global shortage of pandemic vaccine is expected

**Limited global vaccine production capacity**

**Vaccine production capacity concentrated in industrialized countries**

**High price of influenza vaccines**

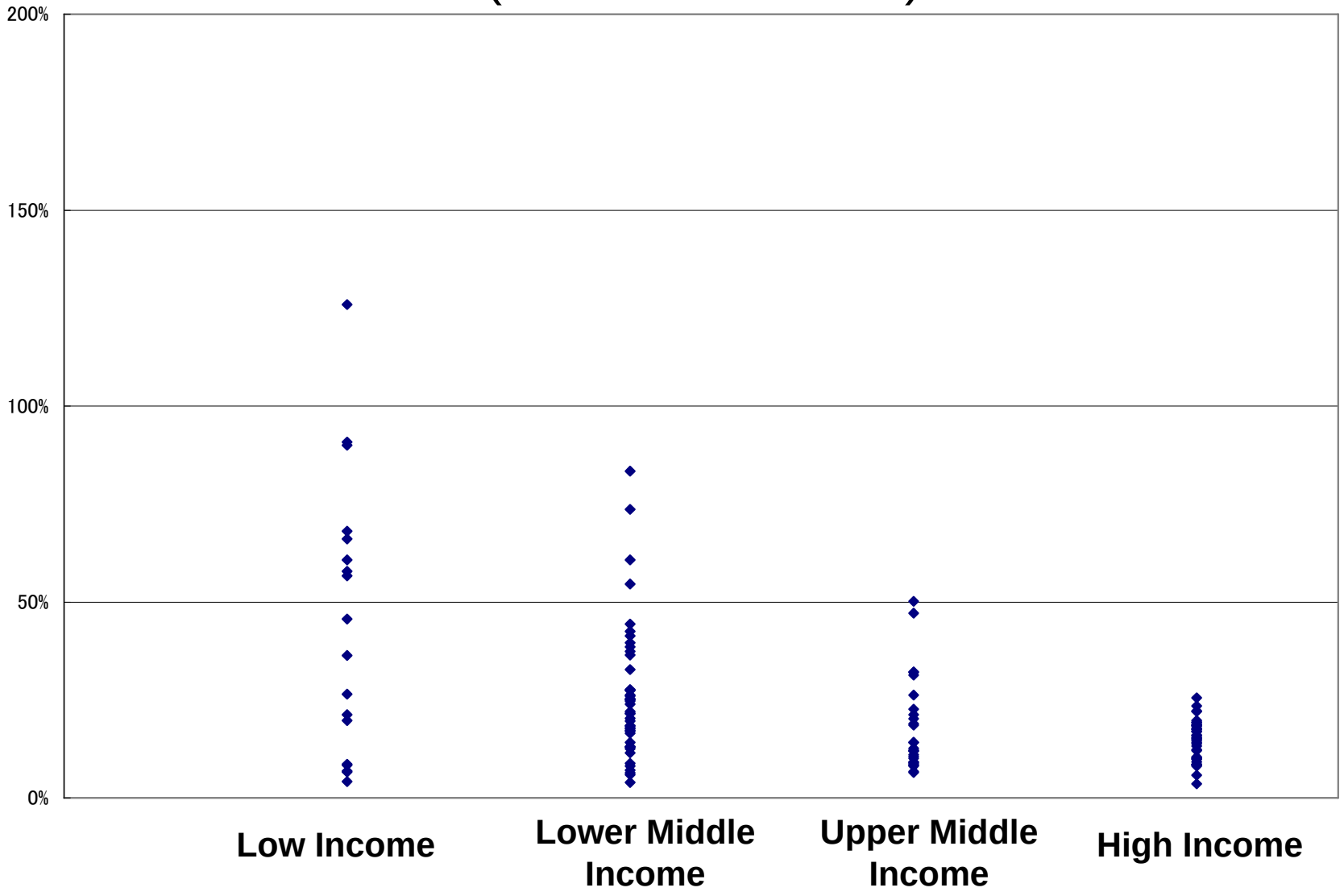


**No / limited supply of pandemic vaccines in most developing countries**

# Limited medical resources in developing countries to deal with influenza pandemic

- Health care facilities
  - Hospital beds
  - Number of clinics
- Medical personnel
  - Doctors
  - Nurses
- Basic medical supplies
  - Antibiotics
  - PPE (masks, gloves etc)
- Mechanical ventilator

# % of Beds Occupied with Patients of Pandemic Influenza (attack rate = 25%)



# Future steps for pandemic preparedness from global perspective

- Influenza pandemic = global issue
  - ➡ Global perspective is required
- Urgent need to fill the gap between countries
  - – Vaccine supply
  - – Antiviral stockpiles
  - – Improved medical care