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Thinking Ahead

Using Scenarios for Pandemic Planning and Preparedness

NAEM Workshop

May 11, 2006
San Diego, CA

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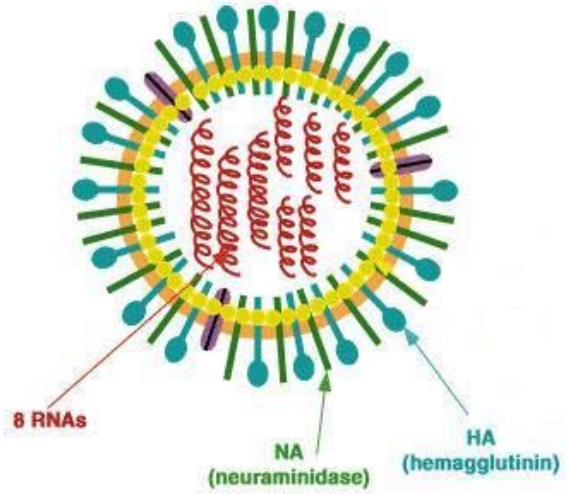
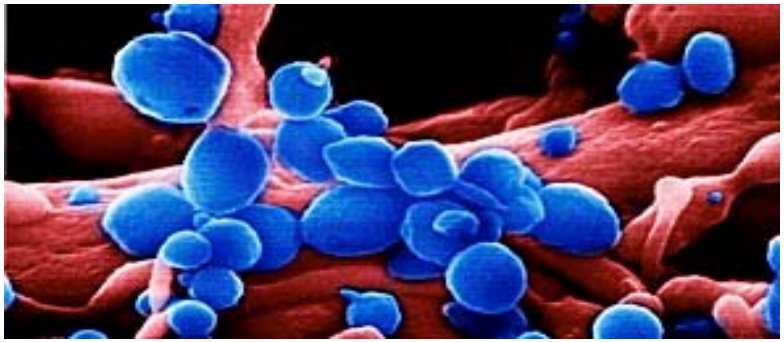
Managing Director, Bio-era

H5N1 Avian Influenza: Why Worry?

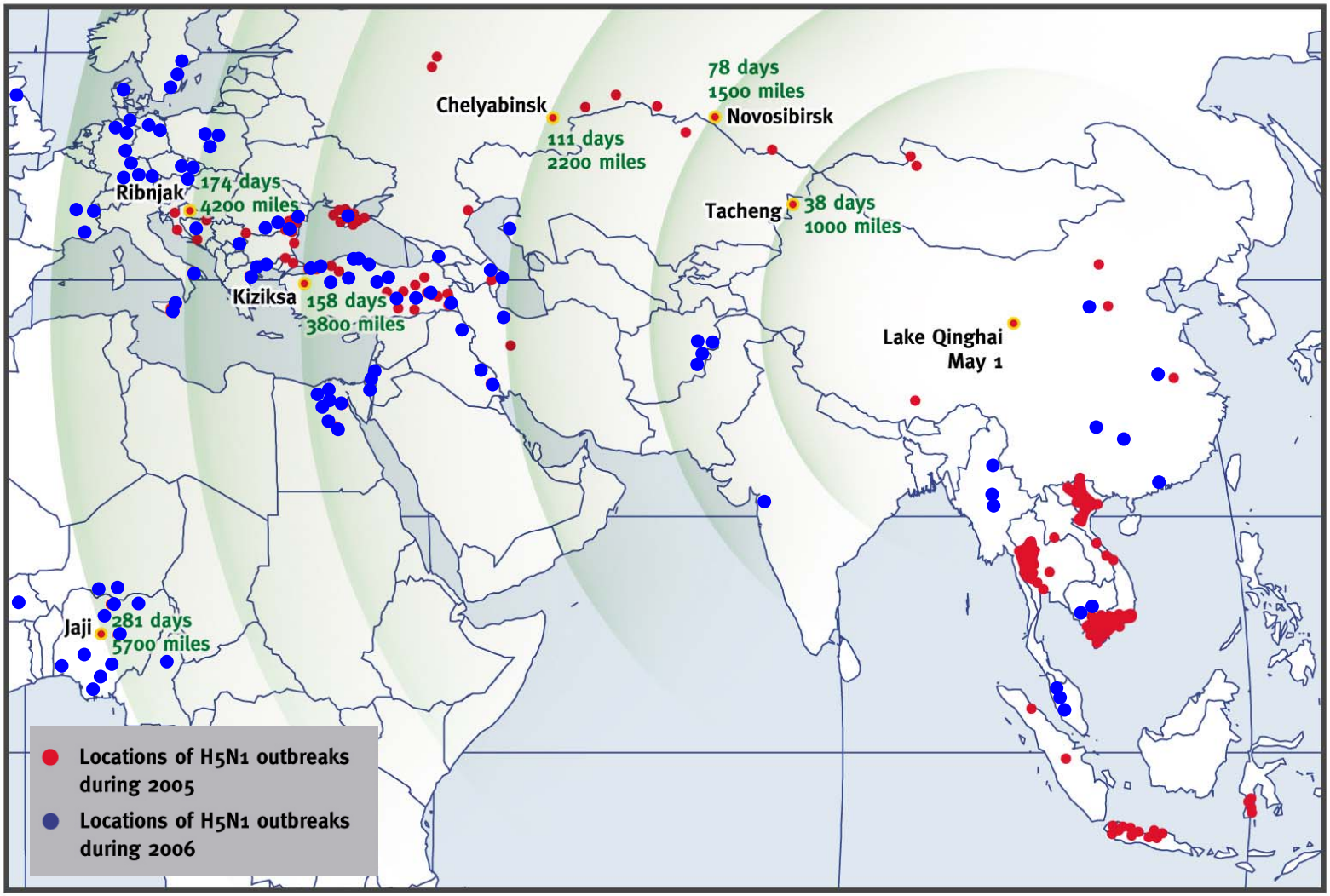




Photograph of the H5N1 virus taken by Lennart Nilsson, November 6, 2005.

- **Primarily a highly virulent (HPAI) disease of poultry and wild birds, but can infect and cause serious disease in a range of mammals, including cats, pigs, ferrets, and humans. Has already caused > $15 Billion (US) in direct economic damages.**
- **Virus is endemic (can't be stamped out) in large areas of Asia, Europe, and Africa, and is expanding its geographic range along migratory flyways**
- **Lack of previous human exposure to H5 influenzas (no communal immunity) coupled with strong H5N1 virulence and broad tissue and species affinities, is causing global concern for its potential to cause a devastating human influenza pandemic.**

The Westward Spread of H5N1

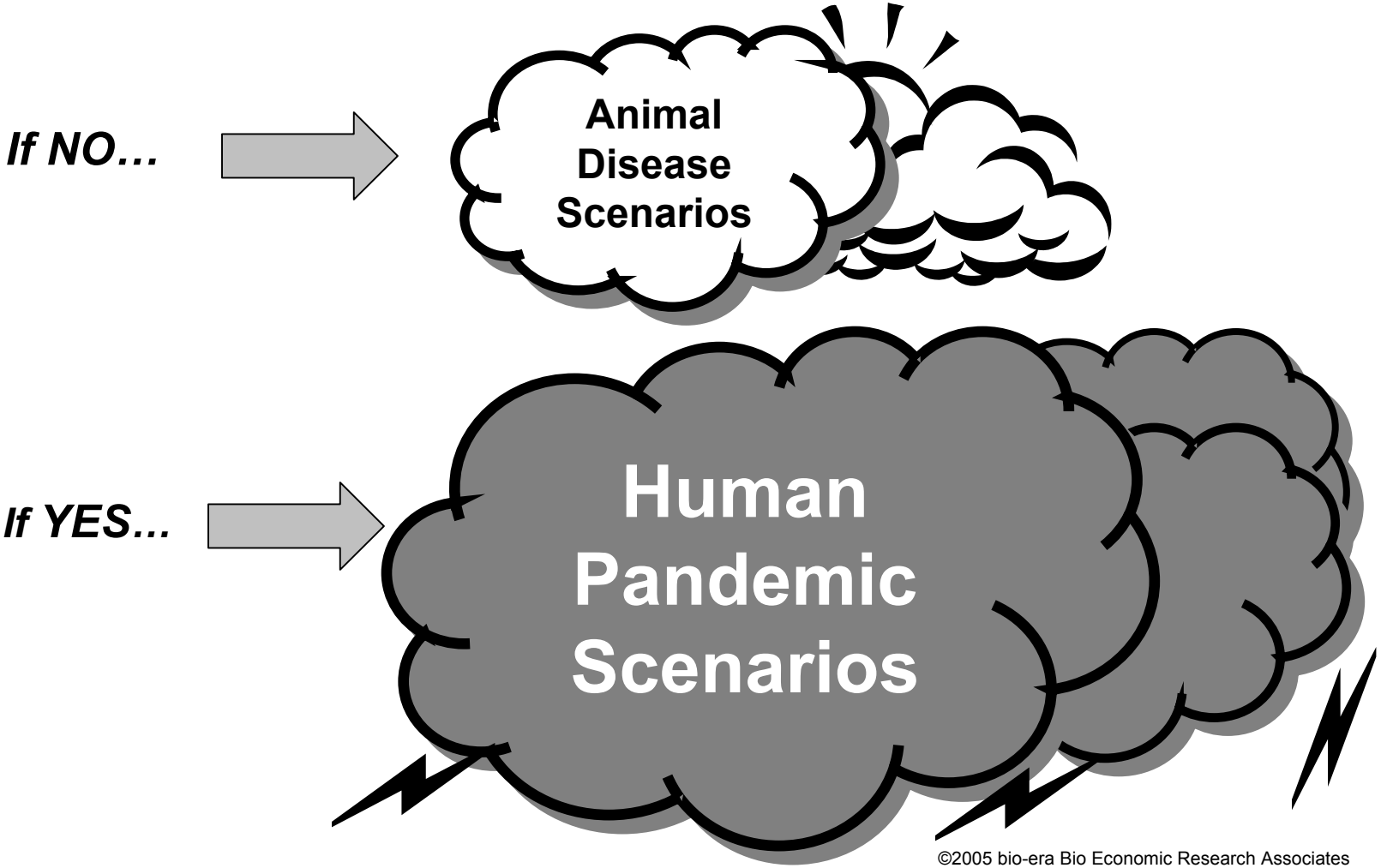


Sources: OIE, FAO, bio-era

The Conceptual Space for H5N1 Scenarios

THE PIVOTAL ISSUE IS…

Will Efficient Human Transmission Emerge?



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The 1918 Influenza Pandemic

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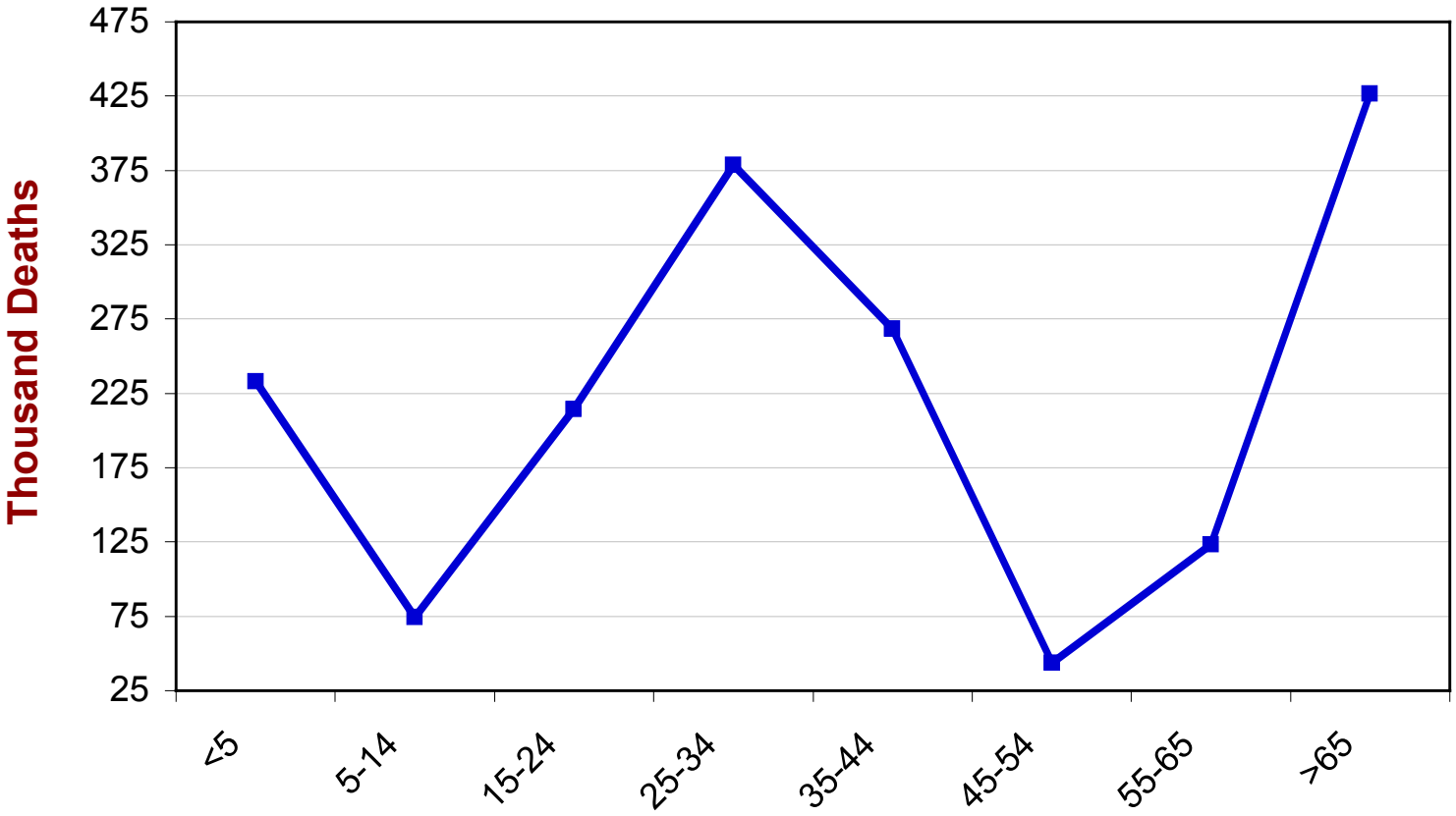
Projected Influenza-Associated Deaths in the United States Based on the 1918 Experience



Source: CIDRAP

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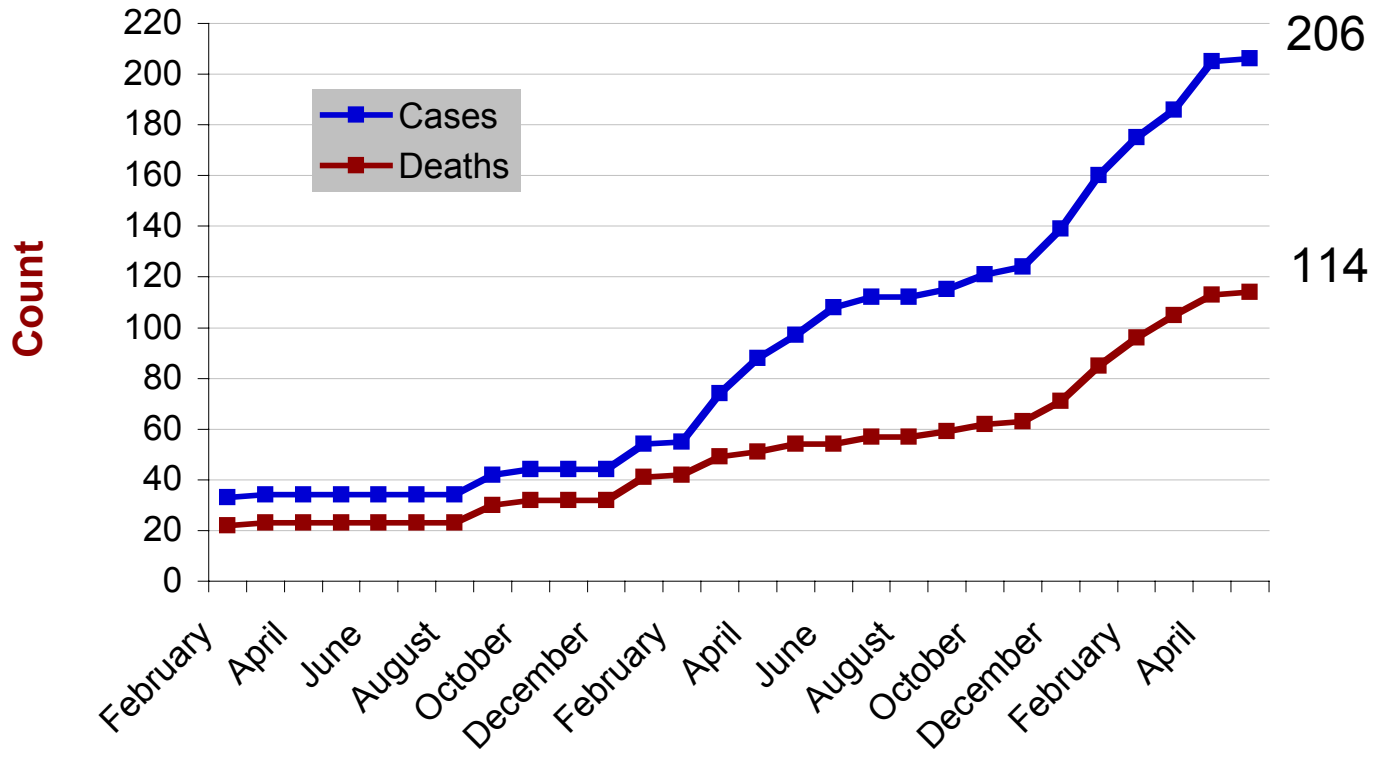
Laboratory Confirmed Human Cases of H5N1 Since Feb. 2004



Source: WHO

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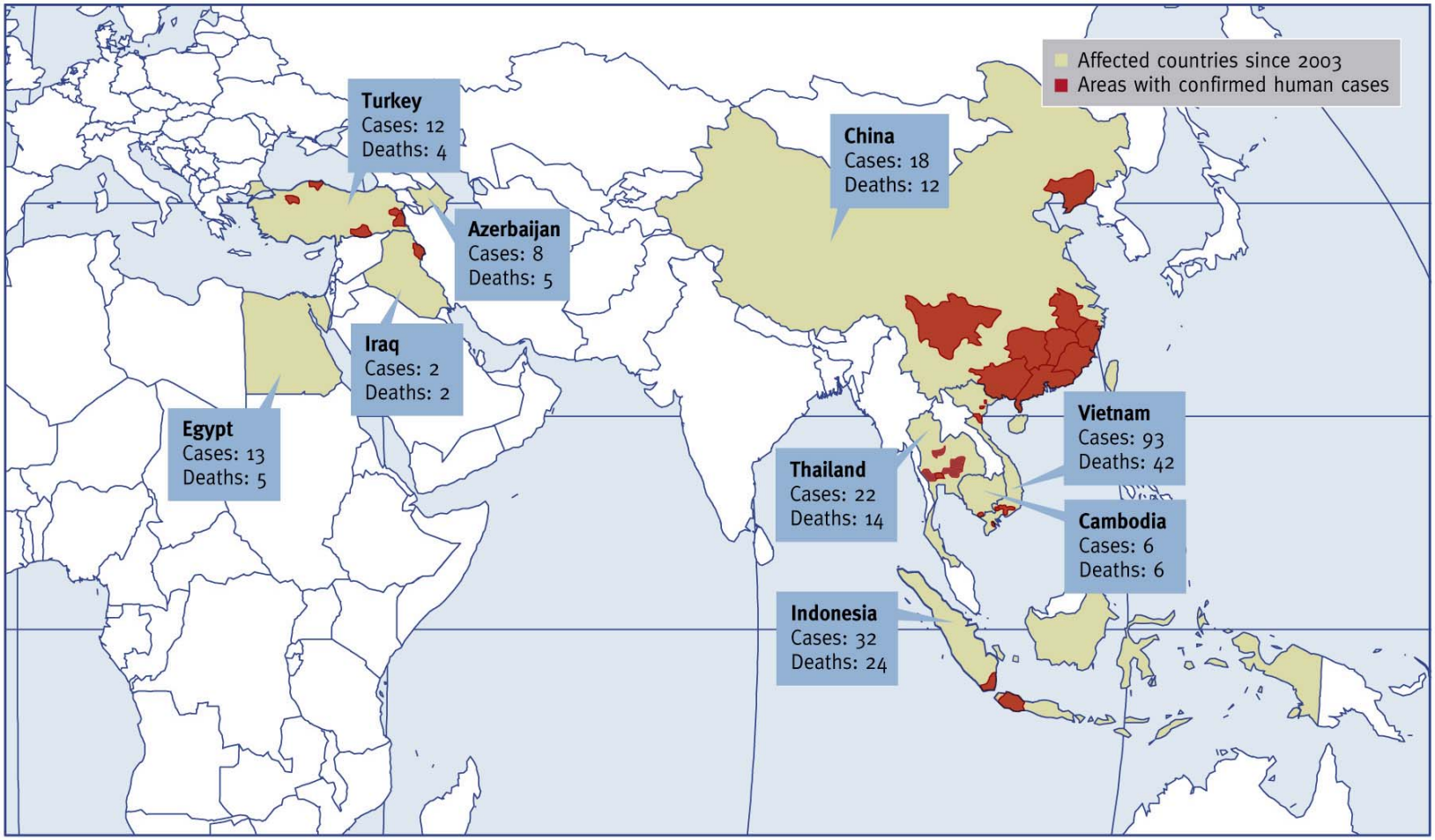
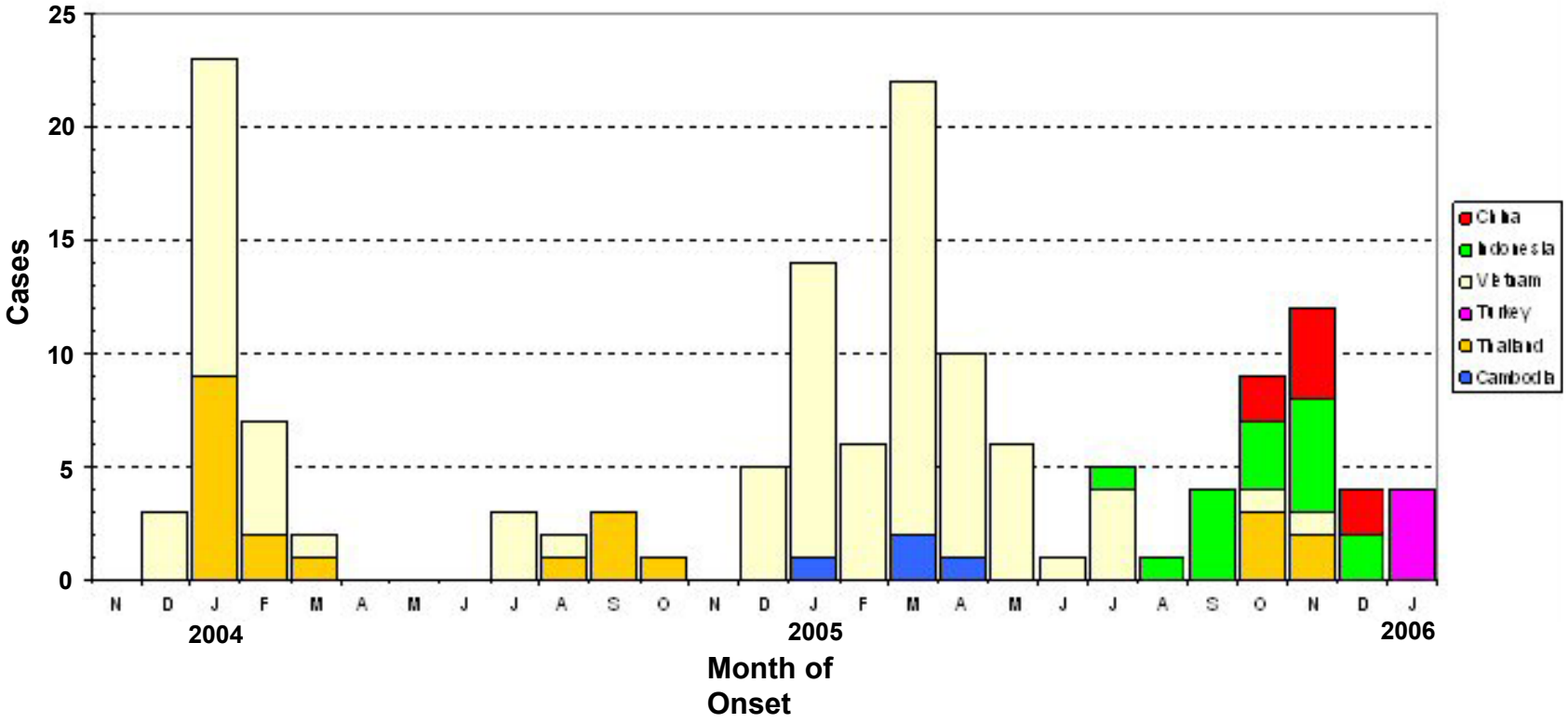
Human cases of H5N1 since December 2003



Source: WHO

Human H5N1 Cases by Date of Onset and Country Since December 2003



Source: ECDC

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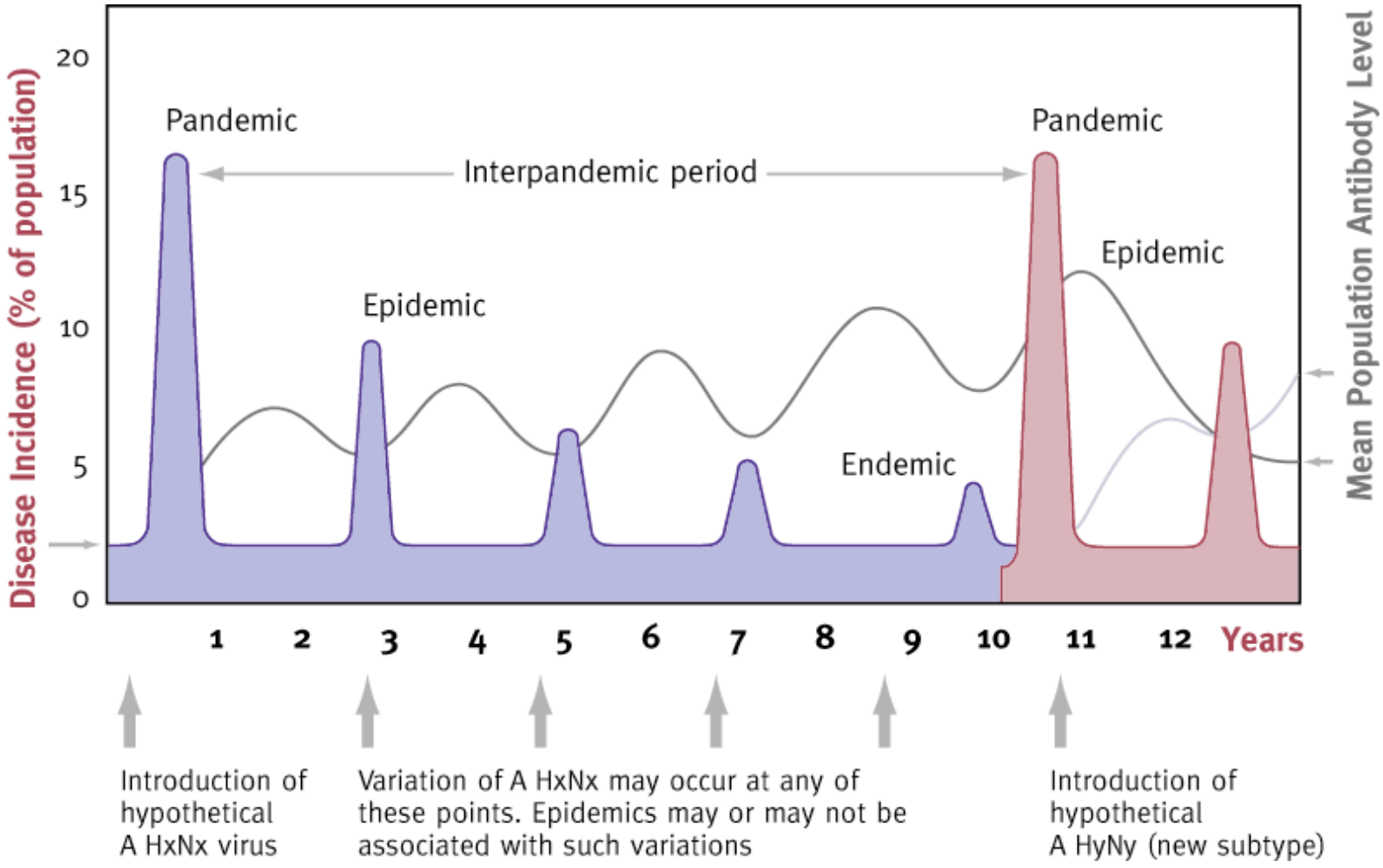
The Pandemic Influenza Cycle



Influenza Pandemics in the 20th Century

Year	Strain	Estimated Deaths	Global Population (Bn)
1918 (Spanish Flu)	H1N1	20-40 million	1.75
1957 (Asian Flu)	H2N2	1-4 million	2.75
1968 (Hong Kong Flu)	H3N2	1-4 million	3.65

Source: WHO, UN, US Dept. of Health & Human Services (HHS)

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WHO Pandemic Phases

Phase 1	An influenza virus subtype that has caused human infection may be present in animals. If present in animals, the risk of human infection or disease is considered to be low.
Phase 2	No new influenza virus subtypes have been detected in humans. However, a circulating animal influenza virus subtype poses a substantial risk of human disease.
Phase 3	Human infection(s) with a new subtype, but no human-to-human spread At most, rare instances of spread to a close contact.
Phase 4	Small cluster(s) with limited human-to-human transmission Spread is highly localized, suggesting that the virus is not well adapted to humans.
Phase 5	Larger cluster(s), but human-to-human transmission is still localized Virus may not yet be fully transmissible.
Phase 6	Pandemic phase: increased and sustained transmission in the general population

Source: WHO

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Infectious Disease Was Thought to Have Been Defeated as a Serious Threat to Global Health…

In 1969 the U.S. Surgeon General testified before Congress that humanity might soon "close the book on infectious disease."

The United Nations "Health for All 2000" accord, adopted in 1978 predicted that by the year 2000, infectious diseases would no longer pose a major danger to human health – even for the poorest nations.

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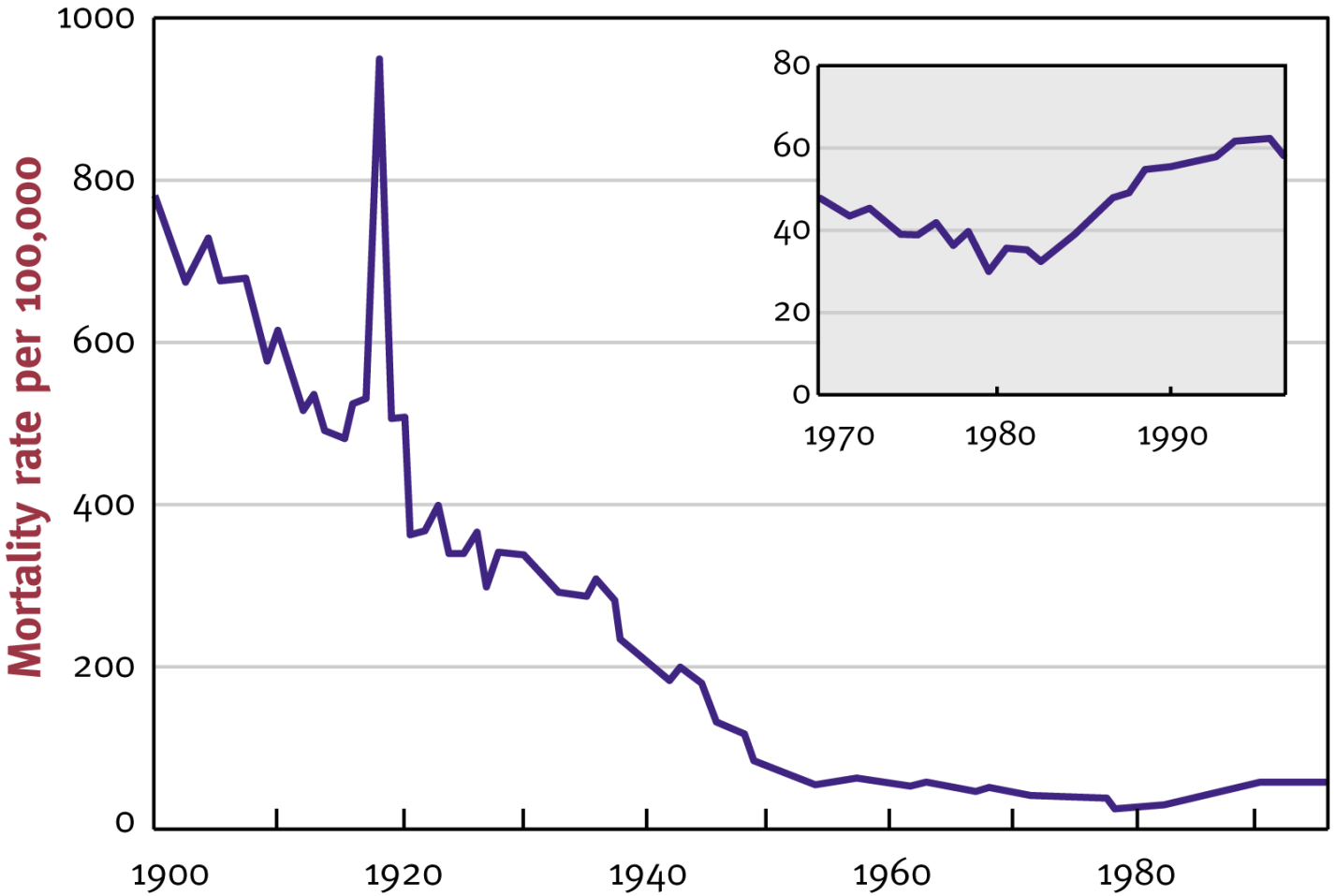
Infectious disease mortality in the U.S., 1900 to 1996



Source: Centers for Disease Control & Prevention

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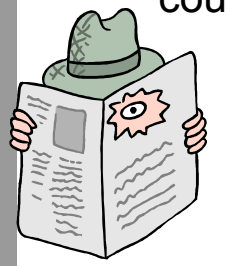
…but by 2000, the CIA Had A Different View

"***Infectious diseases are a leading cause of death, accounting for a quarter to a third of the estimated 54 million deaths worldwide in 1998. The spread of infectious diseases results as much from changes in human behavior--including lifestyles and land use patterns, increased trade and travel, and inappropriate use of antibiotic drugs--as from mutations in pathogens.***

- 20 well-known diseases--including tuberculosis (TB), malaria, and cholera--have reemerged or spread geographically since 1973, often in more virulent and drug-resistant forms.

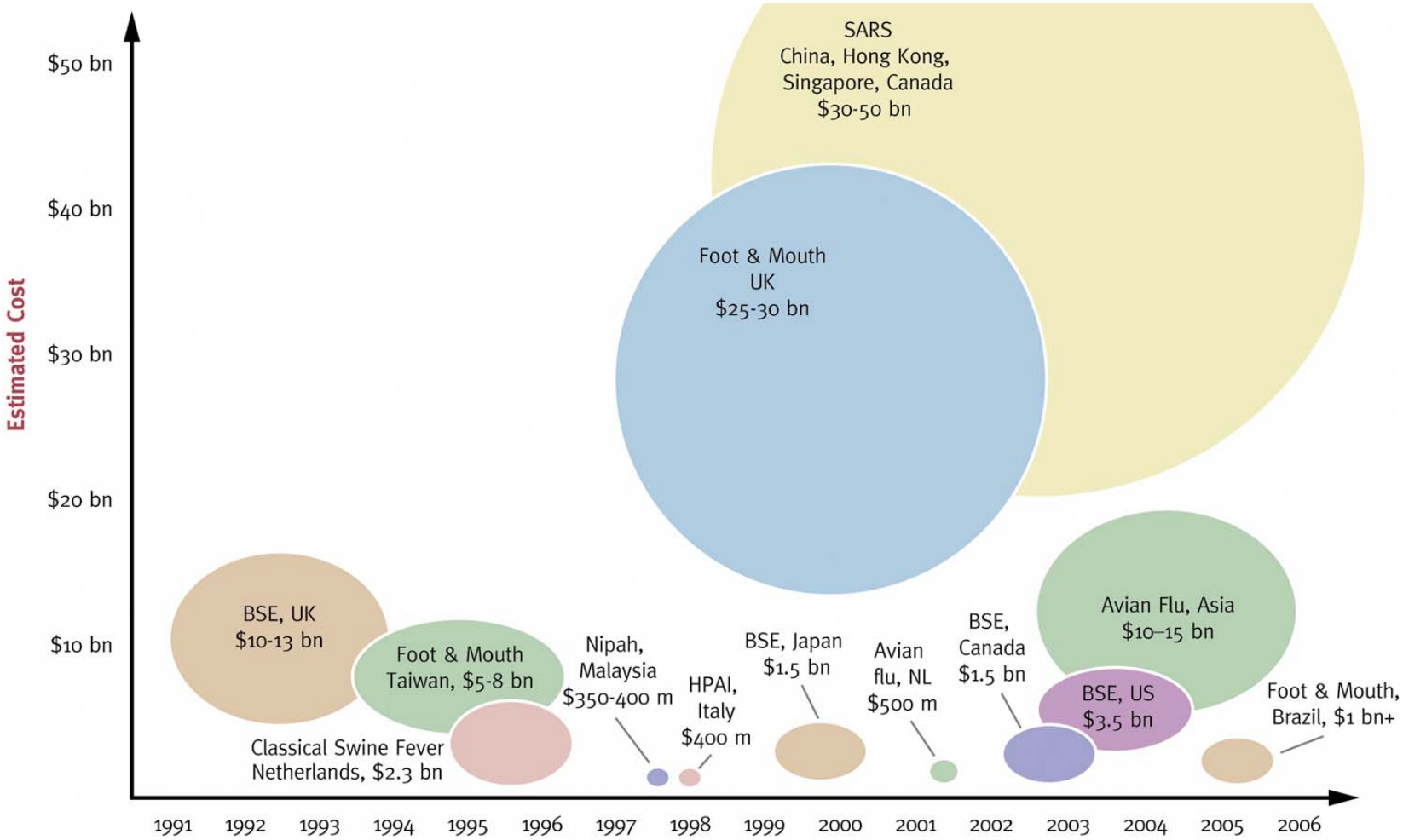
- At least 30 previously unknown disease agents have been identified since 1973, including HIV, Ebola, hepatitis C, and Nipah virus, for which no cures are available.

- Of the seven biggest killers worldwide, TB, malaria, hepatitis, and, in particular, HIV/AIDS continue to surge, with HIV/AIDS and TB likely to account for the overwhelming majority of deaths from infectious diseases in developing countries by 2020…."



The Global Infectious Disease Threat and Its Implications for the United States
CIA Report -- January 2000

Economic Impact of Selected Infectious Diseases



Figures are estimates and are presented as relative size

Source: bio-era

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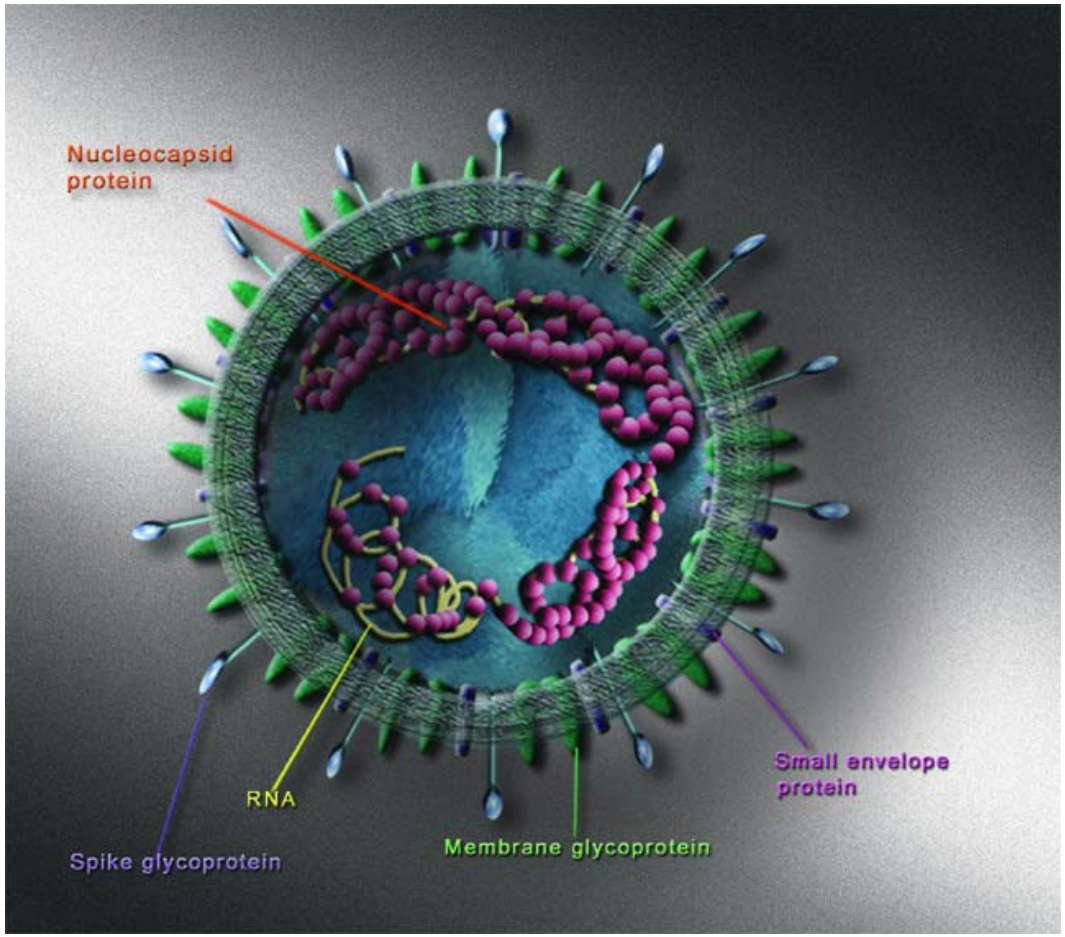
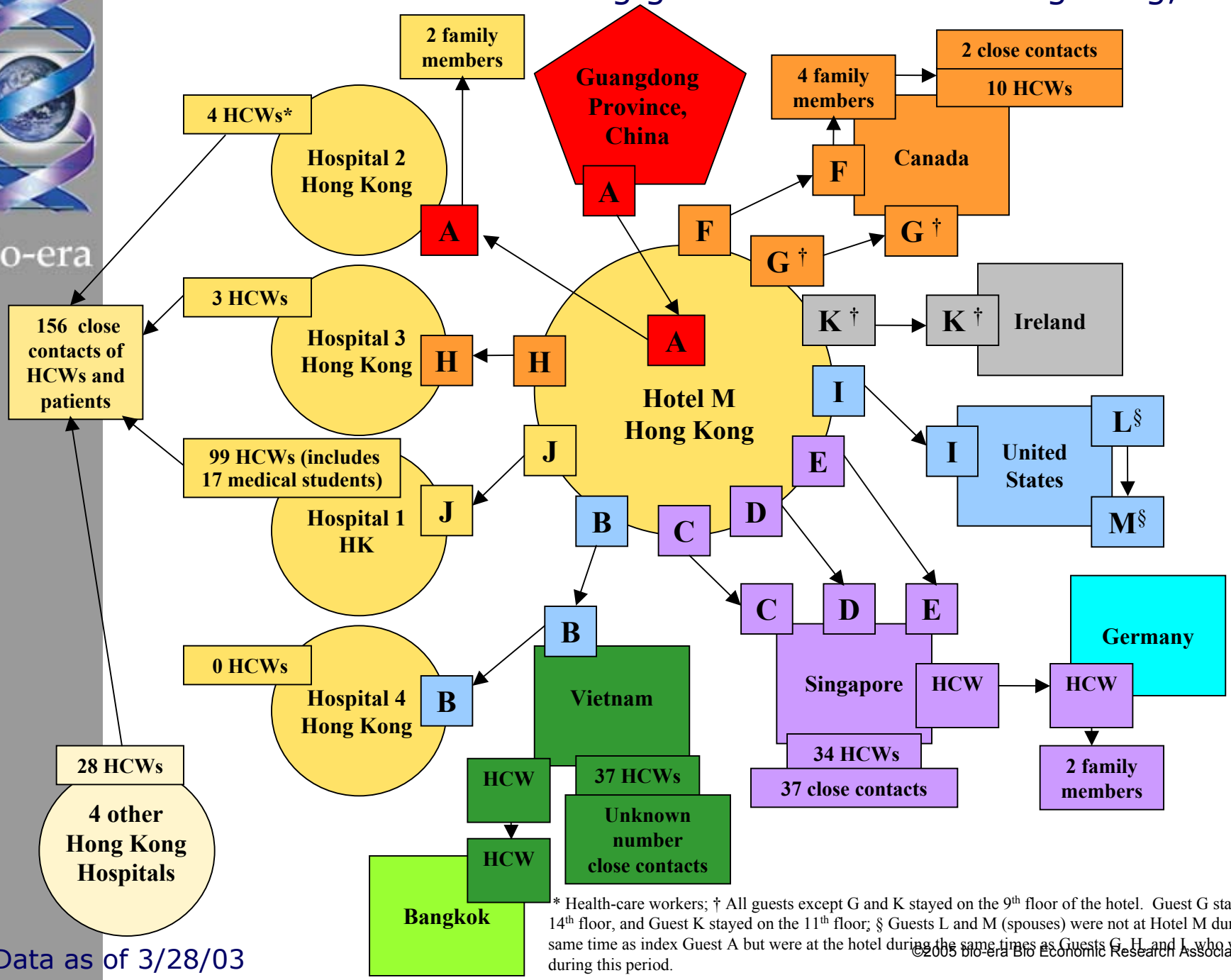
SARS: What Did We Learn?



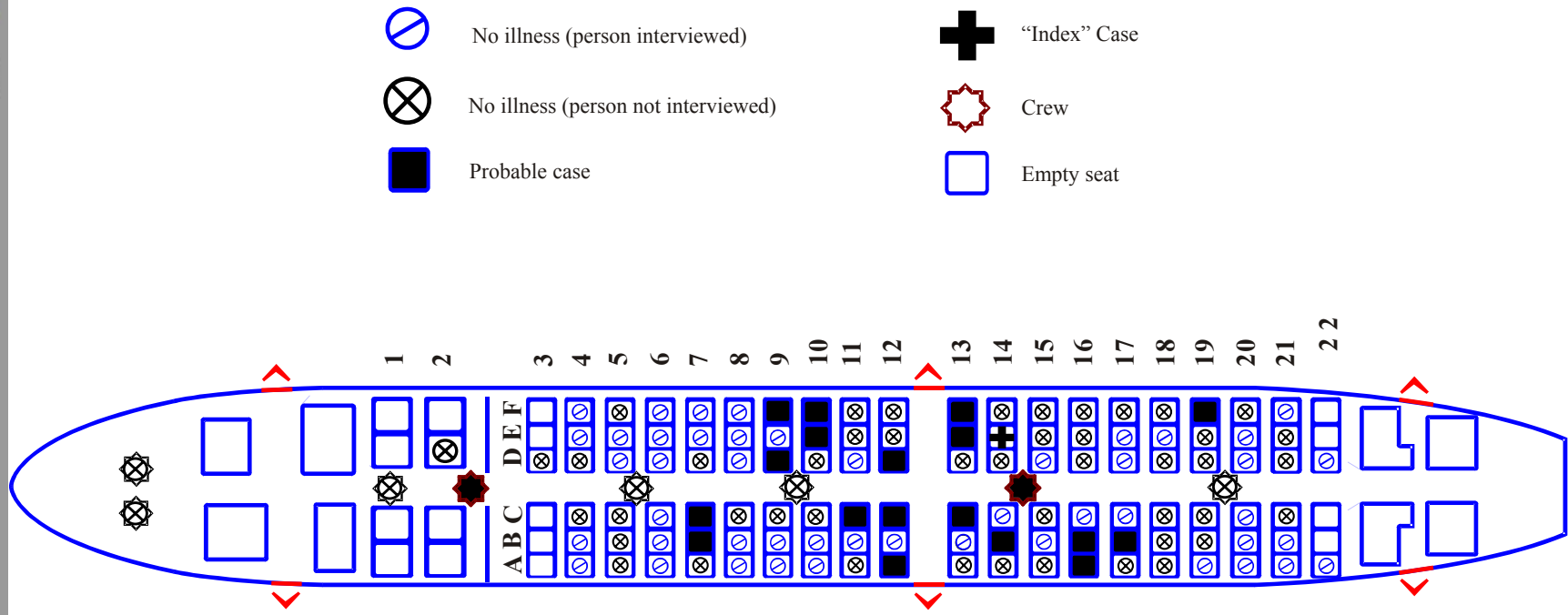
Chain of transmission among guests at Hotel M—Hong Kong, 2003



* Health-care workers; † All guests except G and K stayed on the 9th floor of the hotel. Guest G stayed on the 14th floor, and Guest K stayed on the 11th floor; § Guests L and M (spouses) were not at Hotel M during the same time as index Guest A but were at the hotel during the same times as Guests G, H, and I, who were ill during this period.

Data as of 3/28/03

Airline Transmission of SARS



Source: Olsen et al. NEJM 2003; 349: 2414

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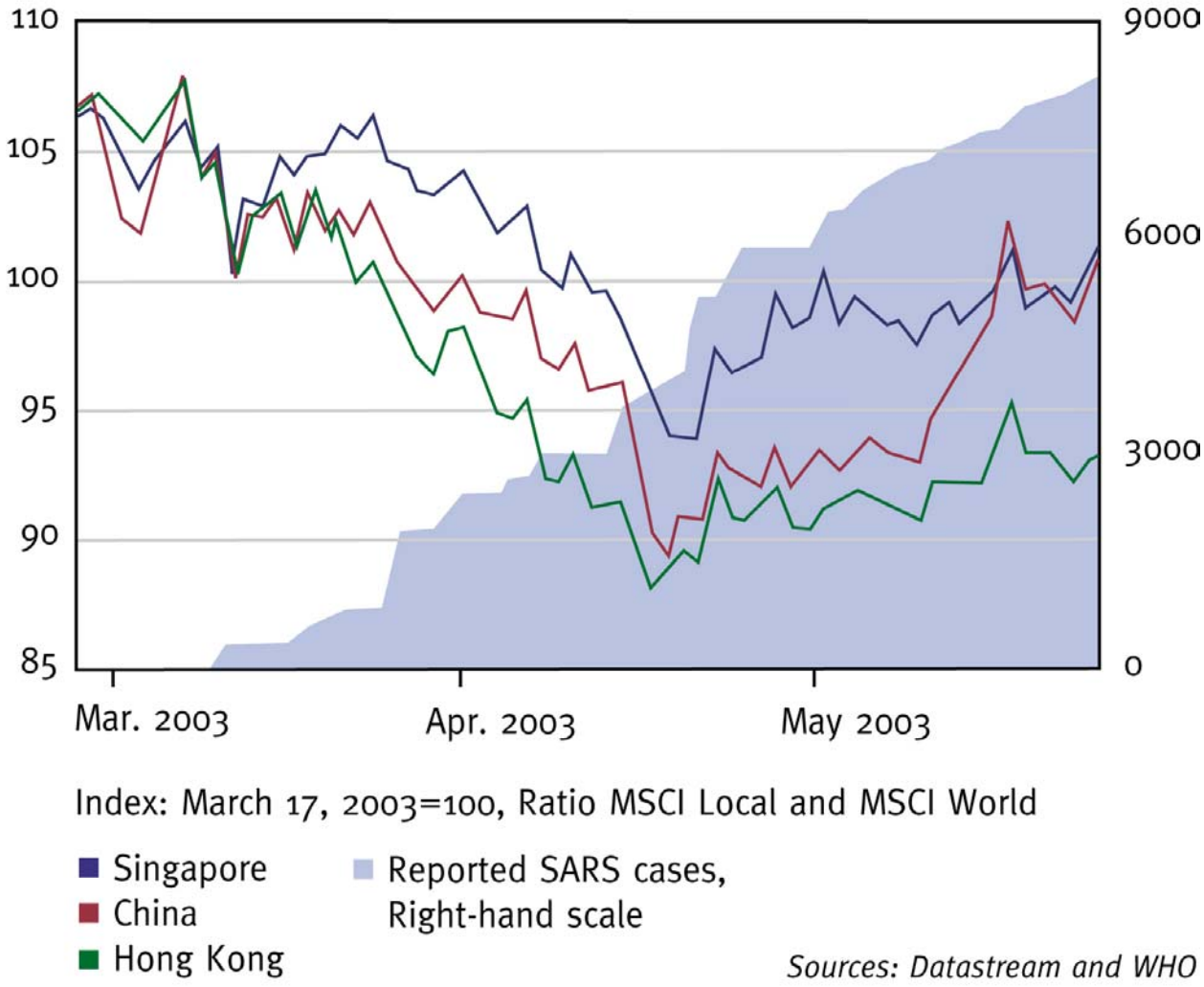
Asian Market Share Prices During SARS



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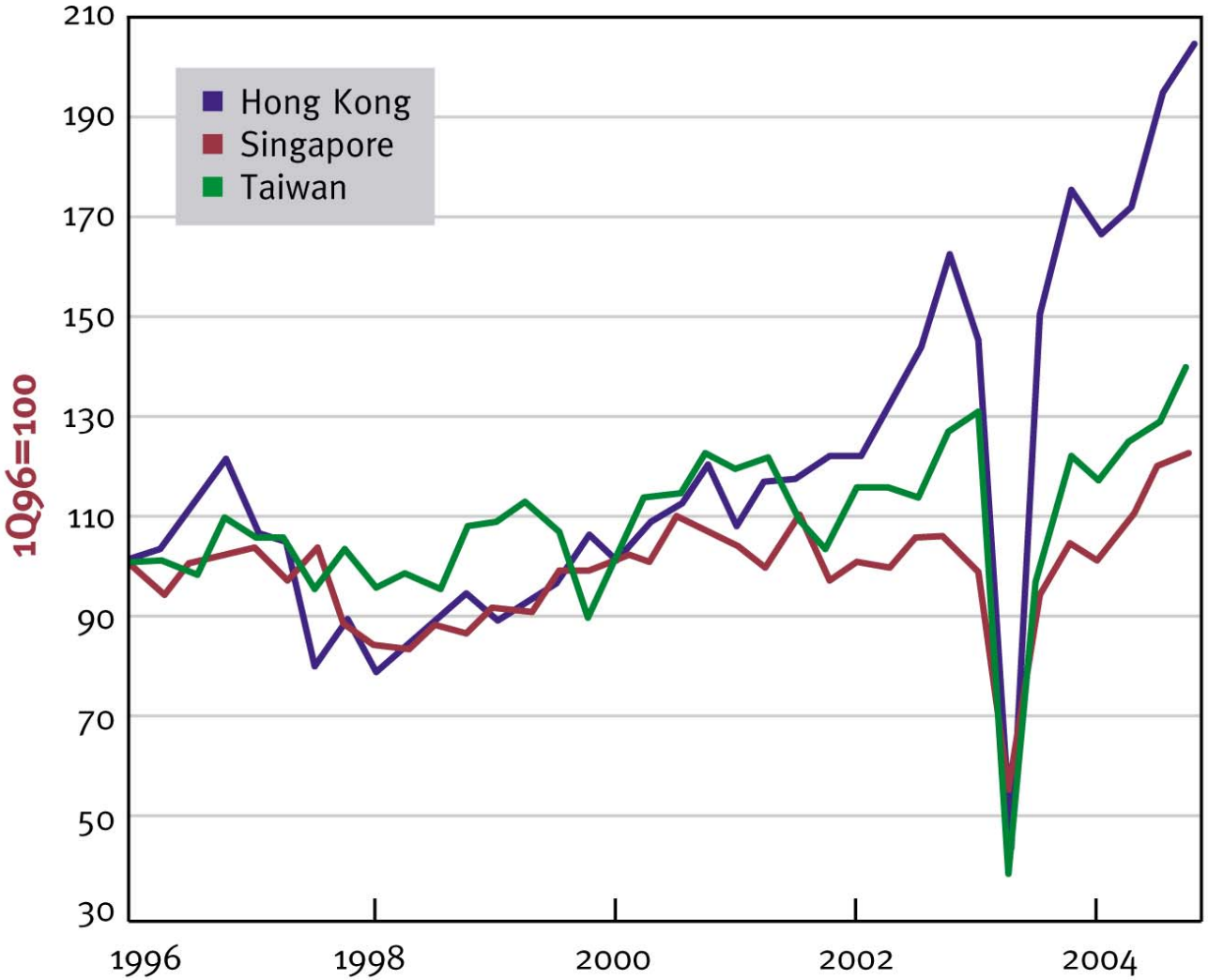
Decline in tourist arrivals during SARS



Source: CEIC data

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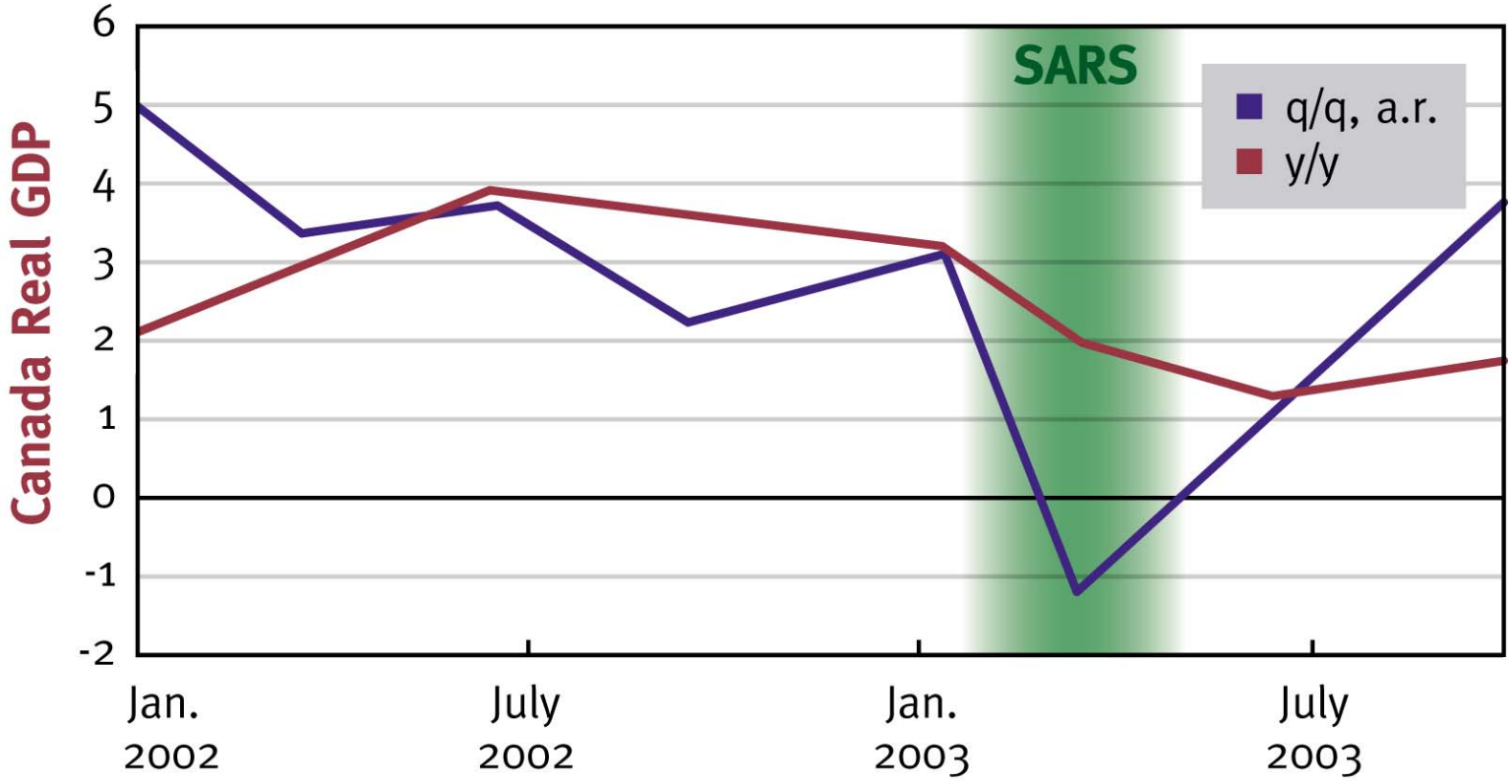
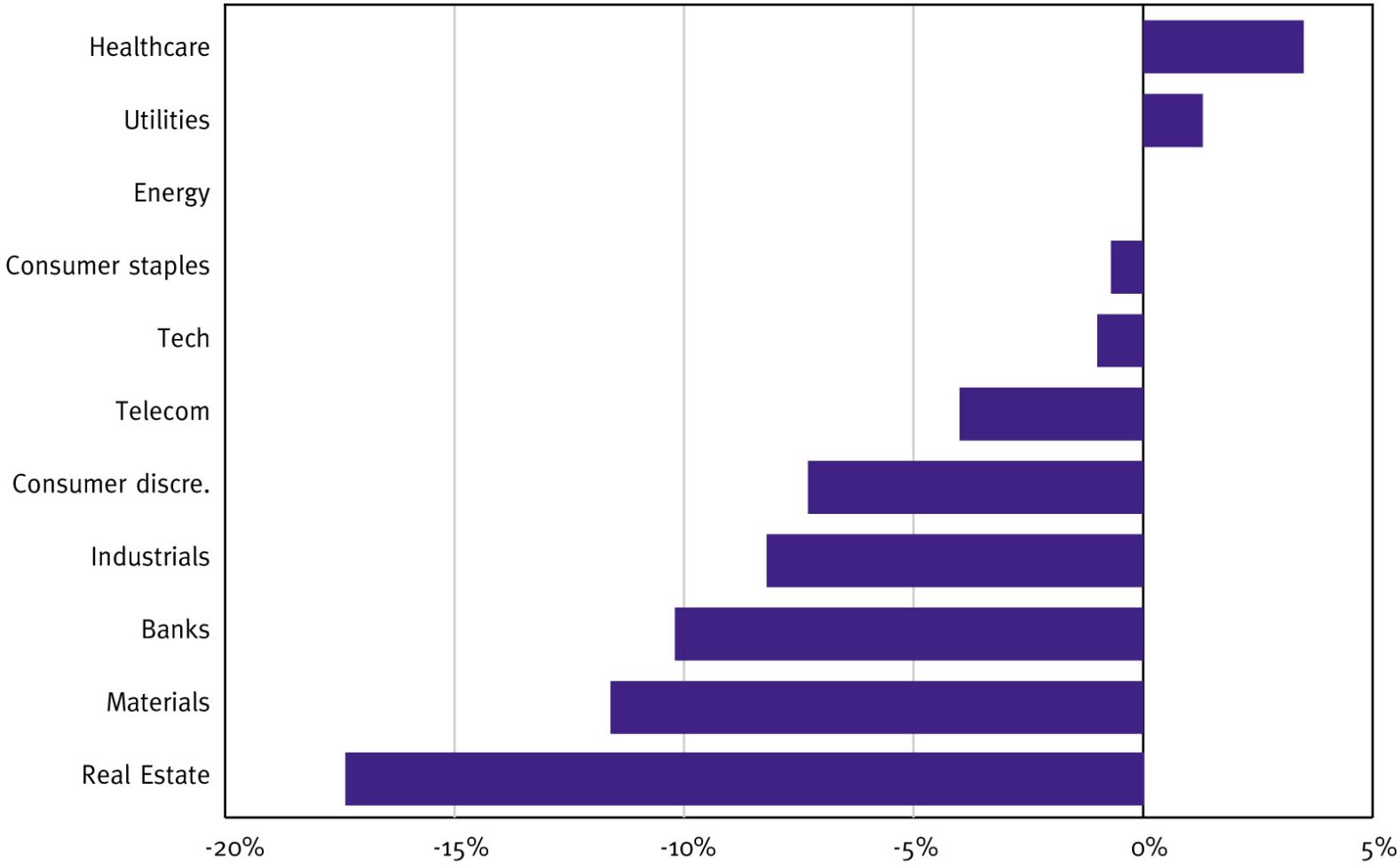
The Effect of SARS on the Canadian Economy



Sources: BMO Nesbitt Burns

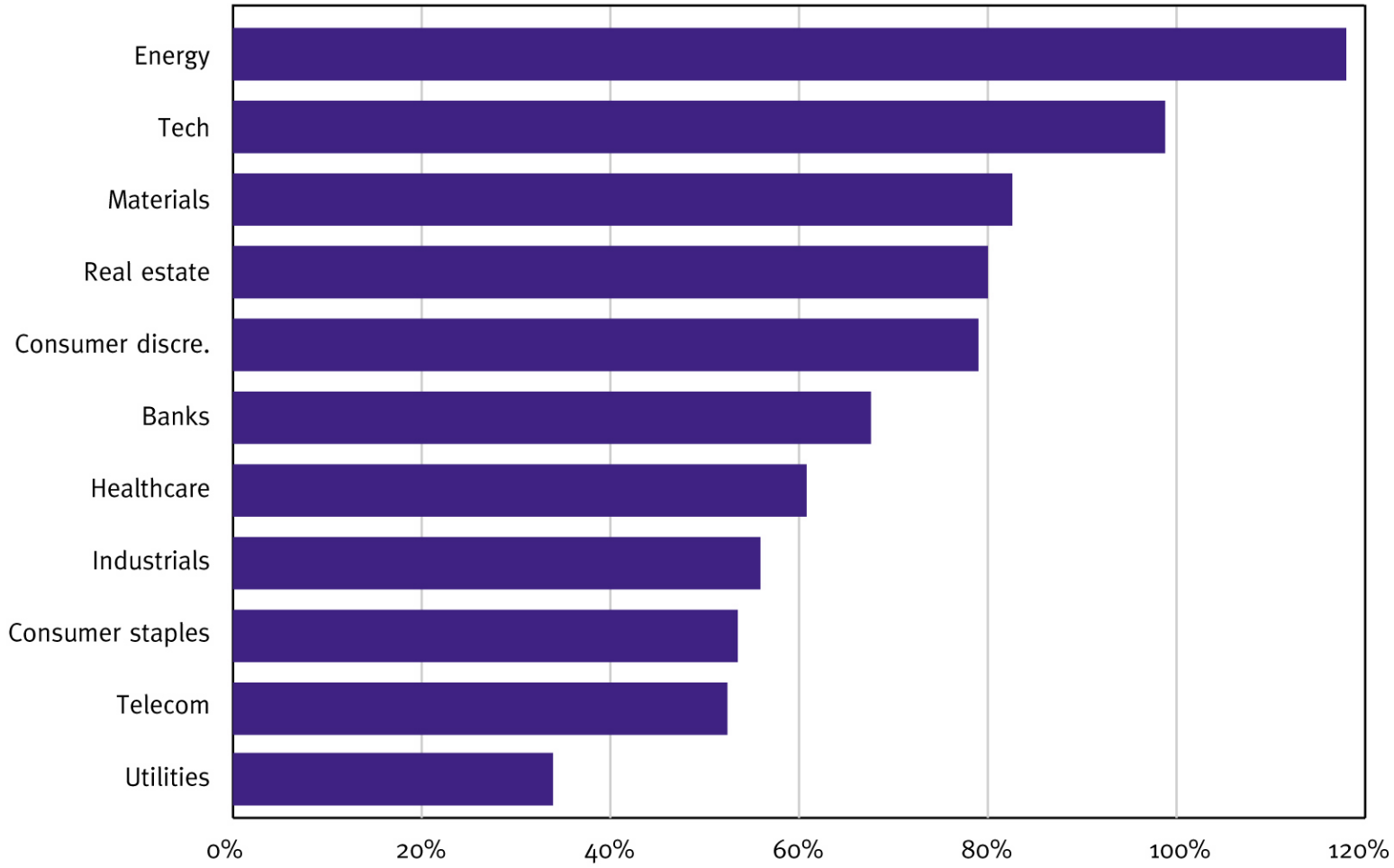
Asian Sector Performance During SARS



Asia ex Jp Performance (US$) from SARS Outbreak to SARS Low by Sector

Source: Citigroup Investment Research

Asian Sector Performance After SARS



Asia ex Jp Performance (US$) from SARS Outbreak to SARS Low by Sector

Source: Citigroup Investment Research

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Seven Lessons from the SARS Outbreak of 2003

1. The economic contagion of fear spread in advance of the pathogen, and did much greater economic damage than the disease itself.

2. The costs of medical response and lost productivity associated with SARS accounted for only about 1-2% of the $30-$50 billion of economic damage caused by the disease

3. Fear was amplified by a lack of government transparency

4. The most “open” economies were the hardest hit

5. The secondary economic effects included significant, unanticipated disruptions to global supply chains

6. There is no evidence that control measures at national borders had any significant impact on the spread of the disease

7. Once the disease was contained, the economic rebound was swift

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What Are the Elements of Preparedness Planning for an Influenza Pandemic?

- Overall Corporate Scenarios with Signpost Tracking
- Employee health and travel policies
- Workplace health and safety; “social distance” planning
- Vaccination and antiviral drug plans
- Emergency staffing
- Communications
- Security
- Government, public health, and community coordination
- Supply chain and infrastructure planning
- Market impact assessments
- Financial contingency planning

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Using Scenarios for H5N1 Avian Influenza

- Scenario development provides a disciplined but open approach to structuring the cascade of challenges that will be posed by H5N1 Avian Influenza in the future, including the fundamental uncertainties of pandemic
- Good scenarios can be used to work through implications for a diverse range of interests, stakeholders, operations and networks, and to identify gaps in preparedness
- Fundamentally, good scenario development yields a deeper, clearer understanding of the dynamics shaping the present, while creating a common framework and language for interpreting and responding to events as they unfold.

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Why Scenarios?

The most important choices we make in the present depend on the assumptions we hold about the future

Scenarios provide a way of making sense of the uncertainties we face and of challenging our assumptions about what the future holds

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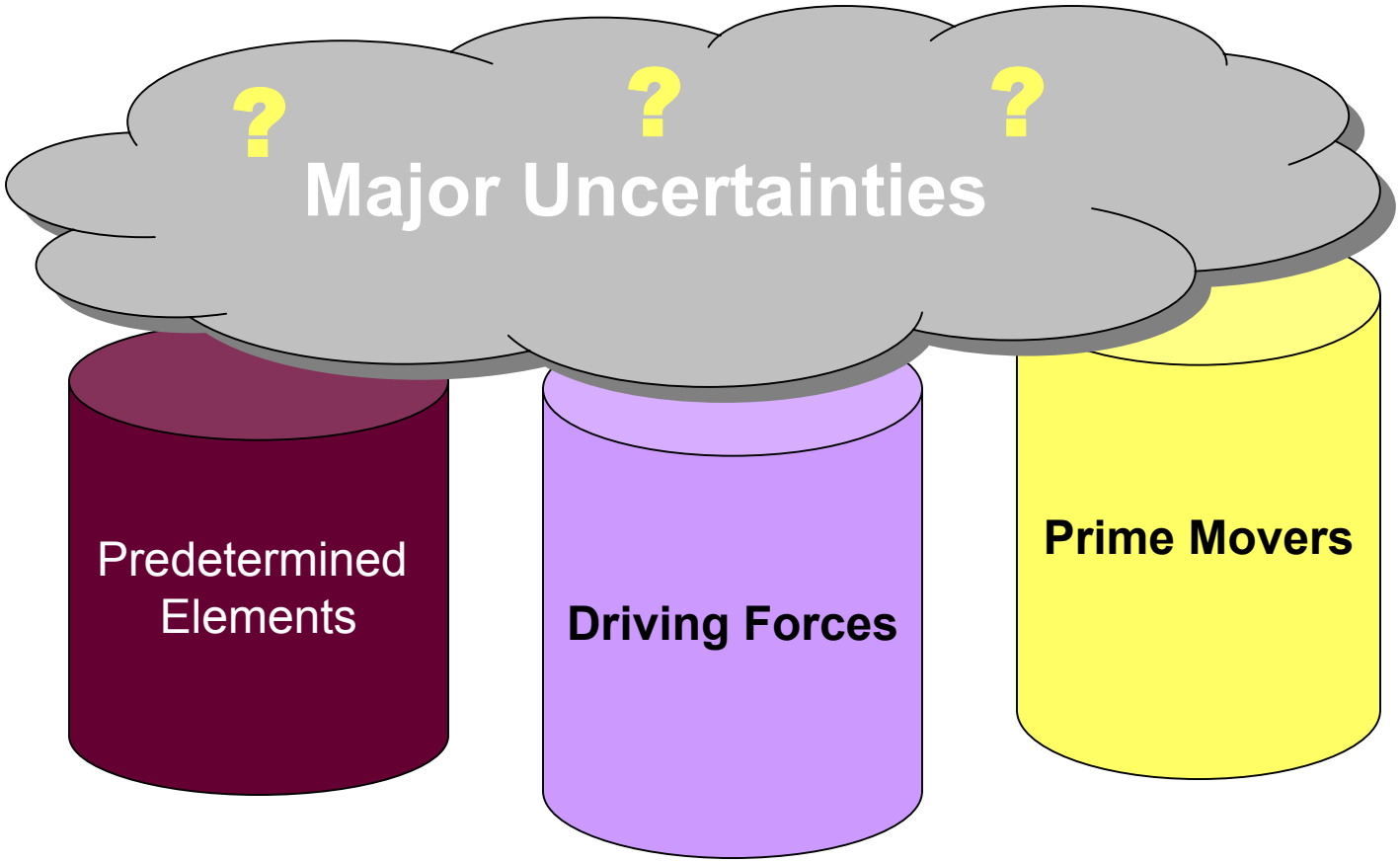
The Elements of Scenario Building



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Driving Forces

- Viral mutation, recombination and reassortment
- Human susceptibility to influenza pandemic
- Pathogen exchange among wildlife, livestock, and humans
- Globalization of trade and travel
- Increasing meat demand and livestock populations

Major Uncertainties

- Evolution of H5N1 to highly human-transmissible form
- Speed of dissemination of a pandemic
- Effectiveness of antiviral drugs in treating pandemic strain
- Effectiveness of human vaccines in treating pandemic influenza

Predetermined Elements

- H5N1 endemic in parts of Asia
- Human H5N1 infections will continue to occur
- H5N1 continues to evolve in the environment
- Vaccine manufacturing capacity with current technology is limited

Prime Movers

- H5N1 virus
- WHO and world public health community
- Suppliers of unapproved treatments
- FDA and other regulators
- Poultry farmers/industry
- Internet bloggers

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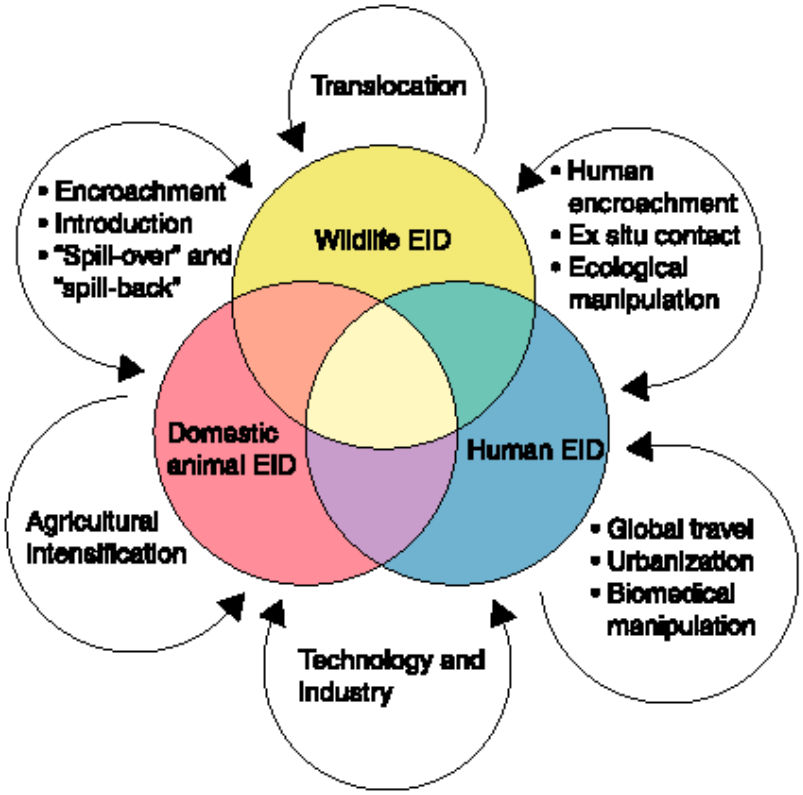
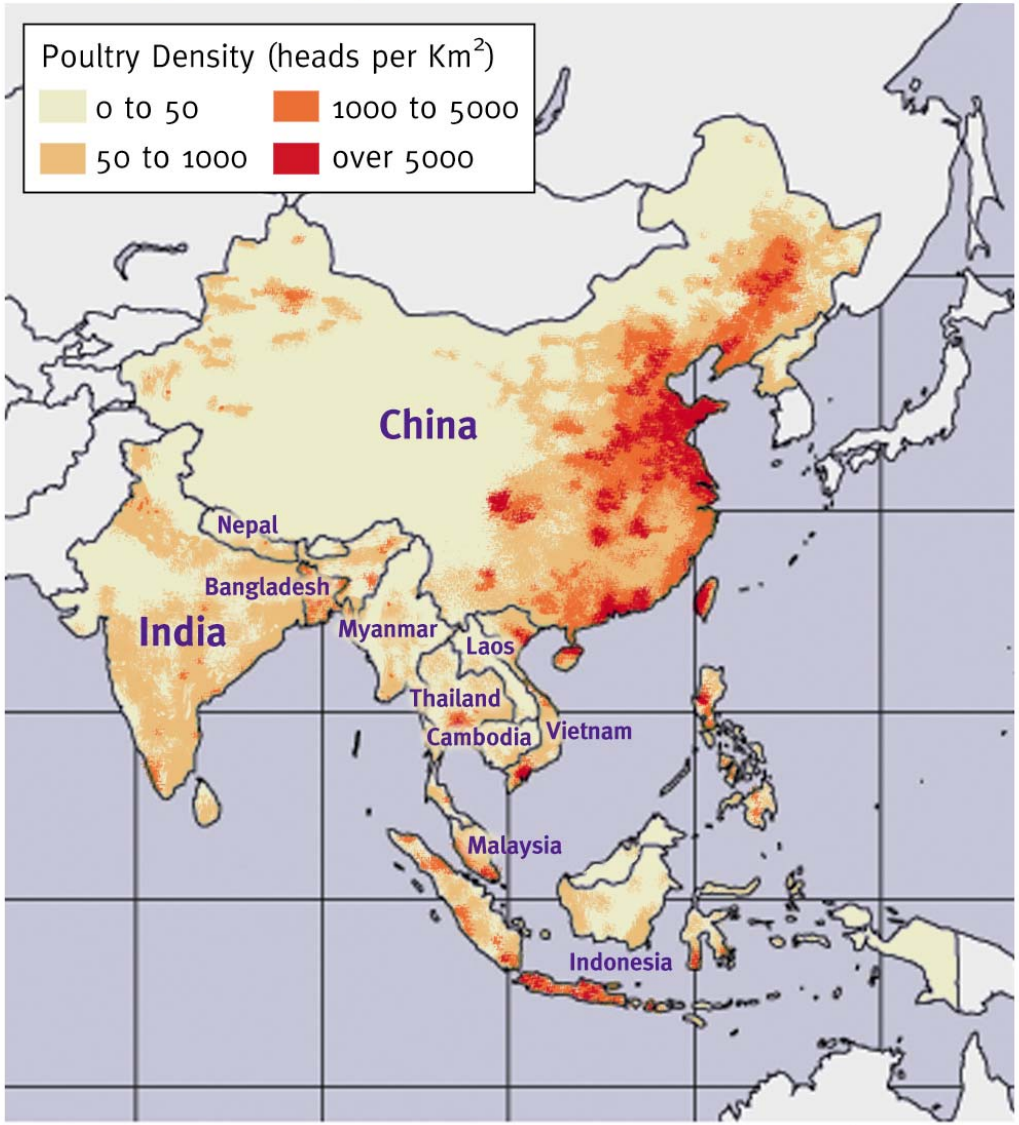
The Story of Emerging Infectious Disease:
Increasing Interactions Between Wildlife, Livestock, & Human Populations

- **Fundamental forces are driving new infectious disease threats**
- **Emerging diseases are causing increasingly significant economic disruptions**
- **Avian influenza poses especially large potential risk**



Poultry Density in Asia



Source: FAO

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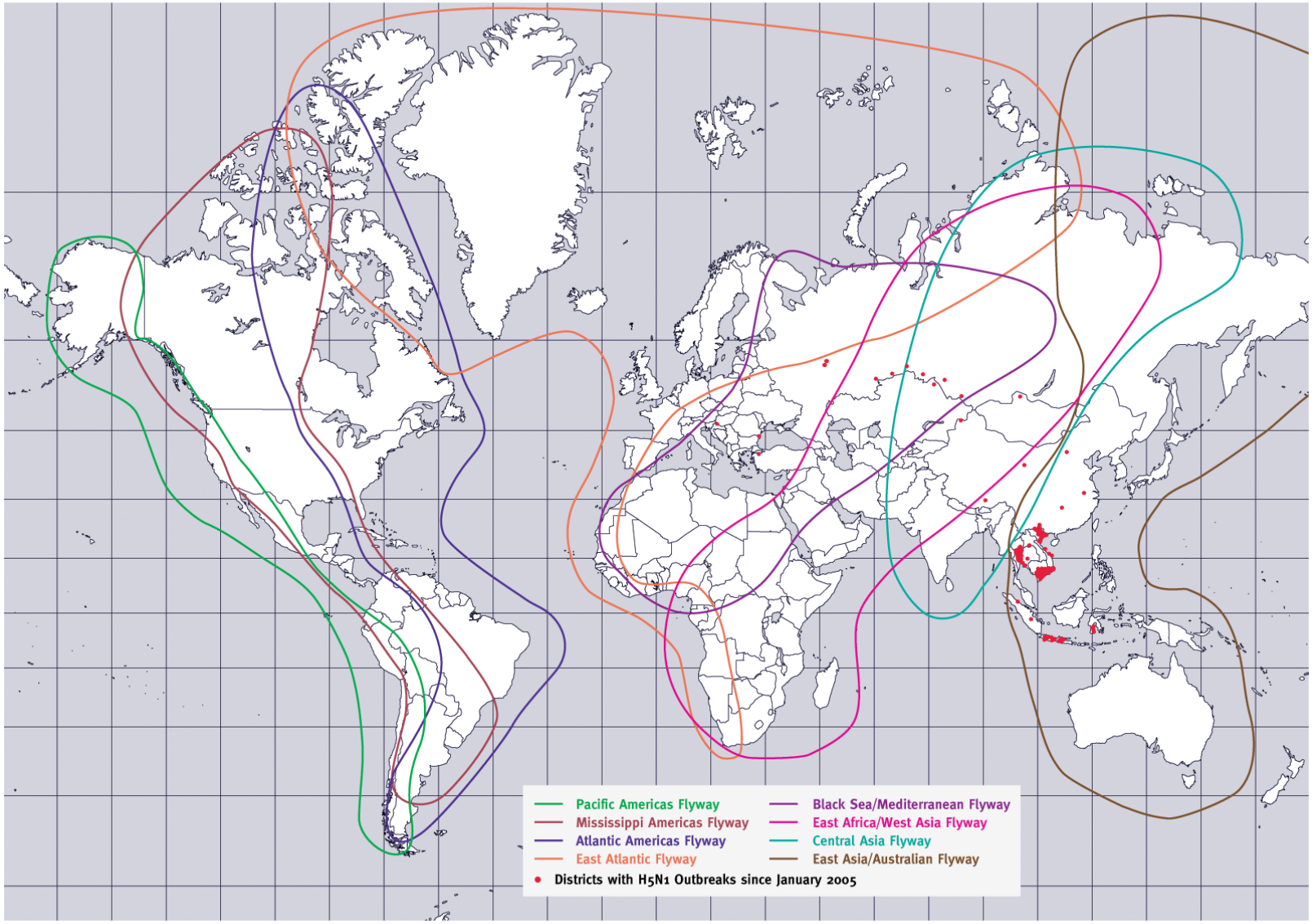
H5N1 Outbreaks in 2005 and Major Migratory Flyways



Sources: AI Outbreaks — OIE, FAO, and government sources; Flyways — Wetlands International

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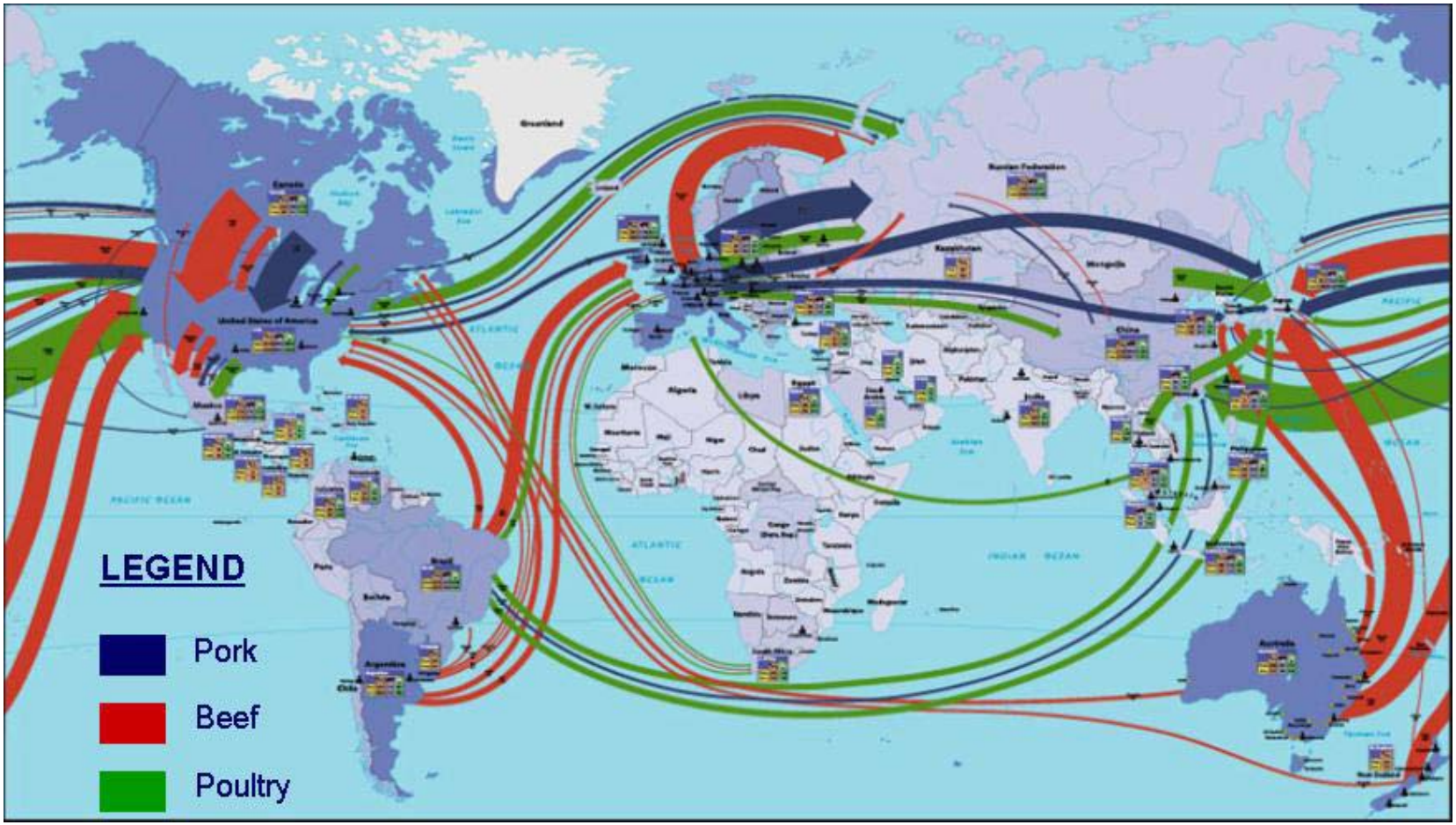
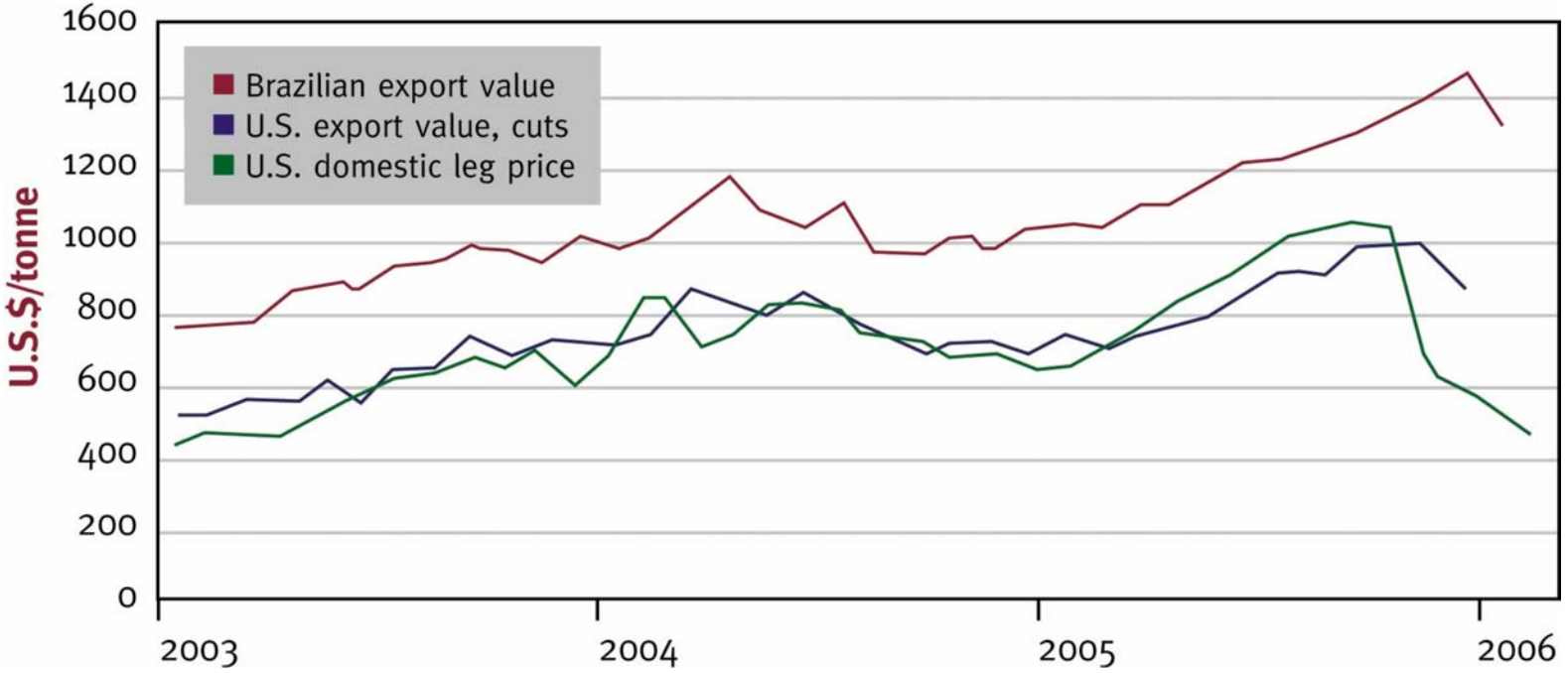
Global Meat and Animal Trade are also Potential Channels for the Spread of H5N1



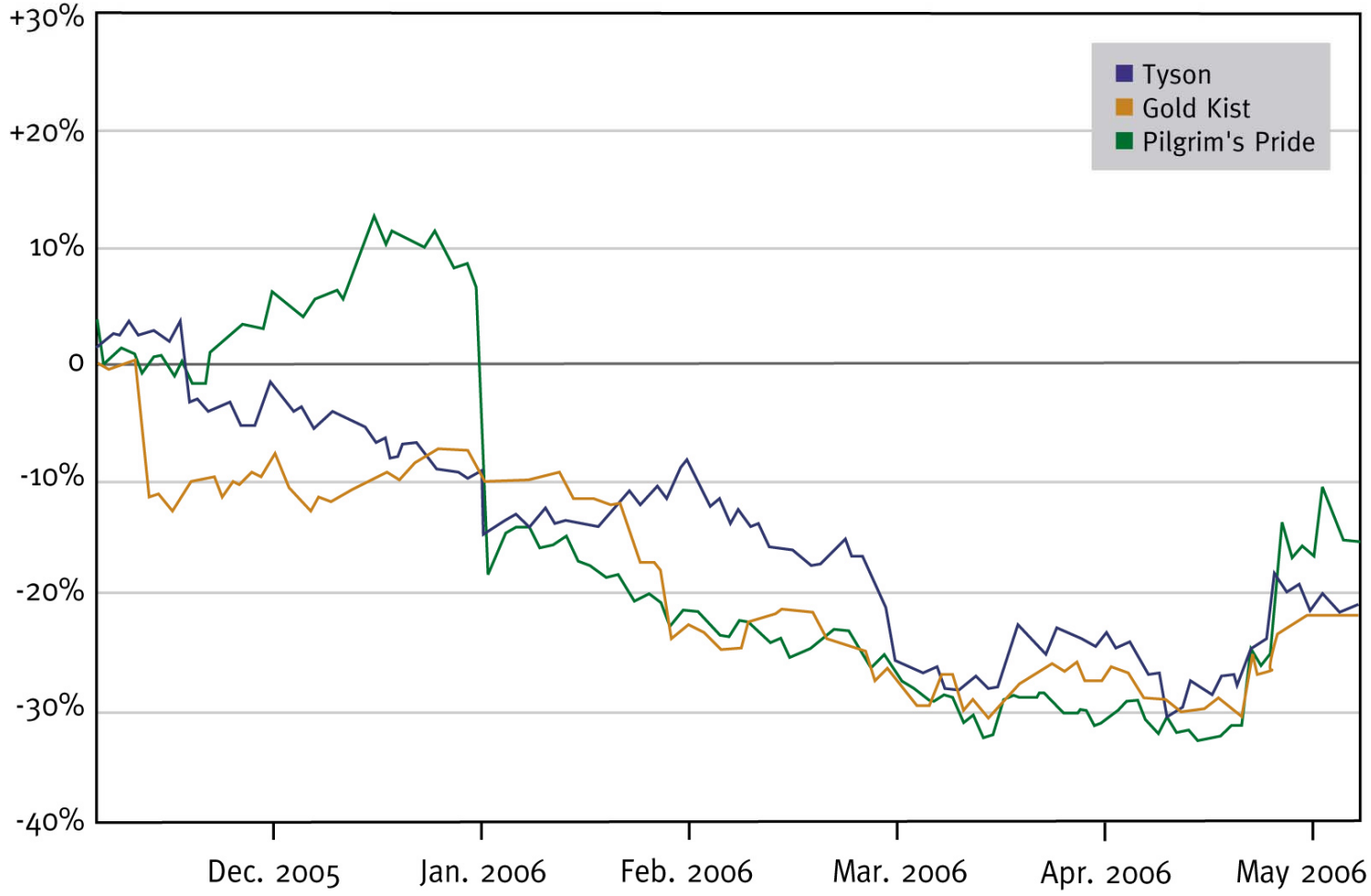
Source: Center for Global Food Issues

Sharp Declines in International Poultry Demand Drive Down Export Prices



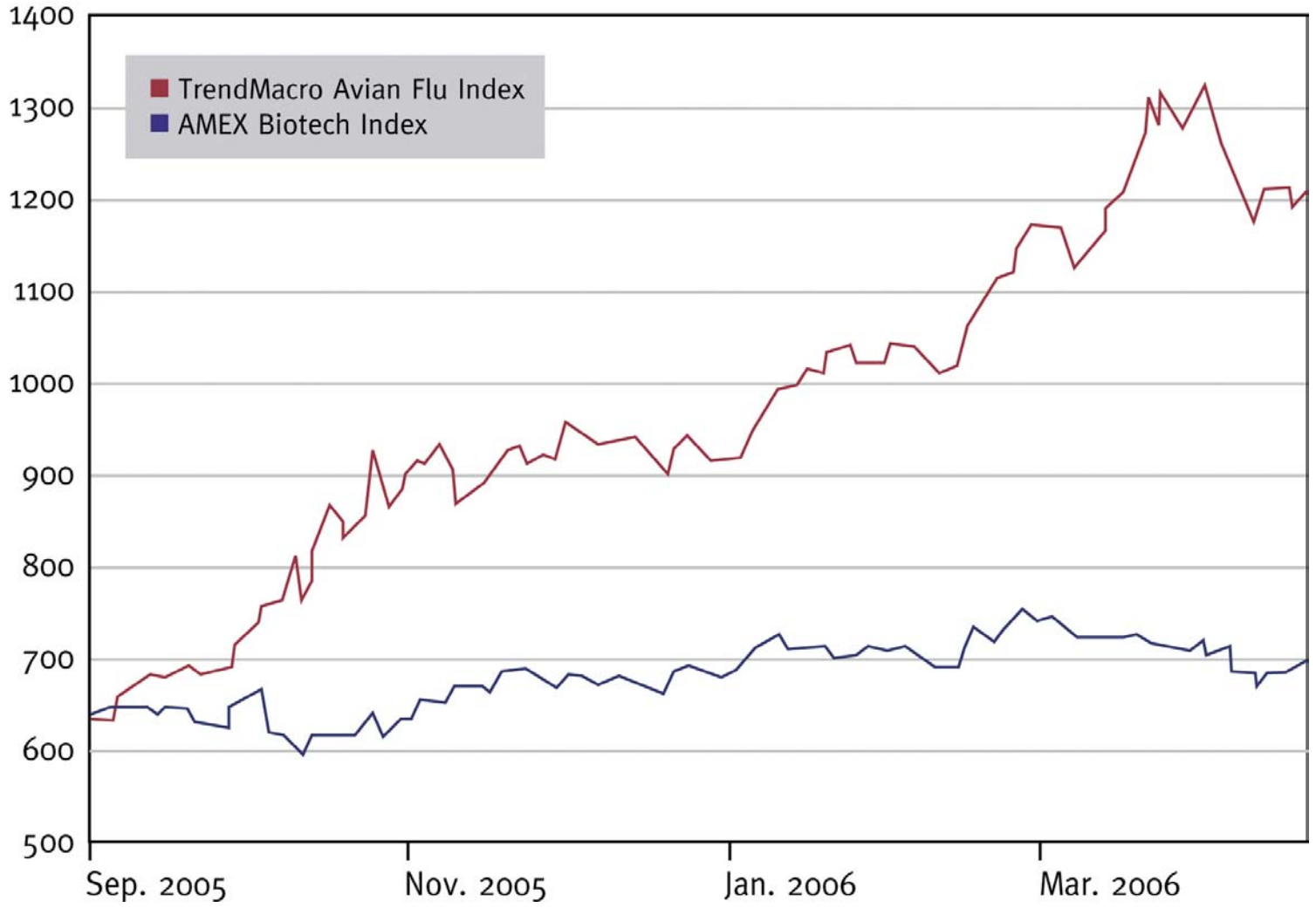
Source: FAO

Share Prices for Major U.S. Poultry Companies



Source: Bloomberg

Avian Influenza Index: Topping Out?



Source: TrendMacrolytics; index stocks: Anylam Pharma, Avant, Avi Biopharma, BioChryst, Carrington Labs, Combimatrix, Cepheid, Crucell, Embrex, Gilead, Generex Biotech, Hemispherx Biopharma, Medimmune, Nastech Pharma, Novavax, Quidel, Sinovac Biotech, Vical

Type A Influenzas with High Pandemic Potential

Neuraminidase (NA or N)	Hemaglutinin (HA or H)								
	N1	N2	N3	N4	N5	N6	N7	N8	N9
H1	H1N1								
H2		H2N2							
H3		H3N2							
H4									
H5	H5N1								
H6									
H7							H7N7		
H8									
H9		H9N2							
H10									
H11									
H12									
H13									
H14									
H15									
H16									

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Epidemiological Models Assess Pandemic Spreading and Impact of Mitigation Measures

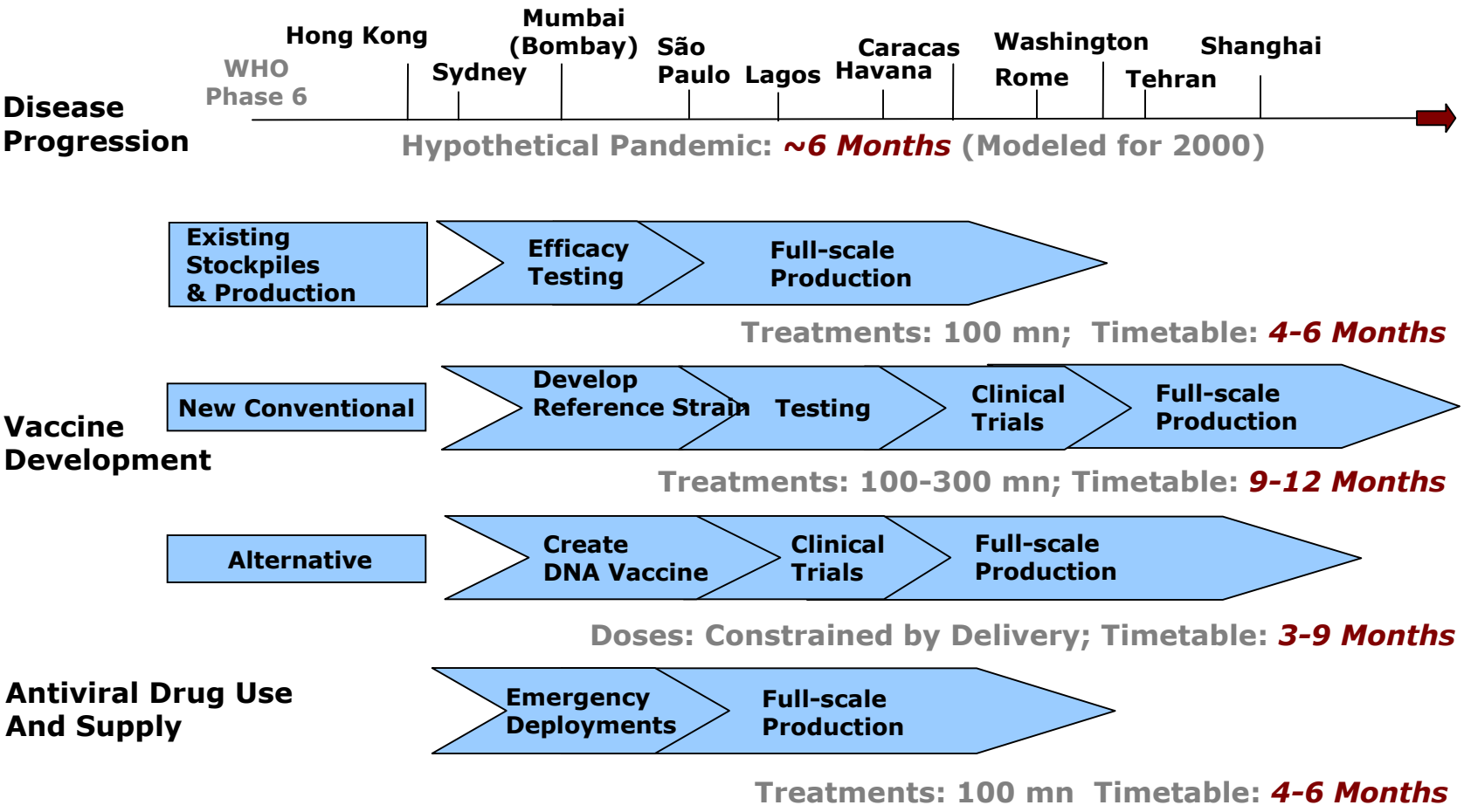
If combined with 99.9% effective border controls, blanket reductions in non-local travel achieve little in delaying the peak of the epidemic…but do reduce the peak attack rate substantially and spread the epidemic over a much longer time period.

School closure…causes a small reduction in cumulative attack rates, but a more substantial reduction in peak attack rates (of up to 40%). Such a reduction in peak incidence could mitigate stresses on healthcare systems and absenteeism in the critical workforce. Closure of 50% of workplaces can enhance the impact of school closure, but at higher economic cost.

Vaccination at the rate of 1% of the population per day would need to begin within 2 months of the initial global outbreak…substantially faster than is possible using current vaccine technologies. A delay of 4 months from the start of the global pandemic would mean that the initial epidemic would be largely over by the time most of the modeled populations could be vaccinated.

Strategies for mitigating an influenza pandemic
Ferguson et al., Nature, April 26, 2006

Timelines for Pandemic Response Measures



Source: bio-era, National Geographic

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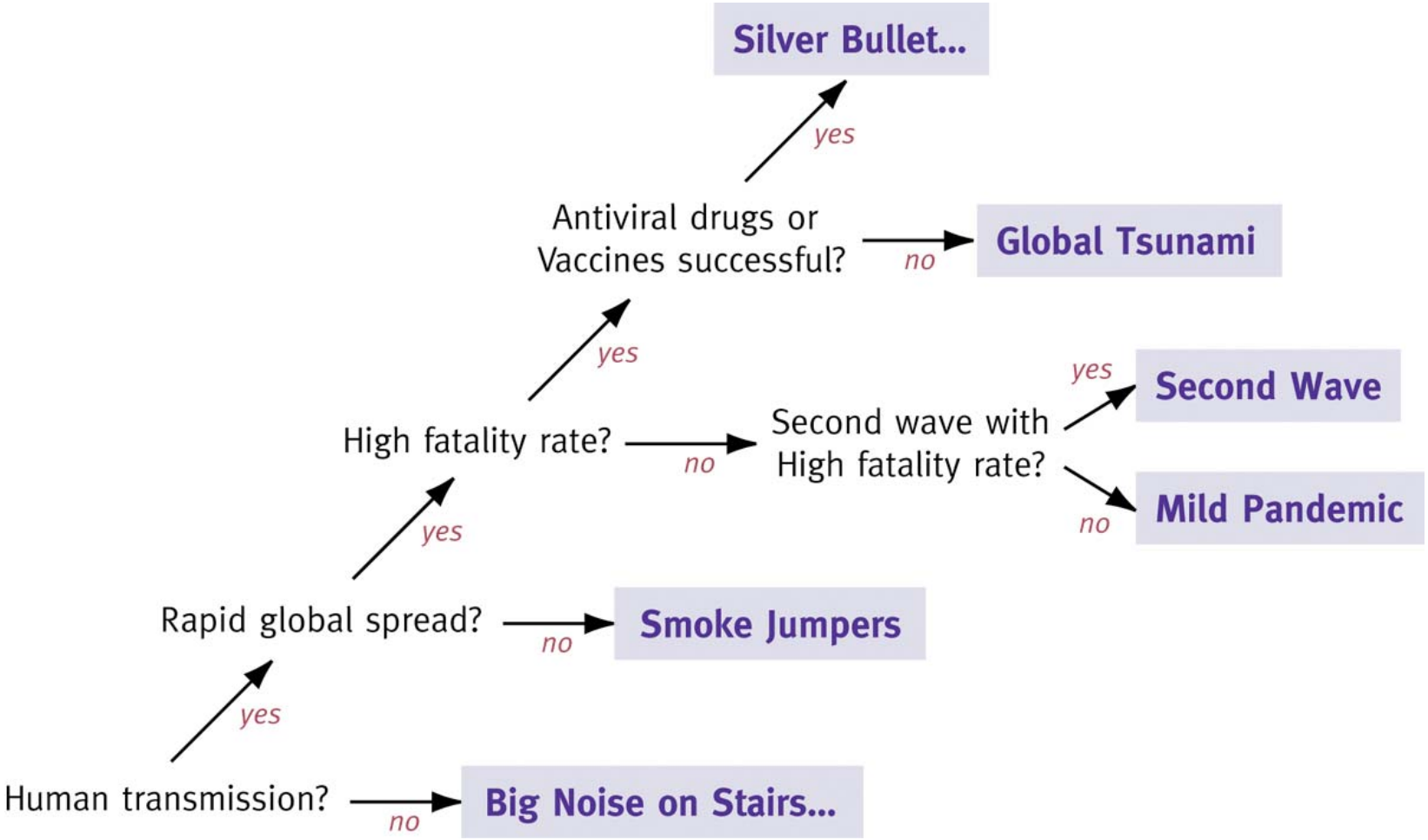
The bio-era Scenarios Map:

A First Step toward Structuring the Conceptual Space…



Evaluate Proposed Actions For Each Scenario

Example: *Stockpile Tamiflu for All Employees and their Families*

Cost = $100 - $200 per month per person for prophylaxis;
½ that for treatment course

Animal Scenario 1

- For use as a prophylactic, only required for poultry workers and possibly for their dependents
- Small psychological value in keeping supplemental supplies for emergency treatments of very rare human cases
- Evaluate ethics of keeping stockpiles away from high-risk outbreak areas
- Could be high ethical and political value in contributing antivirals to public regional stockpiles or the WHO

Pandemic Scenario 1

- Could be overwhelming demand for use as prophylactic over many months; costs could be as high as $2,000 per person
- Need for treatment stockpile very real; may need plan for treating 15%-20% of the workforce and their dependents
- Must develop priority of use (*who gets the drug*) and intention of use (*for what purpose*) plans
- Run high-risk of expropriation of stockpiles, so consider distribution in advance of pandemic

Estimated Macroeconomic Costs of a Pandemic (percentage points of GDP growth decline)

Region	Model	Severity	Demand	Supply	Total
Asia	***ADB***	Mild	2.3	0.3	2.6
		Severe	6.5	0.3	6.8
U.S.	***Lowy***	Mild	0.0	0.6	0.6
		Moderate	0.2	1.2	1.4
		Severe	0.4	2.7	3.0
		Ultra	0.8	4.8	5.5
	CBO	Mild	0.5	1.0	1.5
		Severe	2.0	3.0	5.0
Global	***BMO/Nesbitt***	Mild	0.7	1.3	2.0
		Severe	2.3	3.7	6.0

Source: BMO Nesbitt-Burns; Bio-era analysis

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Corporations Are Assessing the Impacts of Their Operations on Living Systems

Risks:

- McDonalds: AIM launched new policy on antibiotics use in meat production
- Unilever: sustainable food supply initiative
- DuPont-Pioneer: resistance management and drought resistant traits in seed development
- BSR: Clean Cargo initiative addresses invasive species

Opportunities:

- Biofuels production
- Biomaterials
- Biological pathways for production processes (biomimicry)
- Synthetic biology pathway engineering (artemisinin, taxol, etc.)

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New Tools to Manage Biosecurity Risks

	Commodity Price Risk	Bioeconomic Risk
Fundamentals analysis	Supply/demand, trade & investment	Evolutionary biology, ecology, epidemiology
Scenario planning	Signposts, market dynamics	Emergence & florescence
Intelligence/monitoring	Market benchmarks, basis risk	Sentinels, testing, global tracking
Financial risk management	Futures, options, derivatives, forward markets, insurance	Futures, options, derivatives, forward markets, insurance
Operational management	Flexibility, supply chain management	Exclusion, defense, emergency response, supply chain management

Scenario Signposts

Examples:

- **Signs of Outbreak**:
  - — Reports of clusters of human H5N1 disease, with suspected H-H transmission
  - — WHO declares we are in Stage 4 of pandemic
  - — WHO rushing in countermeasures
  - — Increased and sustained transmission

- **Signs of Early Economic Reaction**
  - — Gold Prices
  - — Crude oil vs. Jet Fuel Spread
  - — Local country currency values
  - — US Treasuries

- **Signs of Political Tension**
  - — Finger-pointing between governments
  - — Nationalization or confiscation of private countermeasure stockpiles
  - — Trade and travel embargoes against outbreak countries

- **Signs of Fear**
  - — Internet search word volumes
  - — Spikes in website hits
  - — Countermeasure sales and shortages
  - — Growing TV and media coverage

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A Vital Linkage in the Economic Transmissibility of an "Asian Flu"

US National Strategy for Pandemic Influenza

- **The strategy contains three pillars:**
  - Preparedness and Communication
  - Surveillance and Detection
  - Response and Containment
- ***Who is in Charge?***
  - **Secretary of Homeland Security**: responsible for coordination of Federal operations and resources, the establishment of reporting mechanisms, and communication with Federal, State, local and tribal governments, the private sector, and NGOs.
  - **Secretary of Health and Human Services:** responsible for Federal health and medical responses, and will be the principal Federal spokesperson during a pandemic.
  - **The White House** will chair a group of senior government decision makers on the monitoring of daily events, strategic policy development, and domestic responses.

US National Strategy for Pandemic Influenza

- ***International Partnerships and Protocols:***
  - The *U.S. International Partnership on Avian and Pandemic Influenza* will be responsible for promoting transparency from governments and multilateral institutions, scientific cooperation, and the rapid reporting of human and animal influenza outbreaks.
  - U.S. Embassies and Consulates will be responsible for identifying local resources for obtaining medical supplies and treatment in the event of “stay in place” responses to a pandemic.
- ***Trade and Travel:***
  - Border closures and restrictions on non-essential travel, or mandatory restrictions as a last resort. States are principally responsible for quarantine decisions within their borders.
  - Other control measures will be promoted first: social distance, isolation, and options for vaccination or antiviral medication.
  - The flow of incoming flights from international destinations is likely to be restricted in order to execute screening protocols. Isolation and quarantine could be implemented where appropriate.

US National Strategy for Pandemic Influenza

- ***Vaccines:***
  - The Federal Government will attempt to establish and maintain vaccine stockpiles adequate to immunize 20 million people against influenza strains that present a pandemic threat.
  - Federal Government also aims to expand influenza vaccine manufacturing capacity to cover the entire U.S. population within 6 months of pandemic declaration.
  - National poultry vaccine stockpile will be expanded from 40 to 110 million doses.
  - Department of Health and Human Services has awarded more than $1 billion worth of contracts to improve cell culture-based vaccine production. Novartis AG, GlaxoSmithKline PLC, MedImmune Inc., Solvay Pharmaceuticals, and a unit of Computer Sciences Corp.
- ***Antivirals:***
  - Federal Government will attempt to establish and maintain stockpiles adequate to treat 75 million people (between Federal and State stocks).
  - Federal Govt. also aims to establish and maintain a Federal stockpile of 6 million treatment courses reserved for domestic containment efforts.

US National Strategy for Pandemic Influenza

- ***Personnel Recommendations for the Private Sector:***
  - — Recommended strategies for preventing pandemic influenza are the same as for seasonal influenza:
    1) *Vaccination*
    2) *Early detection and treatment*
    3) *Use of infection control measures to prevent transmission.*
  - — The ability to limit transmission will rely primarily on the application of infection control measures in health care facilities, the workplace and the general community.

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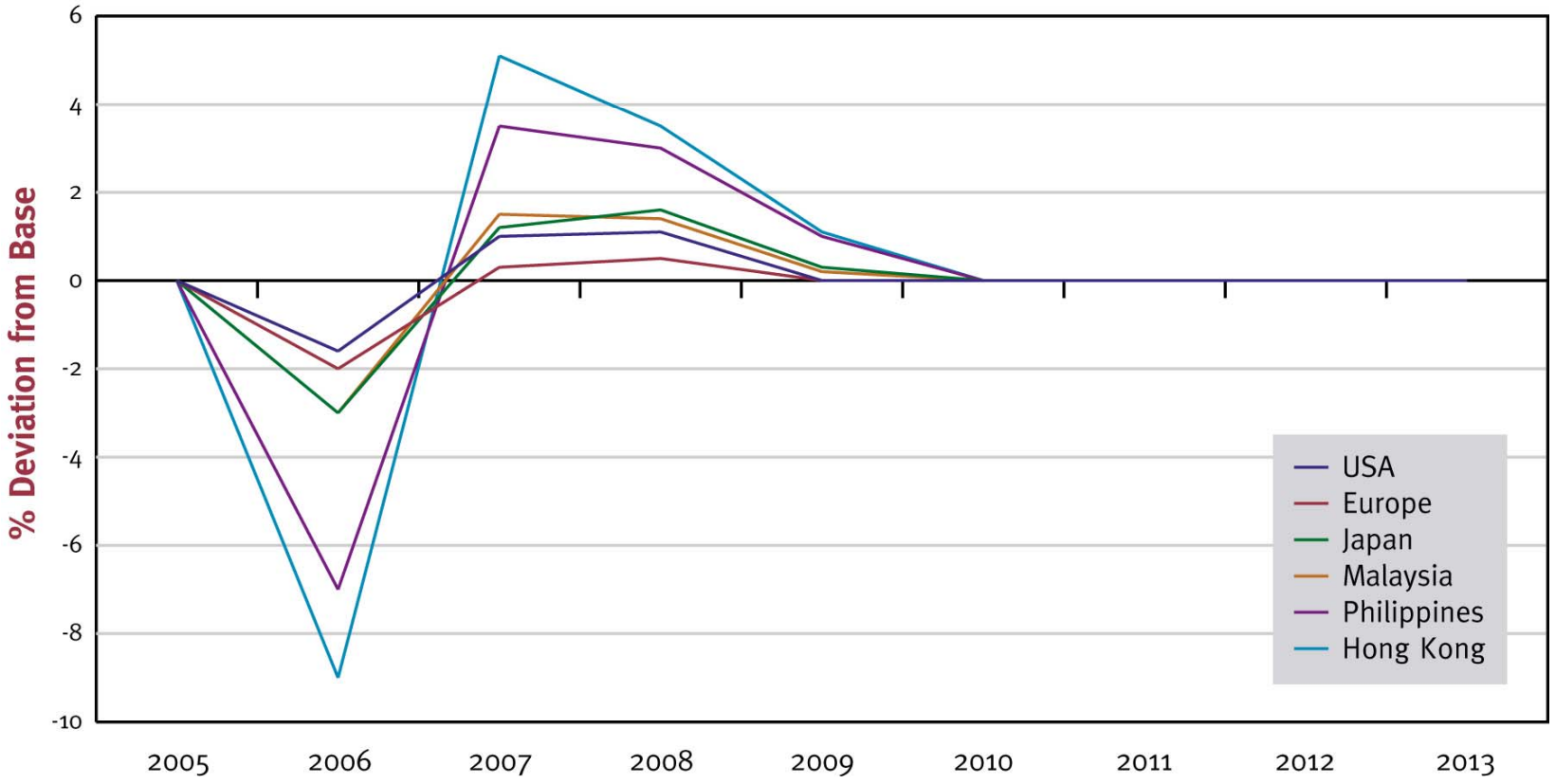
Change in GDP Growth in the Moderate Scenario



Source: Lowy Institute

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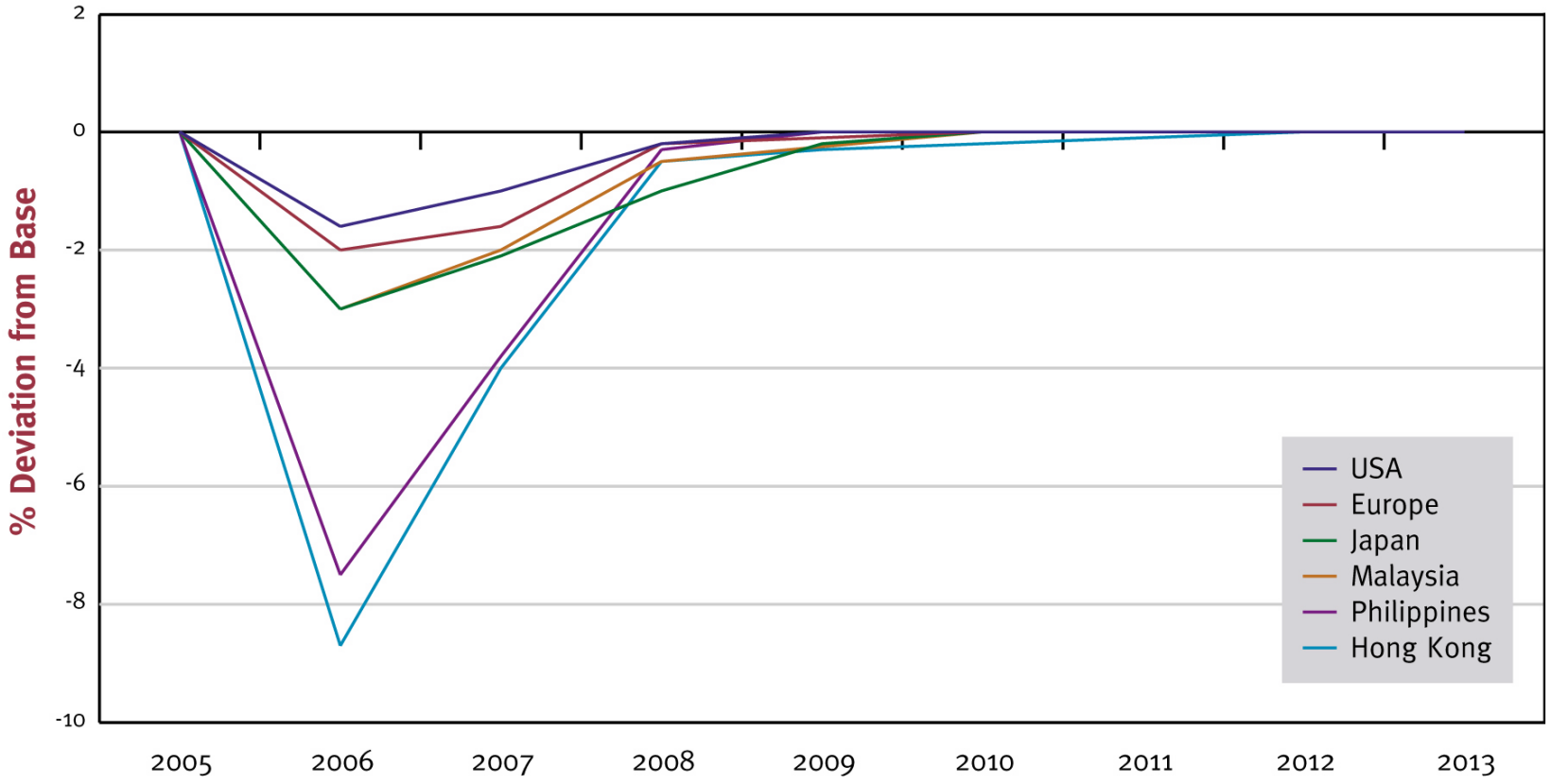
Change in GDP in the Moderate Pandemic Scenario



Source: Lowy Institute

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2006 Percentage GDP Loss by Region

Country	Mild	Moderate	Severe	Ultra
USA	-0.6	-1.4	-3.0	-5.5
Japan	-1.0	-3.3	-8.3	-15.8
UK	-0.7	-2.4	-5.8	-11.1
Europe	-0.7	-1.9	-4.3	-8.0
Canada	-0.7	-1.5	-3.1	-5.7
Australia	-0.8	-2.4	-5.6	-10.6
New Zealand	-1.4	-4.0	-9.4	-17.7
Indonesia	-0.9	-3.6	-9.2	-18.0
Malaysia	-0.8	-3.4	-8.4	-16.3
Philippines	-1.5	-7.3	-19.3	-37.8
Singapore	-0.9	-4.4	-11.1	-21.7
Thailand	-0.4	-2.1	-5.3	-10.3
China	-0.7	-2.1	-4.8	-9.1
India	-0.6	-2.1	-4.9	-9.3
Taiwan	-0.8	-2.9	-7.1	-13.8
Korea	-0.8	-3.2	-7.8	-15.1
Hong Kong	-1.2	-9.3	-26.8	-53.5

Source: Lowy Institute