Institute
and Faculty
of Actuaries

Pandemic Panic

Paul Morden **Munich Re**
Gordon Woo **RMS LifeRisks**

Institute
and Faculty
of Actuaries

Agenda

1. Q&A questions
2. What is a pandemic and who should be worried?
3. Influenza 101
4. Overview of pandemic modelling
5. What mortality is associated with a severe pandemic?
6. Q&A answers

Institute and Faculty of Actuaries

Audience questions

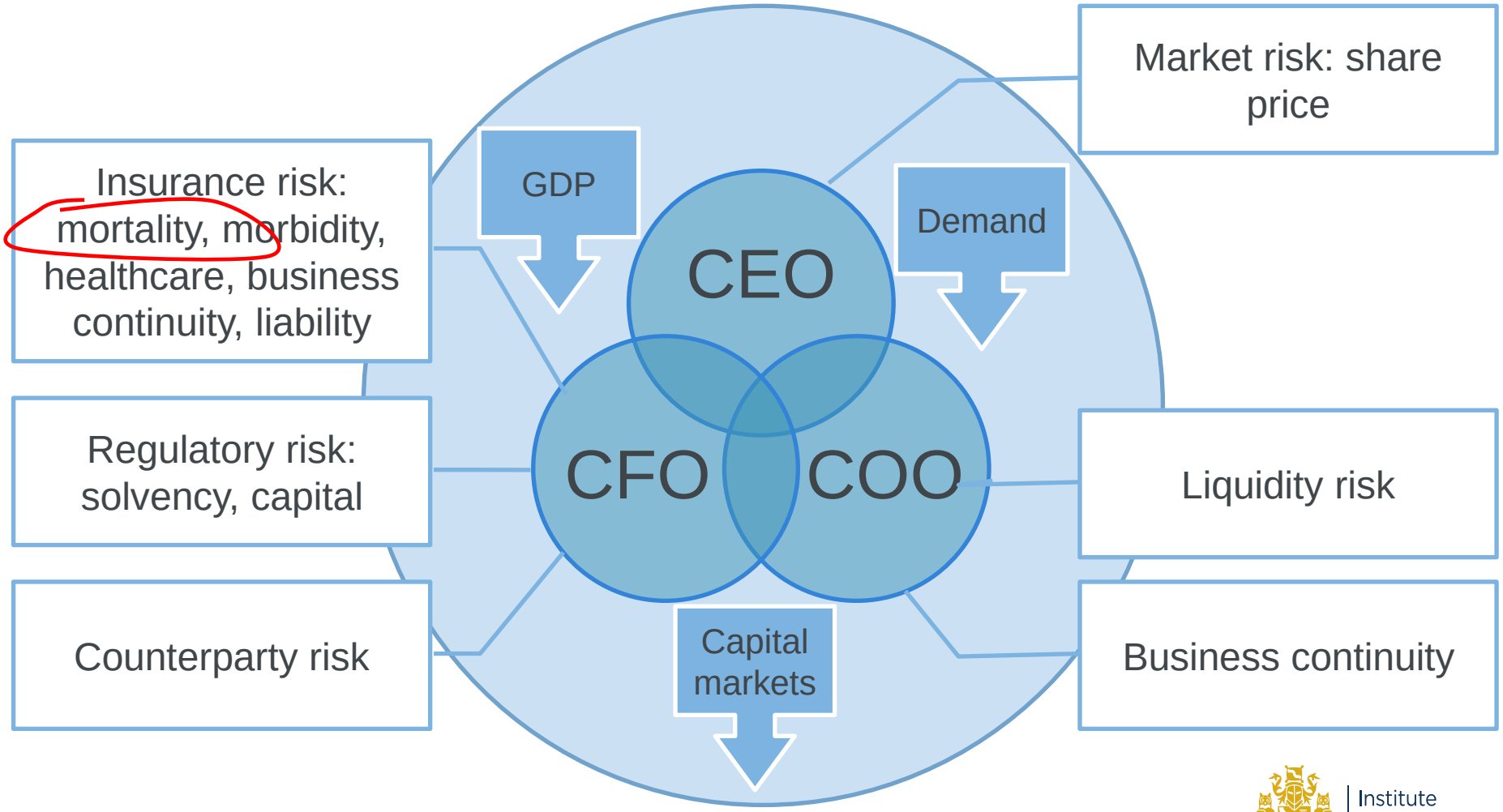
Institute and Faculty of Actuaries

What is a pandemic?

“When an infectious disease spreads to large parts of a continent or even the whole world.”

Institute and Faculty of Actuaries

Who should be worried about a pandemic?



Institute and Faculty of Actuaries

How do pandemic losses compare to other significant insurance events?

“…….even if it were to become a serious pandemic, our exposure would be limited, comparable with our exposure to natural disasters.” Torsten Jeworrek, Munich Re

Institute and Faculty of Actuaries

Structure of the influenza virus

Strains are characterised by two proteins found on their surface: Neuraminidase and Hemagglutinin. Approximately 80% of the spikes are hemagglutinin, which functions in the attachment of the virus to a host cell.

The remaining 20% or so of the spikes consist of neuraminidase, which is predominantly involved in facilitating the release of newly produced virus particles from the host cell.

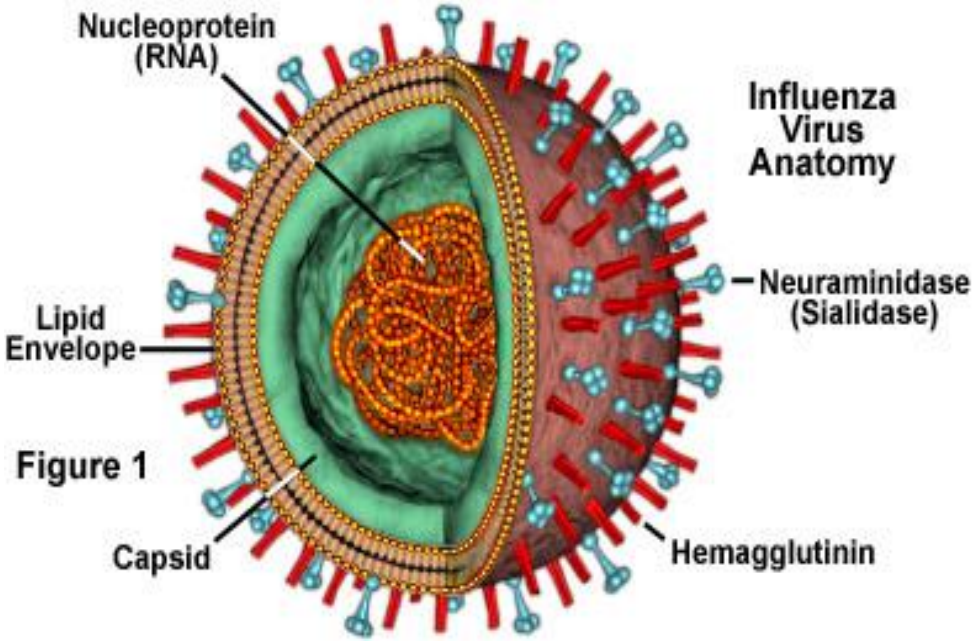


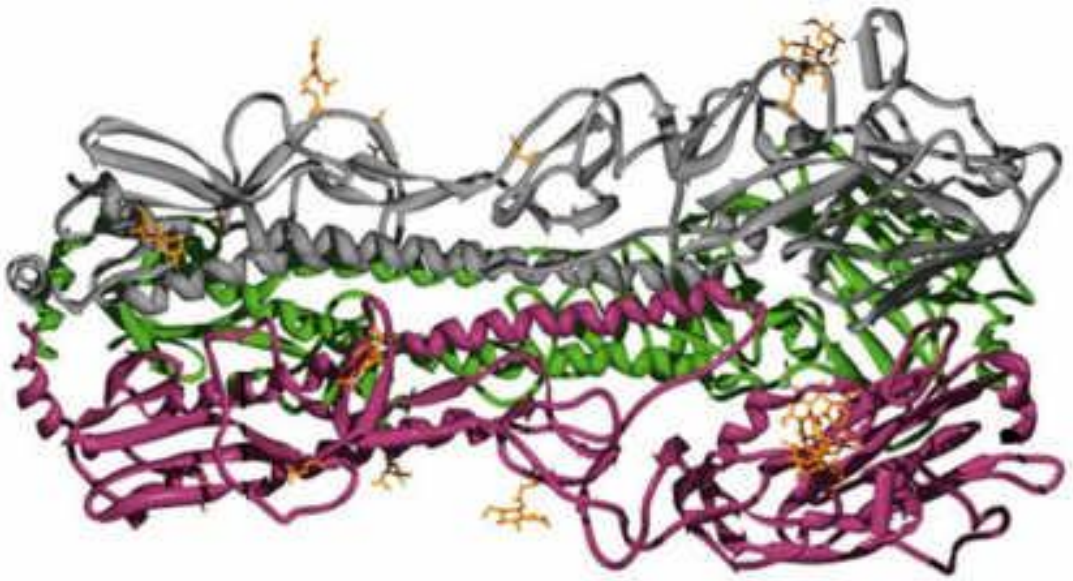
Figure 1

Institute and Faculty of Actuaries

The hemagglutinin molecule

The hemagglutinin (HA) molecule is actually a combination of three identical parts (shown here as grey, green, and purple) that are bound together to form an elongated cylindrical shape.

A mutation that changes just one of hundreds of amino acids in the protein structure can alter the viral properties significantly.



Institute and Faculty of Actuaries

Basics of influenza virus infection

- Influenza virus particles enter the respiratory system.
- Hemagglutinin (HA) is a molecular machine that targets and attacks cells, and is the major virulence factor associated with the virus.
- HA latches onto host cells in throat and upper lungs.
  It binds only to matched receptors in host cells. The structure of HA is very similar between strains, but differs in the specificity of its binding regions.
- The virus enters the nucleus of the host cell, and hijacks the cell's own reproductive machinery to replicate itself numerous times.

Institute and Faculty of Actuaries

Influenza pandemics

The process by which an influenza virus mutates to evade immune systems is called antigenic variation.

Every few years, an ***antigenic drift*** causes epidemics, but every few decades an ***antigenic shift*** causes pandemics.

The most recent influenza pandemics occurred in: 1889; 1918; 1957; 1968, and 2009

Institute and Faculty of Actuaries

Pandemic deaths in USA in 20th century

Date	Strain	Estimate of US Deaths
• 1918-1919: Spanish Flu	[H1N1]	700,000
• 1957-1958: Asian Flu	[H2N2]	70,000
• 1968-1969: Hong Kong Flu	[H3N2]	40,000

A reassorted pandemic virus may be more of a public health risk than the 1918 virus.

Institute and Faculty of Actuaries

H1N1 pandemic 2009

- During the spring of 2009, a novel H1N1 virus of swine origin caused human infection and acute respiratory illness in Mexico. After initially spreading among persons in North America, the virus spread globally, resulting in the first influenza pandemic since 1968.
- Most illnesses caused by the 2009 H1N1 virus were acute and self-limited, with the highest attack rates reported among children and young adults. But the virus was not particularly lethal: the overall case fatality rate was less than 0.5%.
- Studies of hemagglutinin-receptor binding indicated that the 2009 H1N1 virus was well adapted to mammalian hosts.

Institute and Faculty of Actuaries

H5N1 avian flu

- Since 2003, there have been more than 600 confirmed cases of H5N1 virus infection – about 60% died.
- However, the true mortality rate will be lower because there are probably some milder, unrecorded infections of H5N1. Even so, it seems likely that this virus has a greater mortality rate than either ordinary seasonal flu or possibly the 1918 pandemic H1N1 strain.
- But so far, H5N1 has failed to spark a pandemic because it cannot effectively spread between people. It is caught from infected birds.
- Wild H5N1 viruses cannot latch on to the cells in a person's nose and throat.

Institute and Faculty of Actuaries

H7N9 avian flu

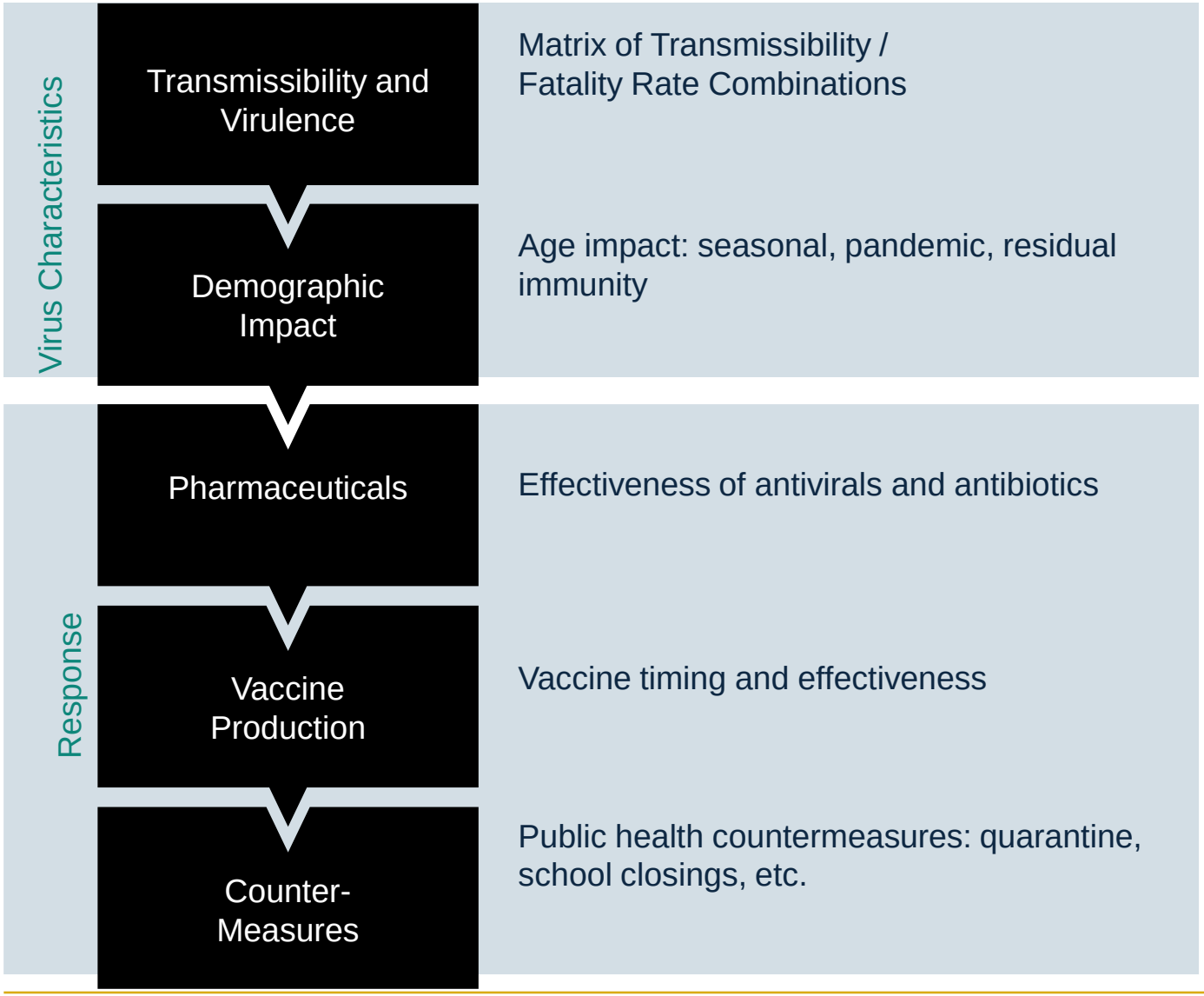
- H7N9 is a new strain of avian flu discovered in China in April 2013, that is transmissible from animals to humans.
- Similar to other avian influenza viruses, H7N9 attaches more strongly to tissues in the lower than the upper airway. But unlike other avian flu viruses, H7N9 attaches to a broader range of cell types. The attachment pattern emerging with the H7N9 virus in China suggests the future potential for severe disease and efficient transmission.
- The H7N9 lethality rate is currently above 30%.

Institute and Faculty of Actuaries

Stochastic Modelling of Pandemic Mortality

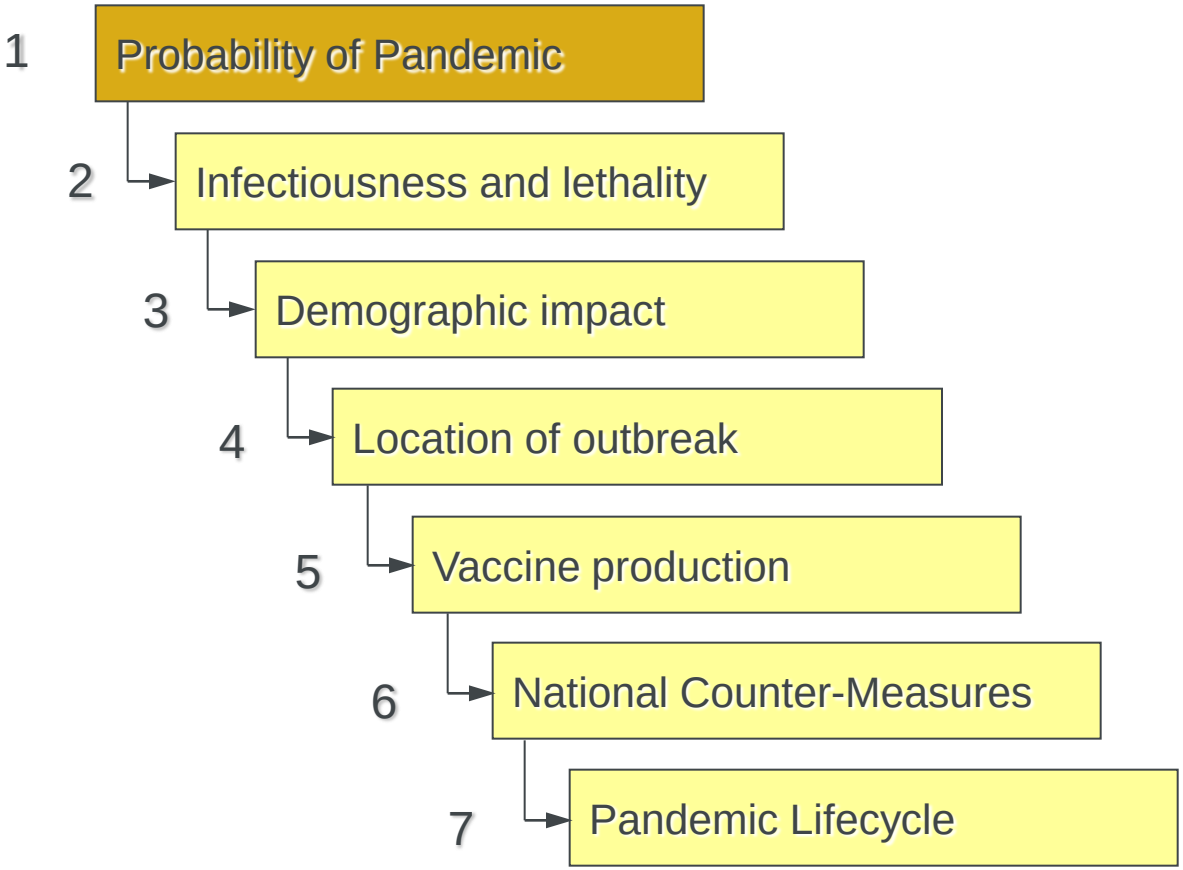
Institute and Faculty of Actuaries

Infectious disease model overview



Institute and Faculty of Actuaries

RMS dynamic event-tree model of influenza pandemic



Institute and Faculty of Actuaries

Annual probability of pandemic

- In the 20th century, influenza pandemics occurred in 1918, 1957 and most recently in 1968. Before then, a pandemic occurred in 1889.
- Pandemics occur randomly in time. The elapsed interval since the previous pandemic is not necessarily a guide to the imminence of the next pandemic. An empirical baseline historical average estimate of pandemic frequency is 11 per 300 years, i.e. 3.6%.
- Man-made laboratory experiments, if they continue, potentially might increase the likelihood of a new pandemic virus.

Institute and Faculty of Actuaries

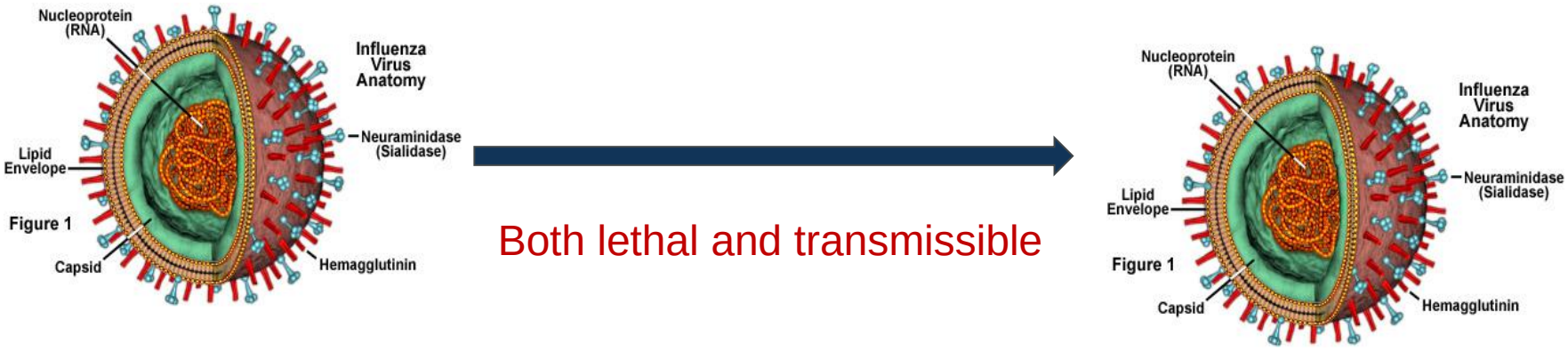
Cracking the combinatorial problem

- There are many millions of possible combinations of genetic changes that might potentially lead to dangerous characteristics.
- However, the probability distribution for such changes is very high dimensional, and remains poorly known and weakly constrained.
- Hence mathematical biologists are unable to refine the historical estimation of pandemic likelihood.

Institute and Faculty of Actuaries

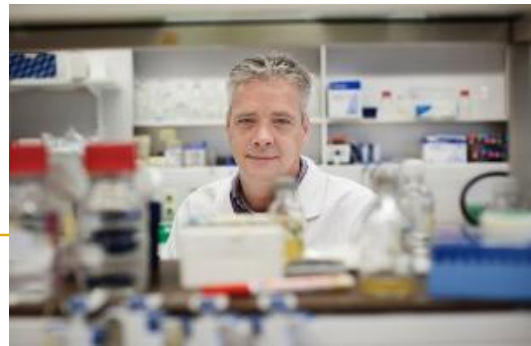
Influenza virus manufacture

- Virologists have for years been experimenting on influenza viruses to see if it is possible to create artificially a lethal and transmissible virus in a laboratory.
- Laboratory tinkering with the HA protein allows some change impacts to be assessed. But laboratory experiments are time-consuming, and resources are limited, so a surrogate method of further experimentation is essential for progress.



The ferret as an influenza mutation engine

- The ferret has been a highly reliable – but not perfect model for human influenza. The virulence and transmissibility of a wide range of influenza viruses are found to be similar between ferrets and humans.
- Human seasonal strains cause mild disease in ferrets and transmit very well between ferrets. Wild H5N1 strains cause severe disease and do not transmit readily.
- Low pathogenic avian influenza strains do not, in general, transmit either among ferrets or humans.
- Ron Fouchier, in Rotterdam, used ferrets as agents for forced mutation change of H5N1.



Syhnthesizing a new hybrid virus

- Yoshihiro Kawaoka introduced random alterations into the H5N1 hemagglutinin protein. From the resulting library of 2.1 million mutant strains, he isolated viruses with two mutations that could stick to receptors in human tracheal cells - something H5N1 viruses cannot usually do.
- Kawaoka then created a hybrid virus by combining this with the 2009 H1N1 pandemic virus.
- This mirrors the natural reassortment process through which wild viruses swap genes.

Risk-benefit of man-made flu research

- Whereas scientists are focused on absolute evidence-based statements of scientific reality, risk analysts are focused on the tail risk of what might happen.
- The prospect remains of future man-made flu experiments for H5N1, H7N9 etc. generating a dangerous outcome.
- Accordingly, biosecurity professionals take a different view from the virologists themselves on the importance of developing new flu strains in a laboratory.

'We would like to assure the public that these experiments have been conducted with appropriate regulatory oversight in secure containment facilities by highly trained and responsible personnel to minimize any risk of accidental release.'

Fouchier, Kawaoka et al., Science express, 20 January 2012

SARS laboratory security failures

- Over the past decade, SARS has accidentally infected staff at high-containment labs in China, Taiwan and Singapore.

A: At the National Institute of Virology in Beijing, a graduate student developed SARS, a few weeks after starting work.

B: The Taiwan case happened in a BSL-4 lab when a military scientist failed to follow procedures in cleaning up a spill of SARS-containing fluid.

C: In Singapore, a sample of West Nile virus contaminated with SARS virus infected a lab worker in a BSL-3 lab at the Environmental Health Institute.

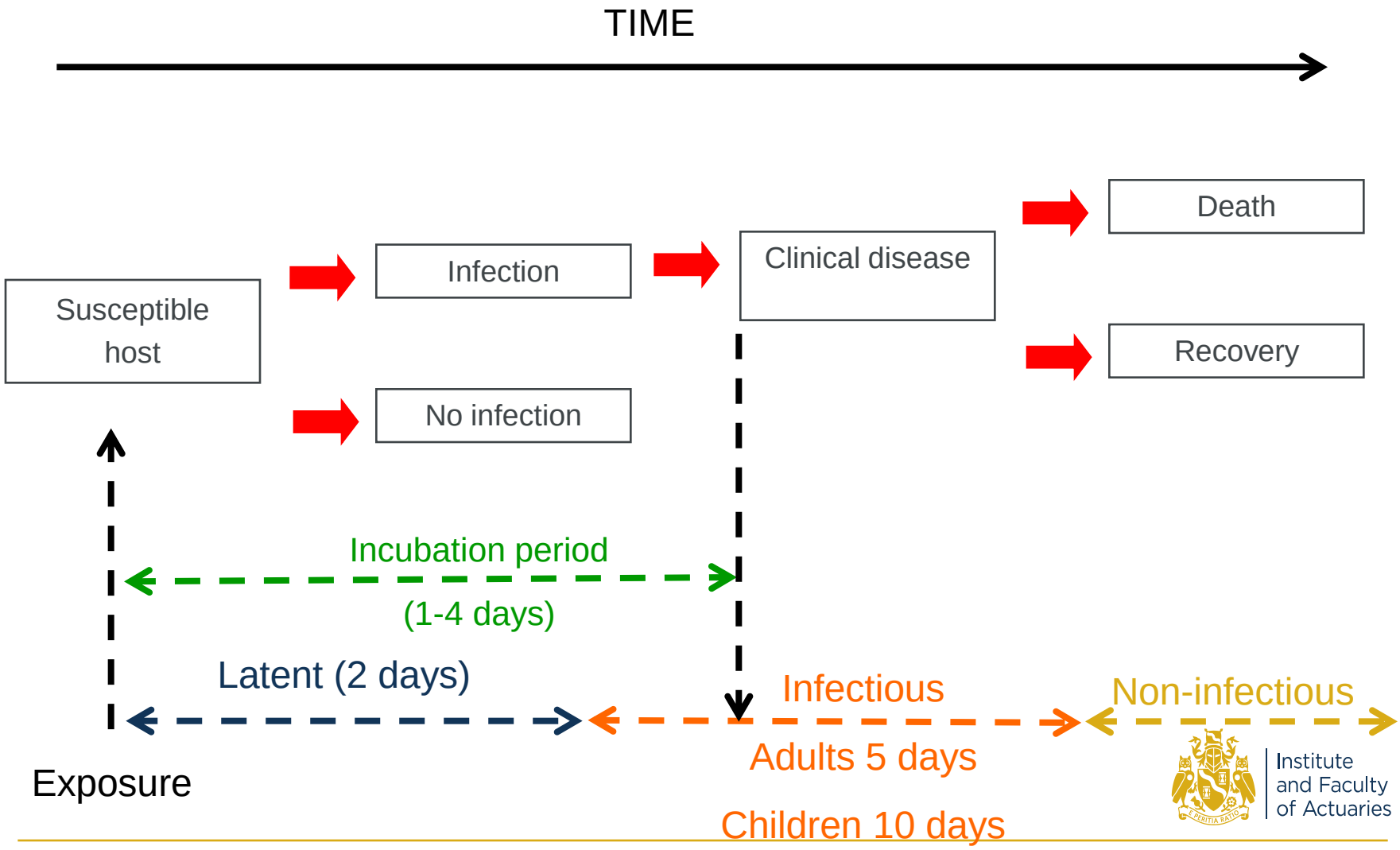
Not mixing SARS with influenza

With SARS, people became sick (symptomatic) *before* they were maximally infective.
The disease was easier to control because apparently well people were not infectious.

With influenza, on the other hand, the infectious period begins about 24 hours *before* the symptomatic period.
This gives influenza a head start in infecting people, before the person knows he or she is sick and thus more likely to have contact with others.

Institute and Faculty of Actuaries

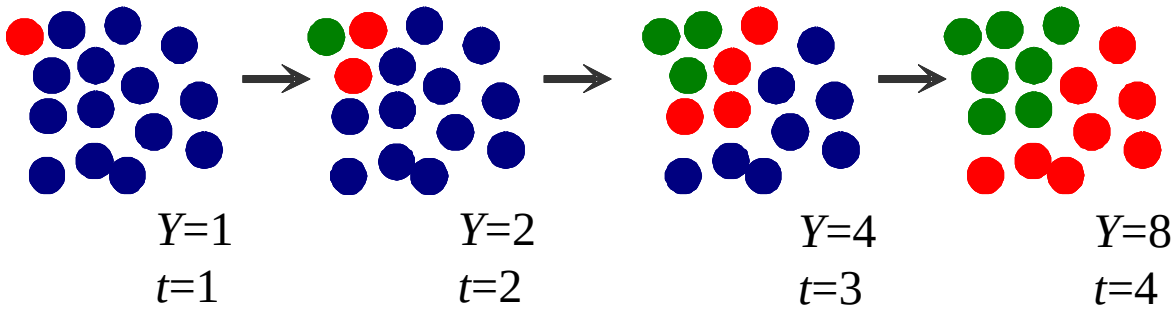
Time development of influenza

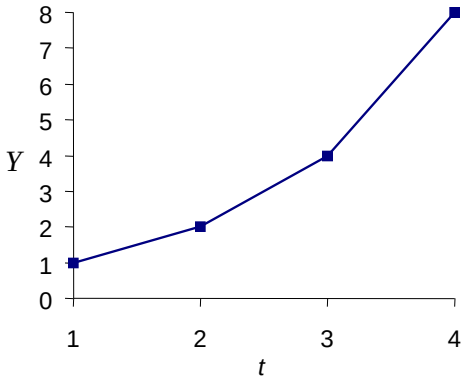


Institute and Faculty of Actuaries

Infectious disease epidemics

- Epidemics spread through contact (e.g. person to person):
- A chain reaction gives exponential growth until epidemic begins to run out of people to infect.





- R_0 is the number of secondary infections caused by one primary case at the start of an epidemic.
- R_0 needs to be >1 for an epidemic to take off.

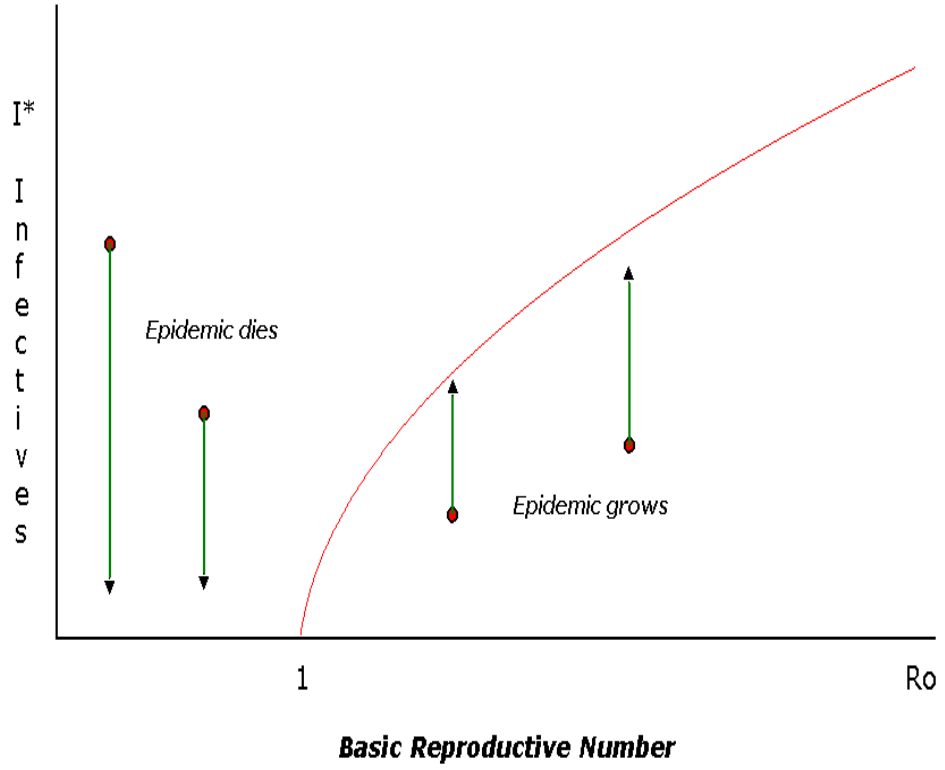
Institute and Faculty of Actuaries

Influenza transmissibility measured by R_0

R_0 = average number of secondary cases an infectious case will cause without intervention

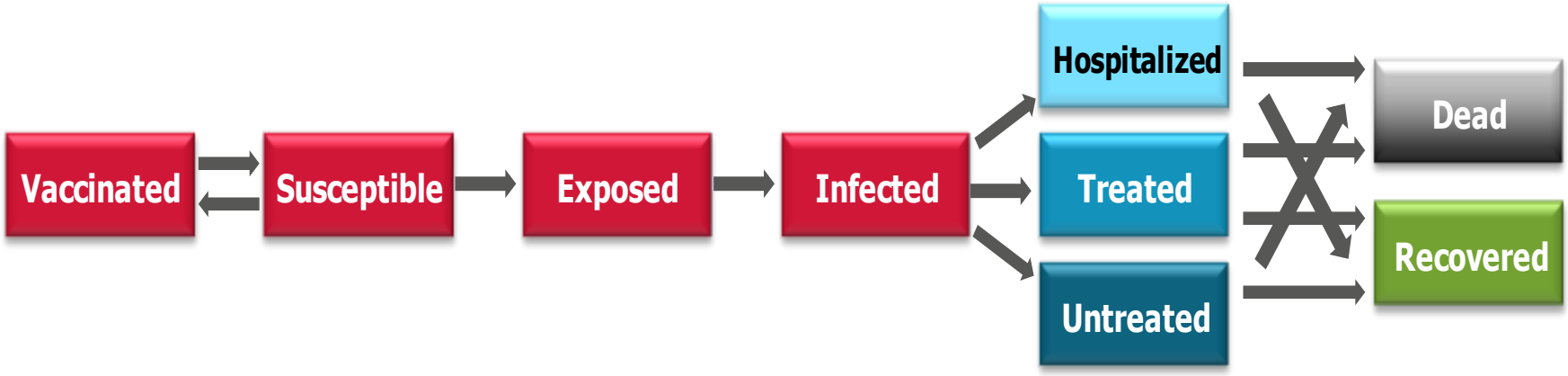
$$R_0 = \beta * \kappa * D$$

(Attack rate) * (Avg. # Contacts per Unit Time) * (Infectiousness Duration)



Year	R_0
1918	1.5-2.5
1957	1.5-1.7
1968	1.5-2.2
2009	1.5-2

Epidemiologic S-I-R modelling



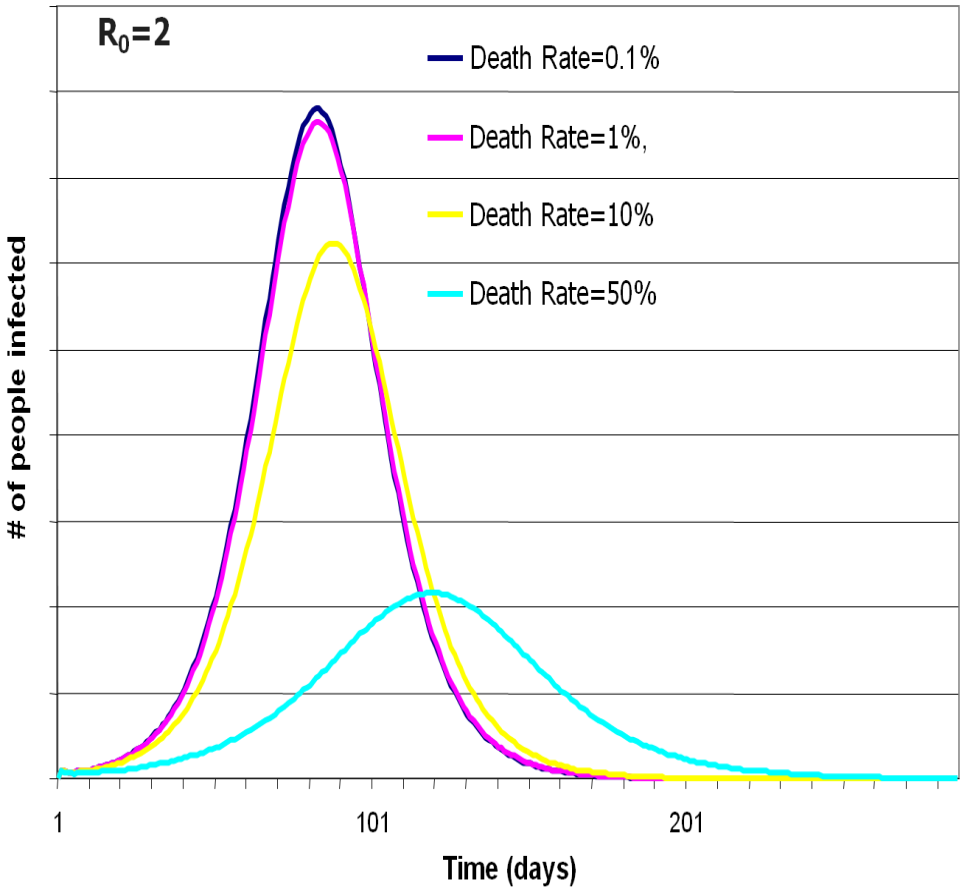
The S-I-R model accounts for:

- Geography
- Vaccination
- Residual Immunity
- Quarantine
- Medical Interventions
- Country Specific Transmission Variables

Institute and Faculty of Actuaries

Transmissibility v Virulence

- In general, diseases with high virulence tend to have lower transmissibility since the dead and injured are not effective transmitters of the disease.
- Worst-case scenario is an infectious disease for which subset of a population suffers high death rates when infected, and another subset has high infection rates but does not suffer greatly.



Institute and Faculty of Actuaries

Virulence: case fatality rate

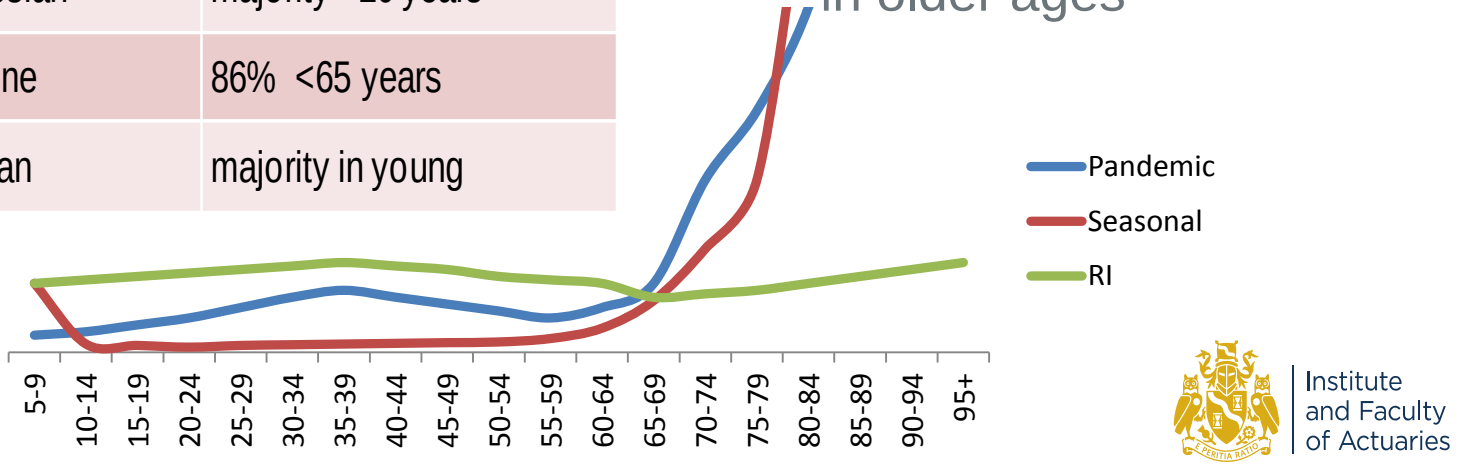
- Virulence is a measure of the relative ability of a pathogen to cause disease and mortality
- Measured in terms of the case fatality rate (CFR): fraction of deaths per case
- Pandemic and seasonal influenza strains since 1900 have had a CFR of less than 2.5% in developed countries

Year(s)	Type	CFR
1510		Very low
1557-1558		Highly fatal
1580		Highly fatal
1729-1730, 1732-1733		High
1761-1762		
1780-1782		Very low
1788-1790		Low
1830-1831, 1832-1833, 1836-1837		Low
1889-1893	H2N2? H3N8?	0.1-0.28%
1918-1919	H1N1	>2%
1957-1958	H2N2	0.13%
1968	H3N2	<0.1%
1977-1978	H1N1	
2009	H1N1	0.05%

Demographic impact of influenza

Year	Name	Demographic mortality
	Seasonal	90% >65 years
1889	Russian	
1918	Spanish	>95% <65 years
1957	Asian	36% <65 years
1968	Hong Kong	48% <65 years
1977	Russian	majority <20 years
2009	Swine	86% <65 years
2003	Avian	majority in young

- Three demographic mortality profiles for influenza:
  - **Seasonal**: affects youngest and oldest
  - **Pandemic**: impact working age lives (cytokine storm)
  - **Residual immunity**: flat due to residual immunity in older ages



Institute and Faculty of Actuaries

Differences in the demographic profile

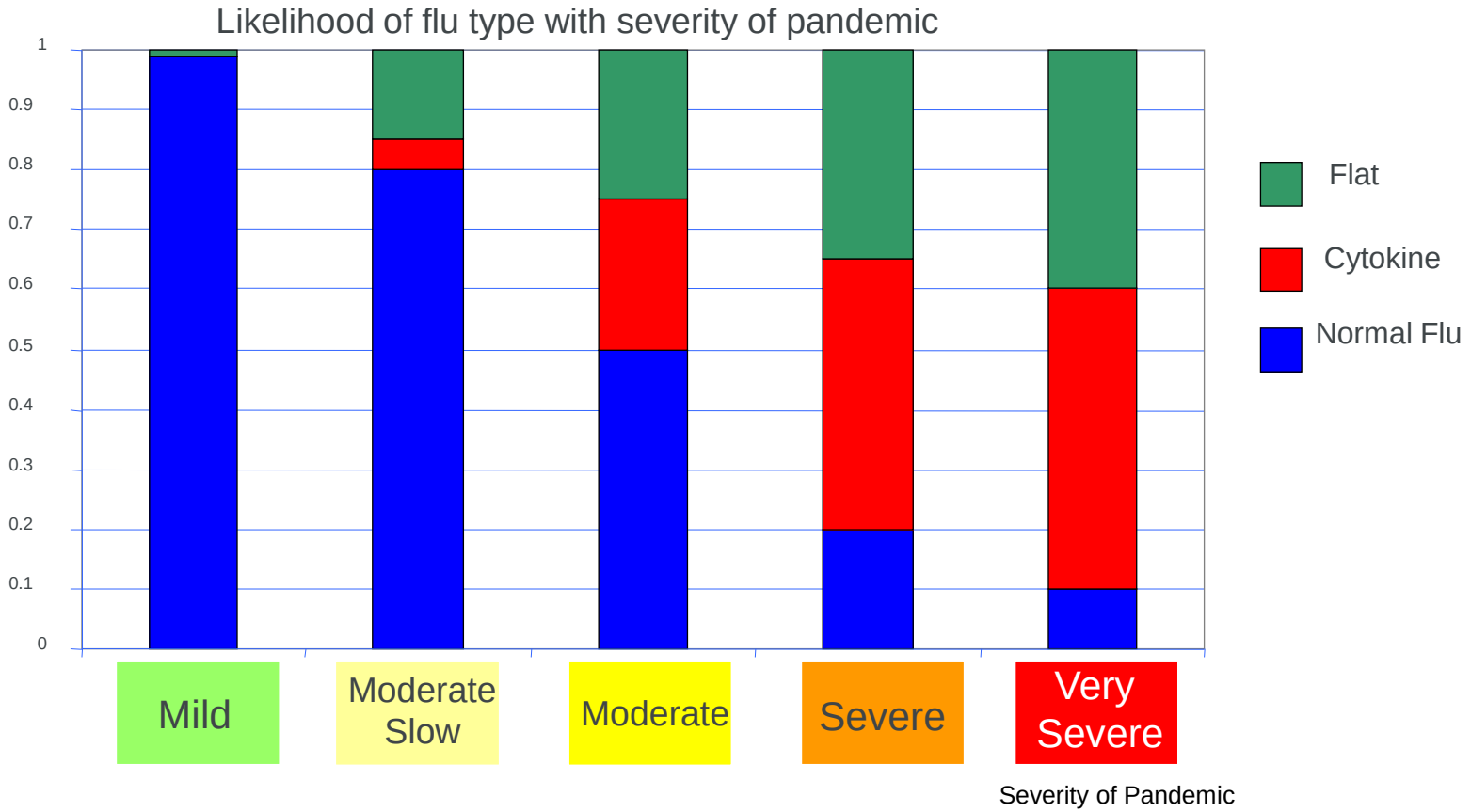
- Annual flu deaths are primarily a result of complications such as bacterial pneumonia, and a weakened immune system increases the risk of complications from flu.

BUT……..

- A **Cytokine Storm** is an immune reaction that results in a positive feedback loop between cytokines and immune cells. Cytokines control reactions of other cells and signal immune cells to go to the site of infection and activate those cells. This stimulates the production of more cytokines.
- The cytokine storm is more severe in those with strong immune systems.

Institute and Faculty of Actuaries

Demographic profile affects loss severity



- 'Cytokine storm' kills young adults with strong immune response systems
- 'Cytokine storm' is more likely in severe pandemics with a pathogenic virus
- More severe pandemics may cause higher losses to those with portfolios consisting mainly of young healthy individuals

Institute and Faculty of Actuaries

Worldwide spread from the source

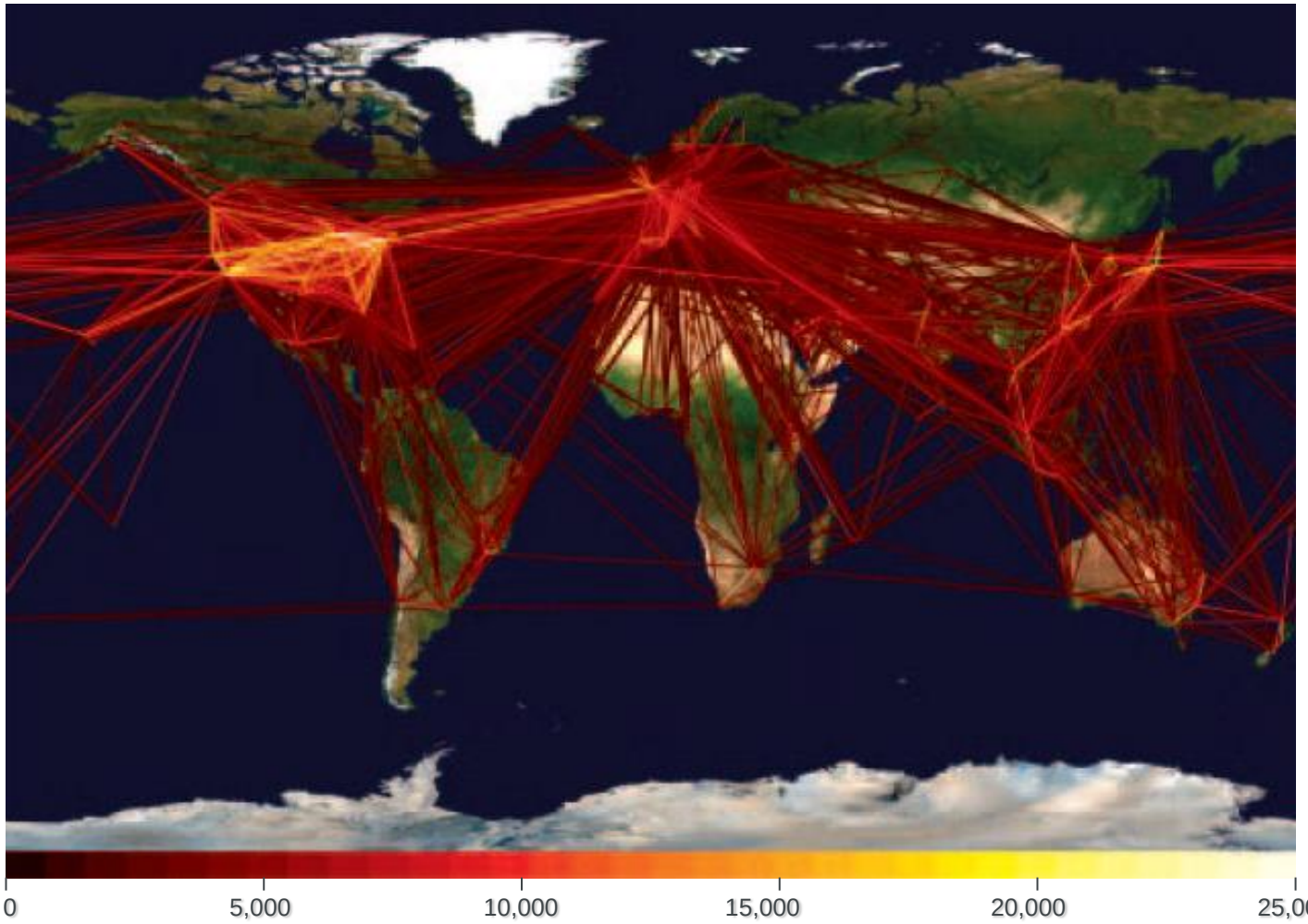
- After increasing and sustained transmission occurs in the general population of even one country, eventual worldwide spread is considered virtually inevitable.

  The public health response focus would shift to reducing impact and delaying spread, to allow time for vaccine development and institution of other response measures (World Health Organization, 2006).

- In 1918, some areas succeeded in delaying the pandemic by several weeks.
- Only severe quarantine measures are successful at delaying a pandemic.

Institute and Faculty of Actuaries

Rapid spread through air travel



Stopping 90% of infections getting in buys 1-2 weeks,

99% buys 2-4 weeks.

Volume of passenger trips per day between international airports

Institute and Faculty of Actuaries

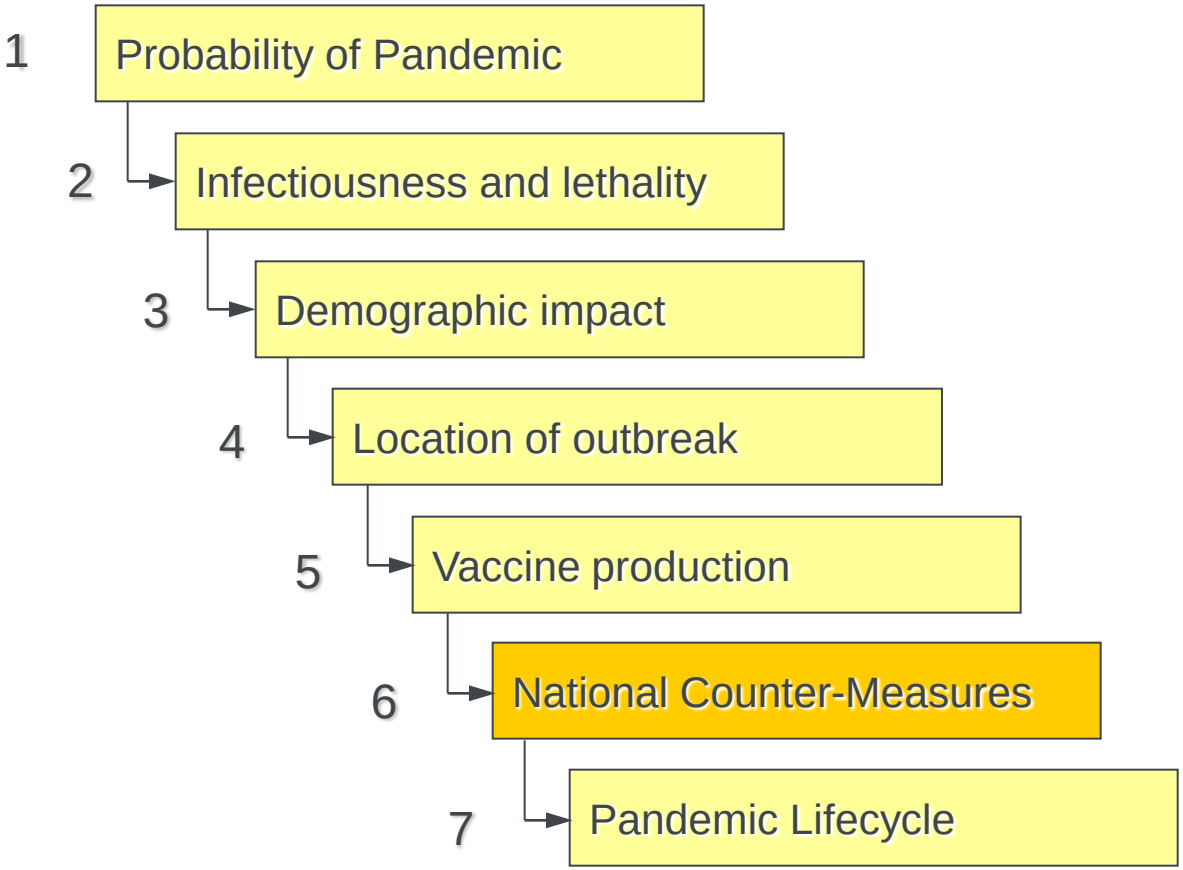
Vaccine production and effectiveness

	Time to Identify	Ramp up to manufacturing	Manufacturing Capacity per month	Vaccine Effectiveness
Better than Normal	1 month	2 months	100m	90%
Normal	2 months	4 months	40m	75%
Worse than Normal	4 months	6 months	10m	60%

- 90% of production is consumed by US, Europe and Japan.
- Vaccination prioritizes health care workers and high-risk groups.
- Significant populations are vaccinated by the end of the year, but not in time to contain spread of cases in year 1.
- Other methods are attempted to produce a vaccine faster but these have negligible impact.

Institute and Faculty of Actuaries

RMS dynamic event-tree model of influenza pandemic



Institute and Faculty of Actuaries

Infectious disease pharmaceuticals

ID Pharmaceuticals Category	Description	Examples
Supportive care	When no specific therapy or drugs are available/effective, and ventilators, management of pain, blood pressure, etc. can provide some reduction in pandemic mortality	Blood transfusions, pain medication, fluid replacement to treat Ebola; Oral rehydration therapy to treat cholera
Antivirals/Antifungals	Drugs used to treat viral infections and drugs used to treat fungal infections are able to reduce pandemic mortality	Antiretroviral therapy (ART) to treat HIV; Fluconazole to treat coccidioimycosis
Secondary Antibiomicrobials	Medications used to treat the secondary infections or complications are able to reduce pandemic mortality	Antibiotic therapy to treat secondary infections (bacterial pneumonia, encephalitis) of measles
Antibiotics/Anti-parasitics	Drugs used to treat bacterial infections and drugs used to treat parasitic infections are able to reduce pandemic mortality	Ciprofloxacin to treat anthrax; Chloroquine to treat malaria

There are many different pathogens, and many pharmaceuticals.
For bacterial infections, there are several classes of antibiotics.
For viral infections, there is a limited range of antivirals.

Institute and Faculty of Actuaries

Effectiveness of pharmaceuticals

- Usefulness and supply of antiviral drugs are uncertain.
- Multiple country and viral characteristic specific response scenarios are modelled to address these issues.
- For a 1918 type scenario the difference in response assumptions can result in a two-fold difference in event losses.

Institute and Faculty of Actuaries

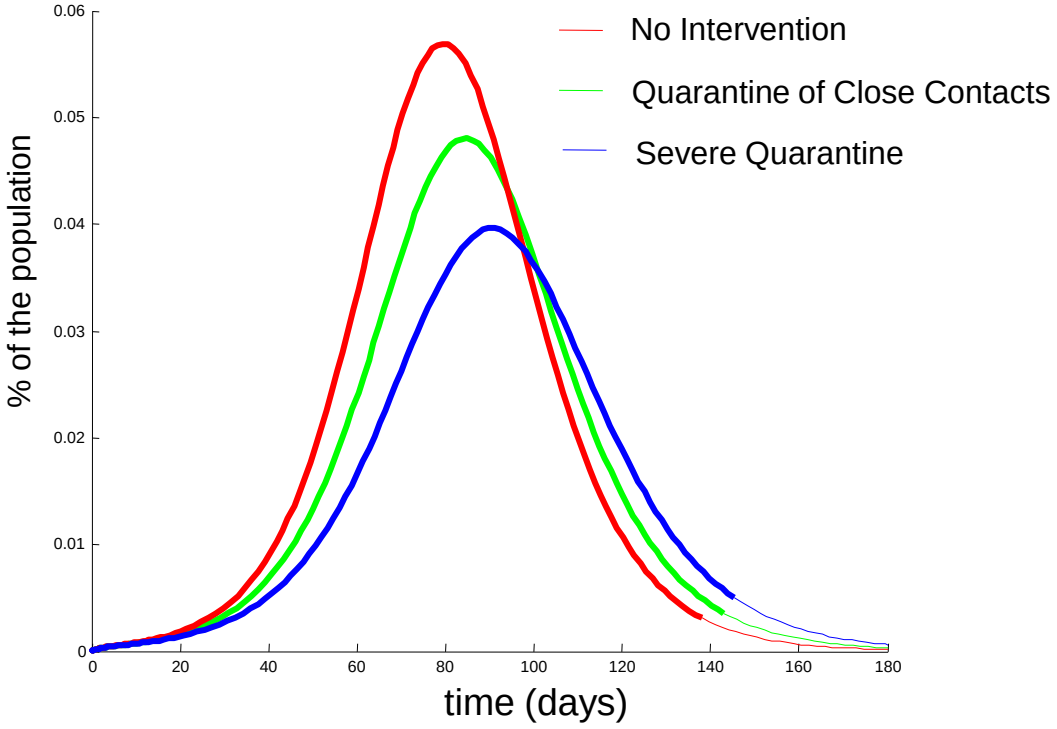
Response of the healthcare system

- Hospital equipment and bed space will be limited.
- Healthcare workers are likely to get ill.
- Preparedness and response are likely to vary widely on both local and national levels.
- Response plans and resources need to be evaluated in making assessments of quality of care in a pandemic.

Institute and Faculty of Actuaries

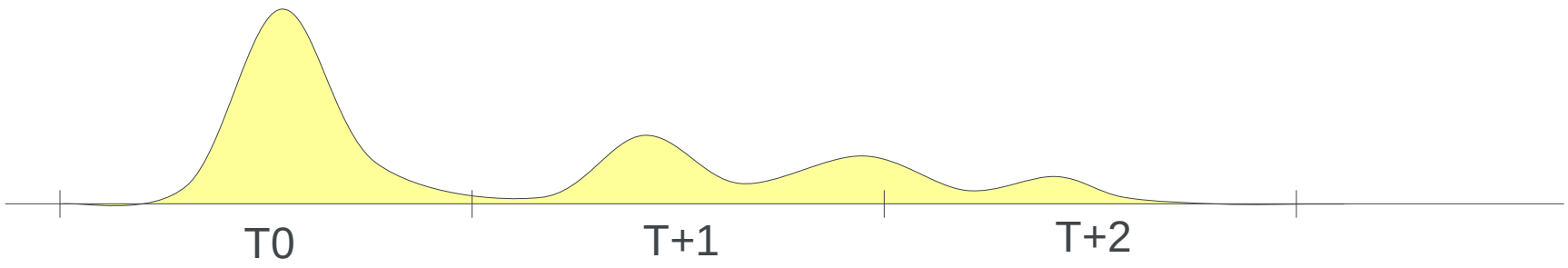
Effectiveness of quarantine

- Community level quarantine is only effective when there are very few cases.
- May be realistic for short periods of time, but pandemic is likely to last for months or even years with multiple waves.
- Short incubation period, non-specific symptoms, and asymptomatic infections make tracking exposed difficult.



Institute and Faculty of Actuaries

Multi-year pandemic waves



- Vaccination cycle (manufacture of vaccine and vaccination of population) will likely take many months, spanning more than one flu season.
- Pandemics of 1918 and 1889 had second waves that caused significant losses in subsequent years.
- Initial genetic reassortment may be followed by additional genetic shifts that can cause additional waves of infection.
- Once a virus is in a population it becomes endemic – residual immunity takes time to build up.

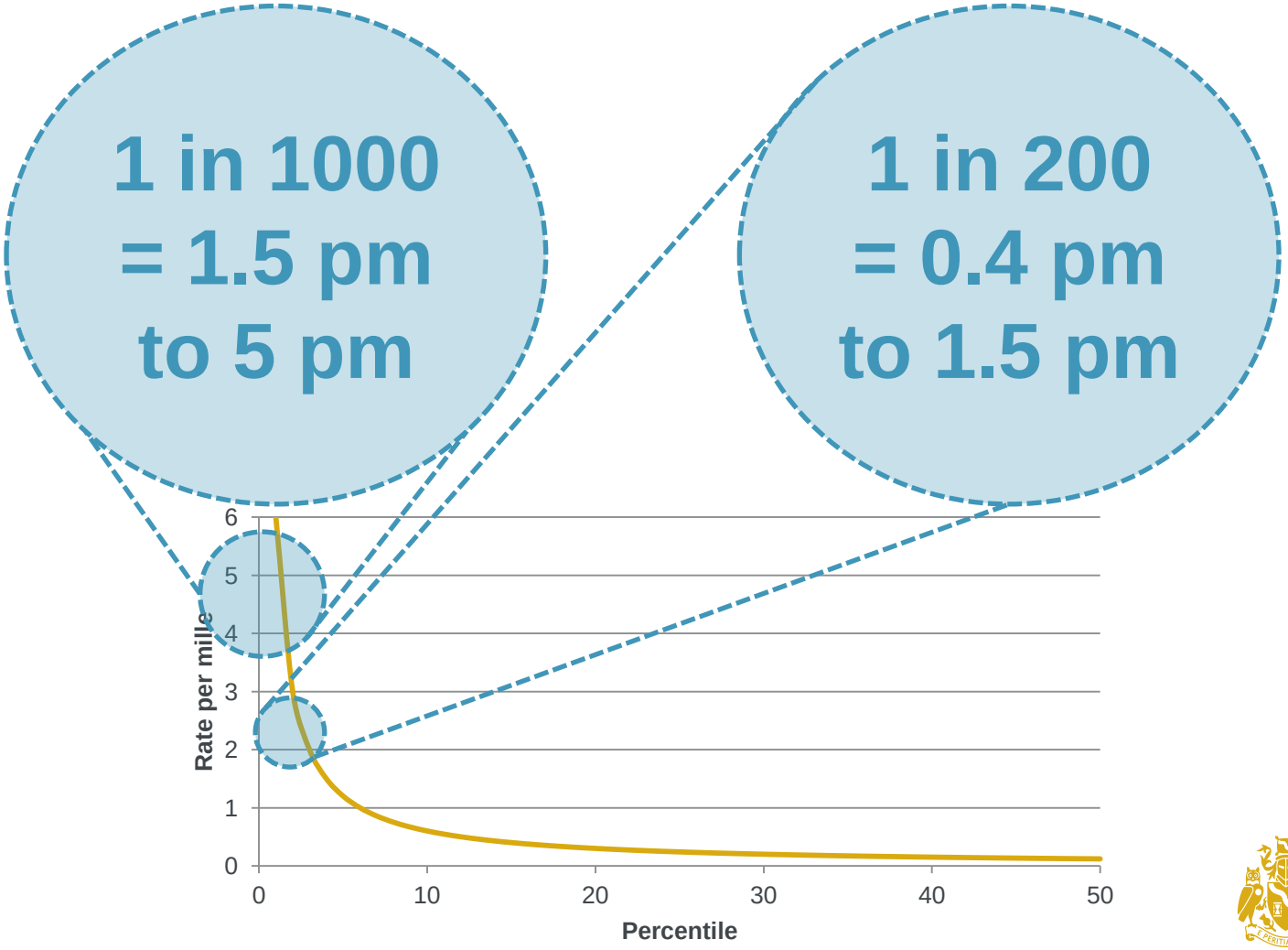
Institute and Faculty of Actuaries

Accounting for an insured portfolio

- The impact of pandemics can vary significantly between the insured population and the general population.
- Insured individuals are screened for conditions such as respiratory and circulatory disease and diabetes, HIV, etc. and have reduced susceptibility to death from infectious diseases.
- In mild to moderate pandemics, individuals with underlying medical conditions have a higher risk of death.
- In severe pandemics, especially those causing cytokine storm-type reactions, healthy individuals exhibit mortality rates comparable to individuals with underlying conditions.
- Correlation between longitudinal all-cause and infectious disease mortality can be used to quantify the mortality difference.

Institute and Faculty of Actuaries

What mortality is associated with a pandemic?



Institute and Faculty of Actuaries

Audience answers

Questions

Comments

Expressions of individual views by members of the Institute and Faculty of Actuaries and its staff are encouraged.

The views expressed in this presentation are those of the presenter.

Institute and Faculty of Actuaries