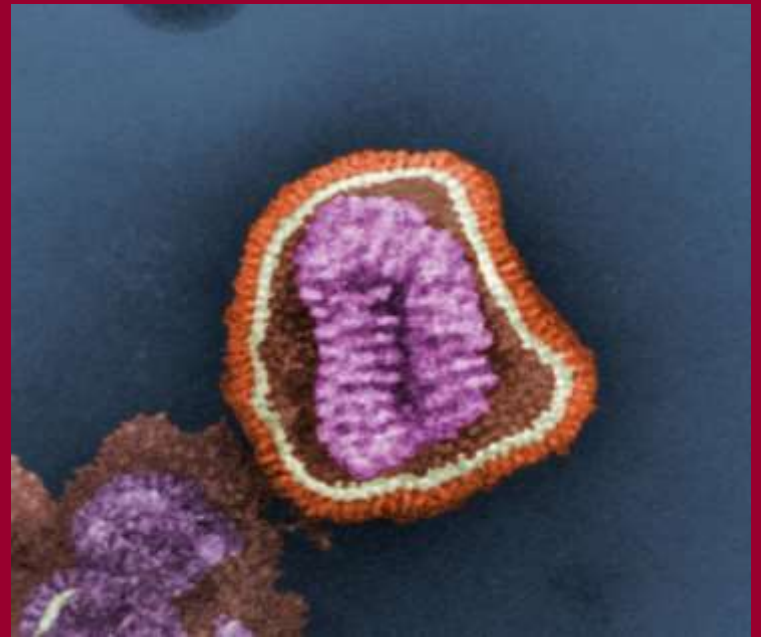




Public Health
England

Influenza



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Image source: Public Health Image Library, CDC



Objectives

- Understand a bit about the flu virus and how it spreads.
- Understand difference between pandemics and seasonal flu.
- Understand important options for treatment and prevention.
- Consider different perspectives when dealing with a pandemic.
- Understand your role as doctors and the protection of the public's health



Public Health
England

Influenza virus

Influenza or 'flu' is an acute respiratory illness caused by infection with influenza viruses.

Member of the Orthomyxoviridae family, with 3 separate genera: influenza A, B and C.

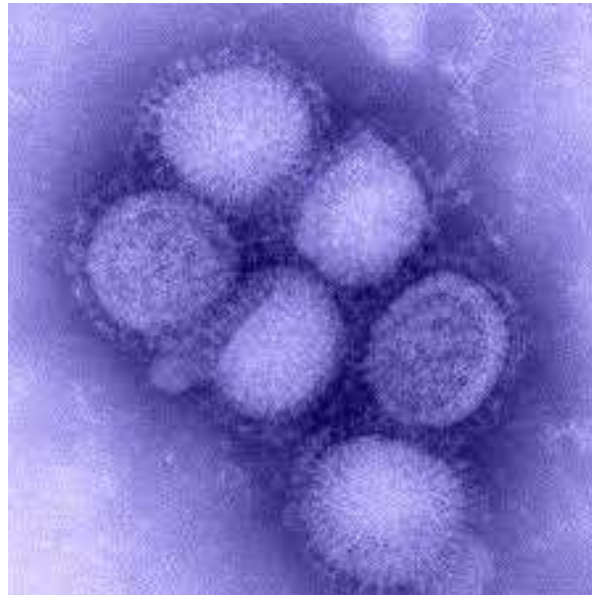
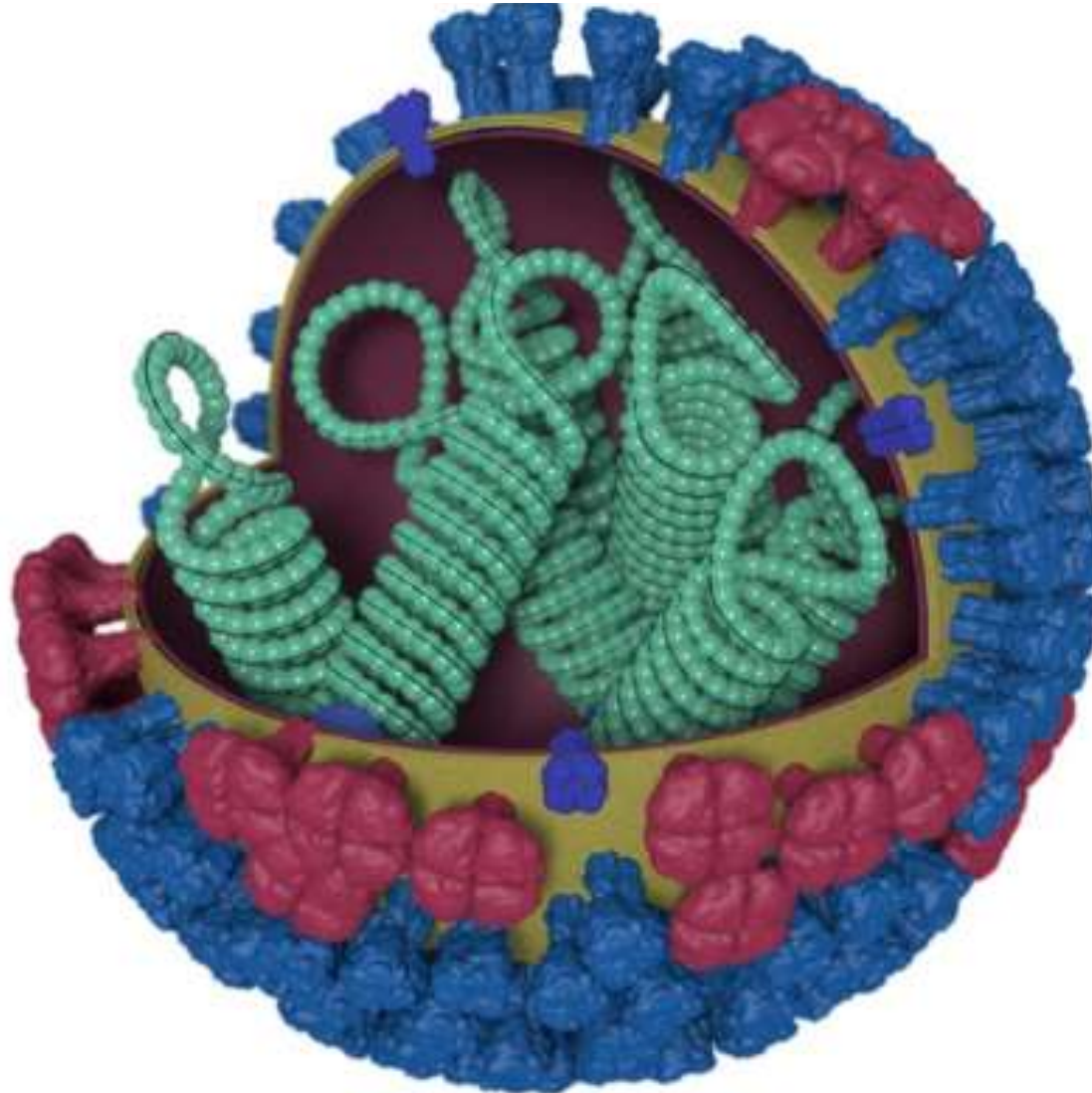


Figure: Electronmicrograph of influenza virus.
(Image source: PHIL, CDC)

Key antigenic sites for the influenza virus

(Image source: PHIL, CDC)



Hemagglutinin



Neuraminidase



M2 ion channel



Ribonucleoprotein



Influenza A subtypes

Influenza A viruses further subdivided by 2 key surface antigens:

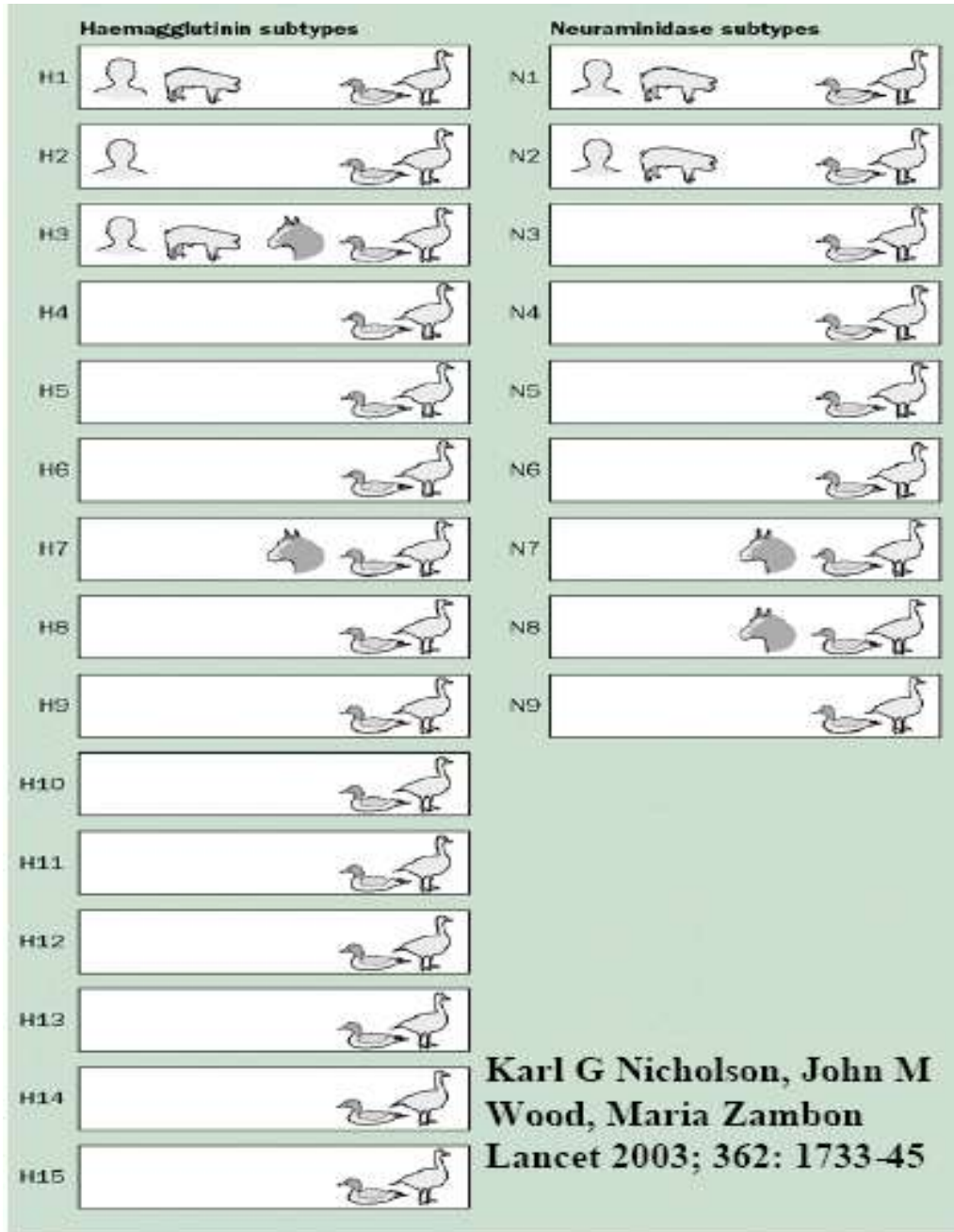
Haemagglutinin (15 subtypes)

- Virus binding and entry to cells: i.e. the “Grappling Hook” for getting in
- Immunity confers protection but only to specific subtype

Neuraminidase (9 subtypes)

- The “Bolt Cutters” for getting out; cuts newly formed virus loose from infected cells and prevents it clumping together
- Immunity to subtype reduces amount of virus released from cells resulting in a less severe disease

All 15H and 9N subtypes have been detected in birds

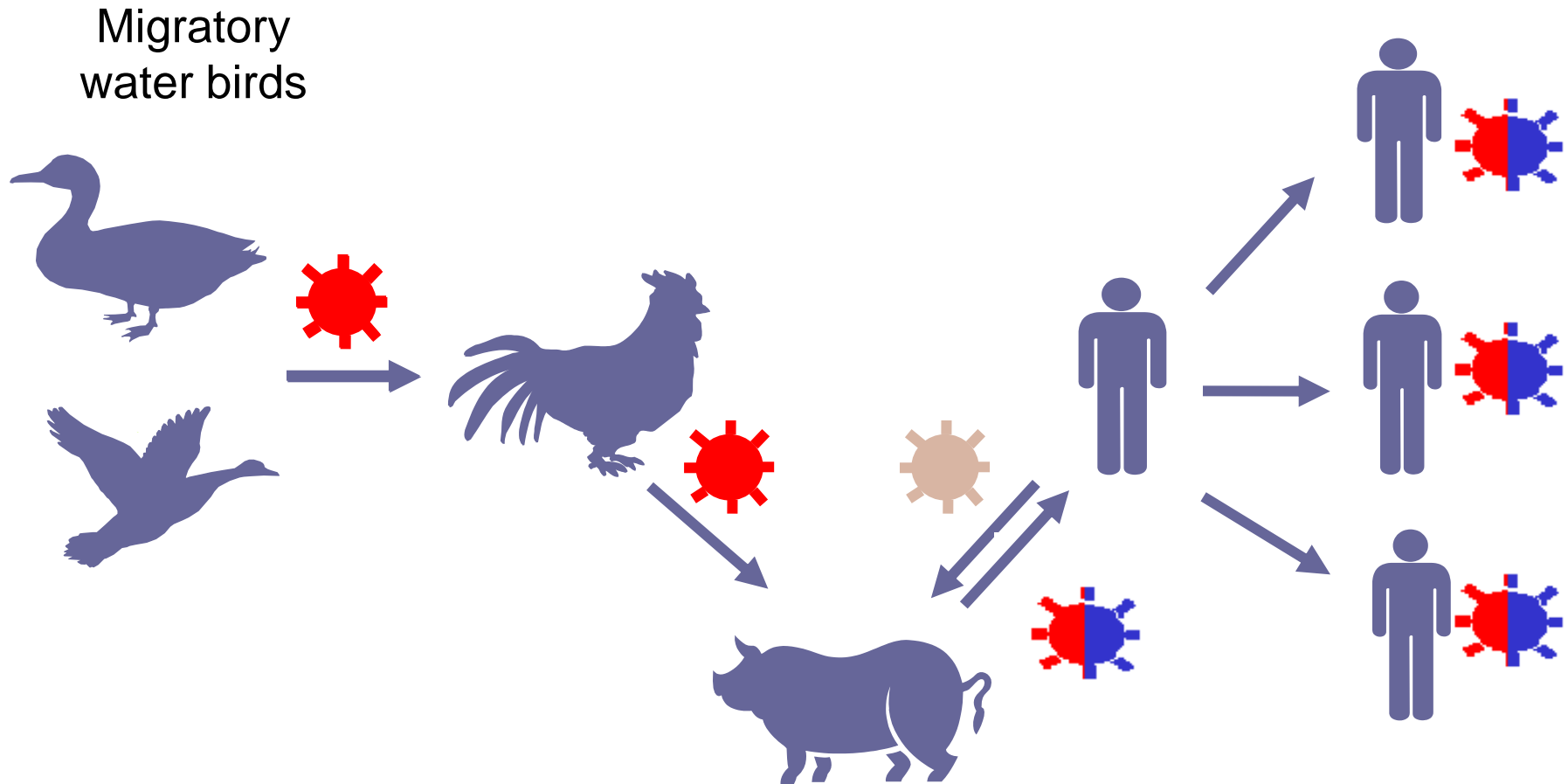
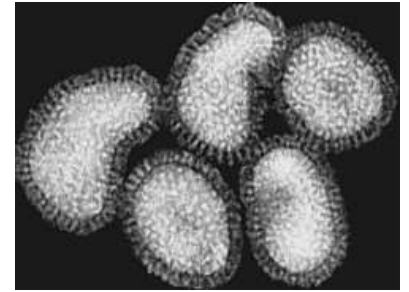




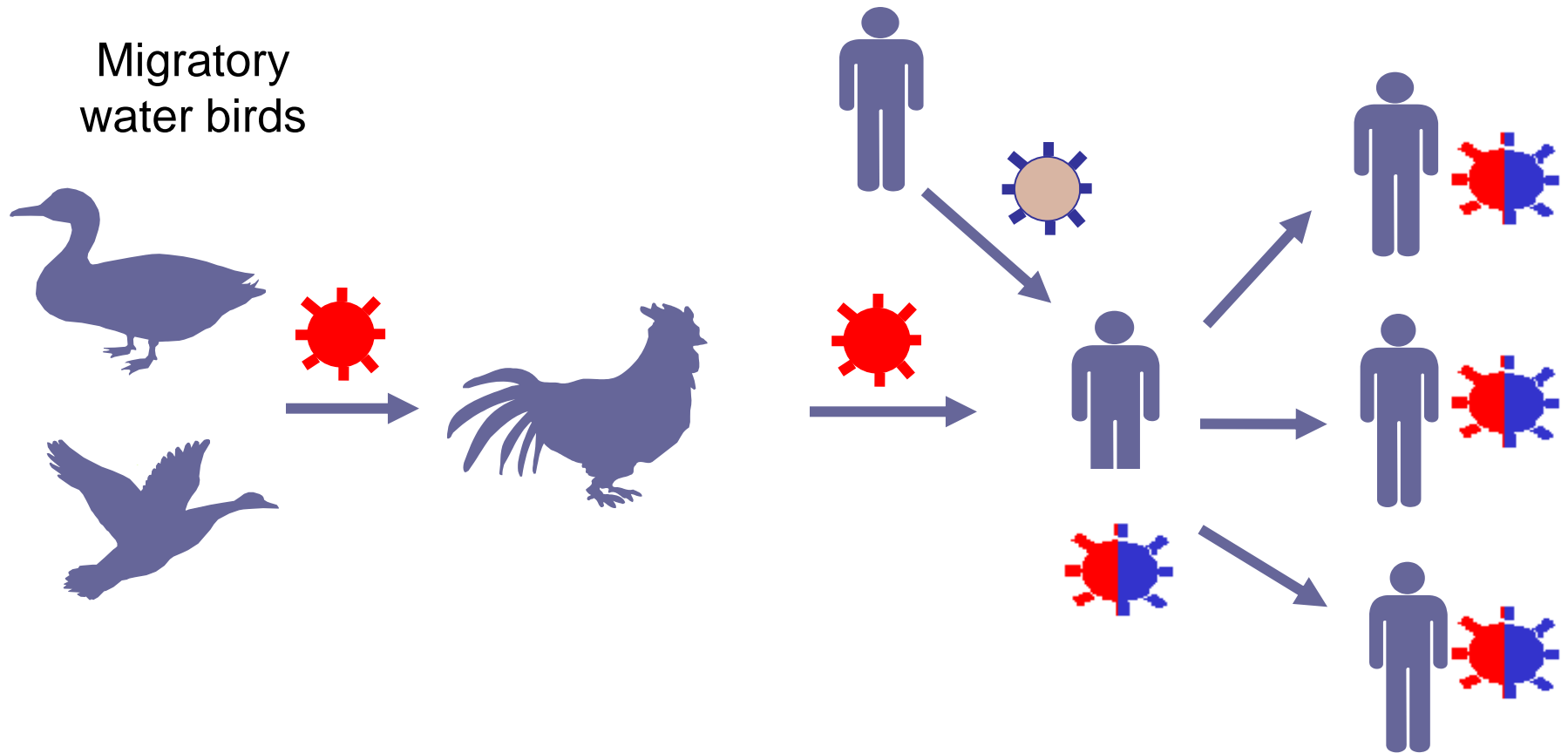
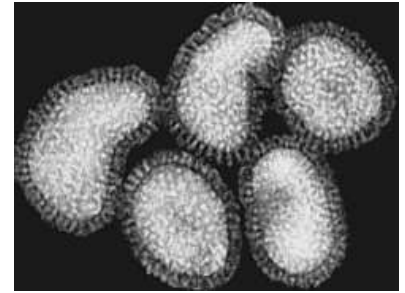
Genetic Epidemiology

- Influenza A and B are the main human pathogens
- Viral genome consists of 8 single-stranded RNA segments.
 - Because the genome is segmented, gene re-assortment can occur in infections.
 - Genes swapping can occur during co-infection with human and avian flu virus
 - Also, no proof reading mechanism so very prone to mutation.
- Minor antigenic variation (***antigenic drift***) causes seasonal epidemics
- Gene re-assortment & major antigenic variation (***antigenic shift***) may be associated with pandemics.

Genetic reassortment in pig



Genetic reassortment in humans





Influenza B and C

- Influenza A

- “Sloppy, capricious, promiscuous”: can infect pigs, cats, horses, birds and sea mammals
- Causes the severe and extensive outbreaks and pandemics.

- Influenza B

- Like Influenza A, also prone to mutation but tend to cause sporadic outbreaks (e.g. schools, care homes, garrisons) that are less severe.
- More often seen in children

- Influenza C

- Relatively minor disease: mild symptoms or even asymptomatic



Public Health
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Influenza transmission

Coughs and sneezes spread diseases!



(Image source: PHIL, CDC)

Transmission mainly via aerosols generated by coughs and sneezes. However, also possible via hand-to-hand contact, other personal contact or fomites.



Quiz: Which has the highest R_0 ?

Rank the following (highest to lowest) in terms of the reproduction number (R_0)

1. Smallpox
2. HIV/AIDS
3. Pandemic influenza
4. Measles
5. Seasonal influenza

The reproduction number, R , is defined as the average number of secondary cases generated by a primary case. It is a crucial quantity for identifying the intensity of interventions required to control an epidemic. R_0 = number of secondary cases you would expect in a totally susceptible population.



Public Health
England

Answer

Disease	Transmission	R_0
Measles	Airborne	12-18
Smallpox	Social contact	5-7
HIV	Sexual contact	2-5
H1N1 Pandemic influenza	Airborne droplet	2-3
Seasonal influenza	Airborne droplet	1.3-1.5



Influenza infection

- Influenza characterised by upper and/or lower respiratory tract symptoms, as well as fever, headache, myalgia and weakness.
- Complications include bacterial pneumonia, and can be life threatening
- Mortality risk higher in persons with underlying medical conditions:
 - Chronic cardiac and pulmonary diseases
 - Old age
 - Chronic metabolic diseases
 - Chronic renal disease
 - Immunosuppressed



Treatment Options

- ‘Supportive care’
 - Oxygenation
 - Hydration / nutrition
 - Maintain homeostasis
 - Prevent / treat secondary infections
- Role of antiviral medication
 - Reduce risk of transmission to others?
 - Reduce severity and duration of symptoms?



Outbreaks, Epidemics & Pandemics

Outbreaks :

- 2 or more linked cases

Epidemics :

- More cases in a region/country

Pandemic :

- Epidemics that span international boundaries

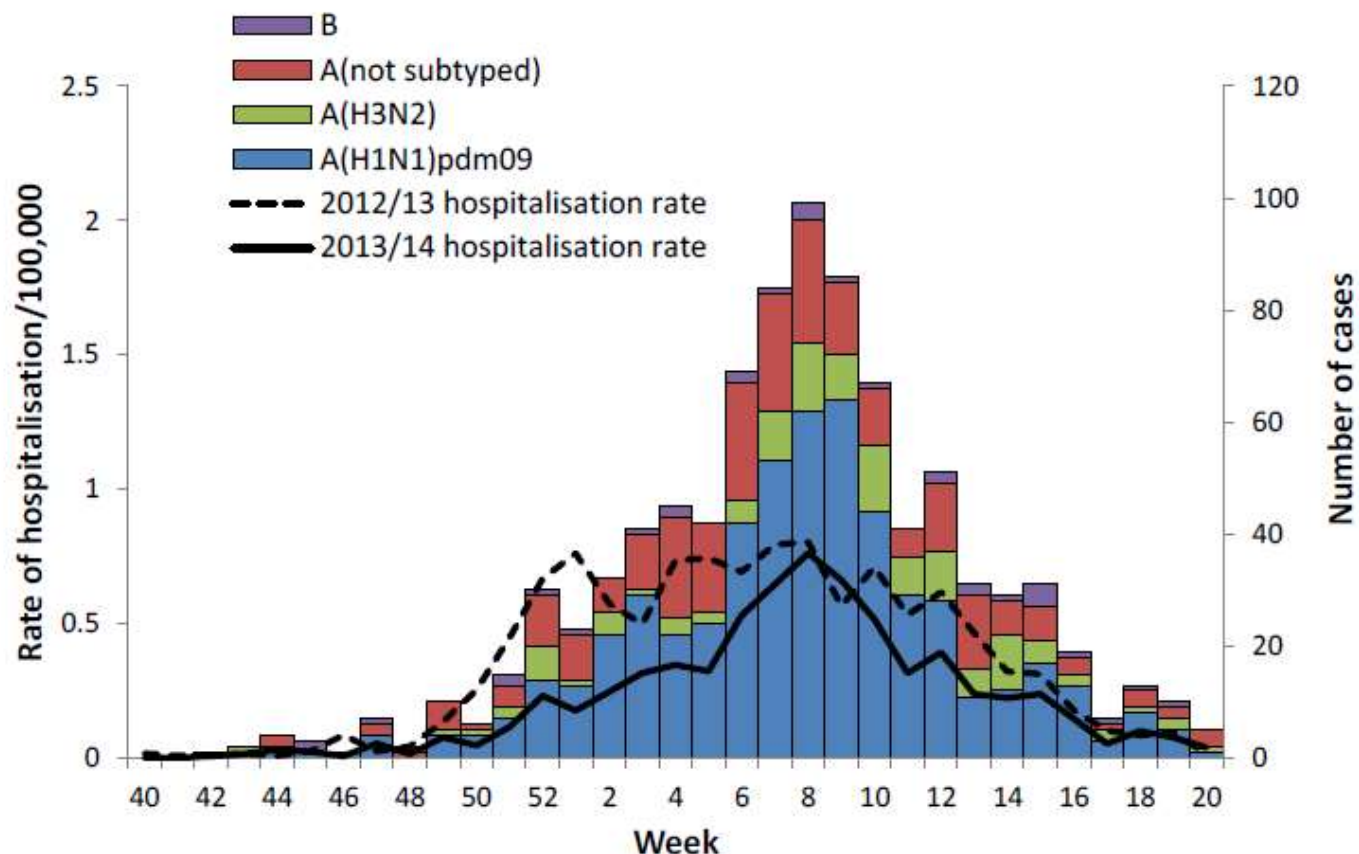


SEASONAL FLU

- Every year the virus changes a little bit ('Antigenic Drift')
- Means it can infect some people who were immune to last year's variant.
- Changes derived from mutation within the people it infects.
- Influenza occurs most often in the winter months and usually peaks between December and March in the northern hemisphere.
- Illnesses resembling influenza may occur in the summer months but they are usually due to other viruses.
- Annual flu vaccination of at risk groups and children offers some protection against infection.



Figure: Weekly number of influenza confirmed admissions to hospital by influenza subtype through the USISS sentinel scheme in England, with crude hospitalisation rate, 2013/14 and 2012-13

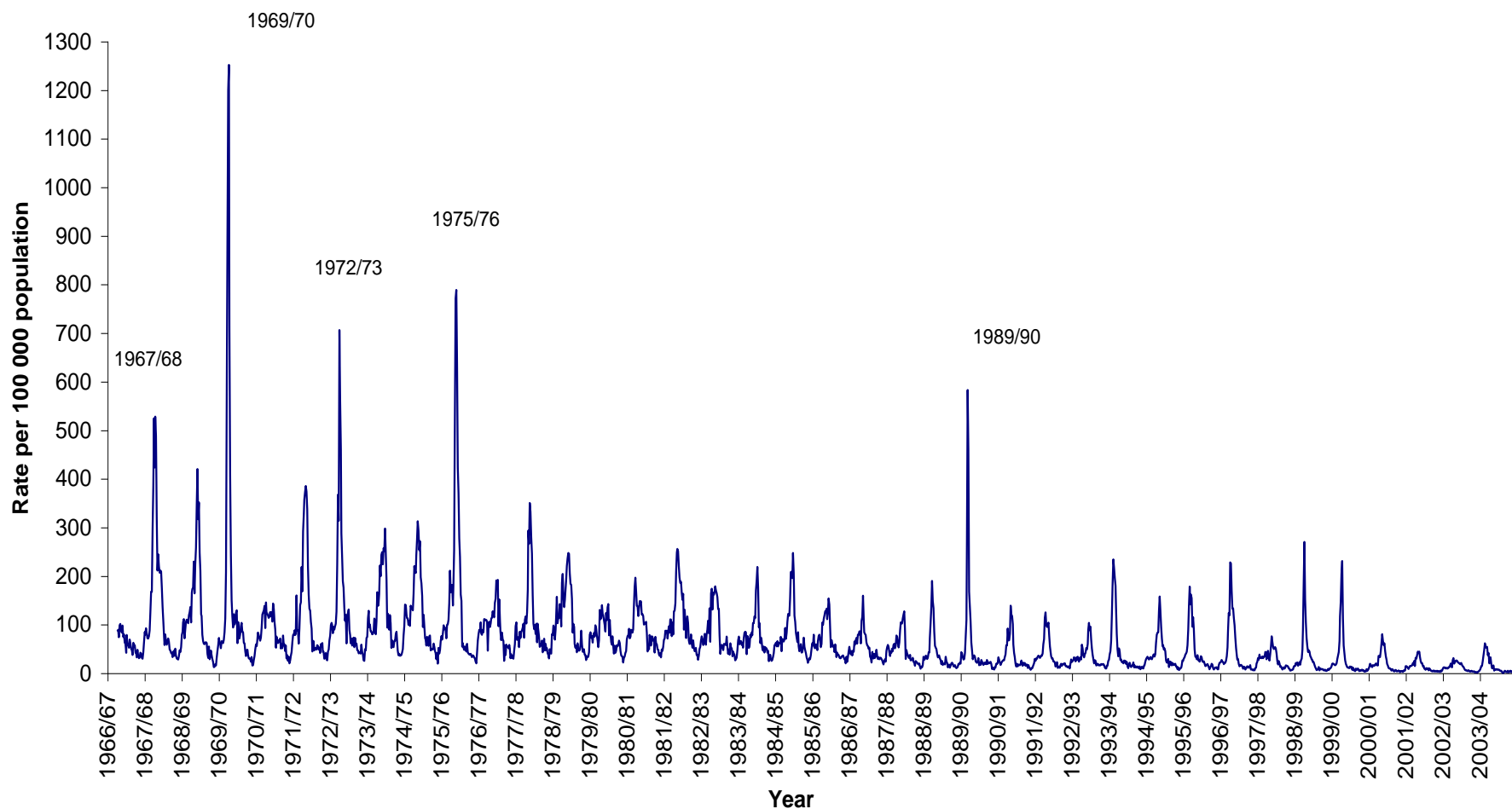


906 hospitalised confirmed influenza cases were reported from the 35 participating sentinel NHS acute trusts across England during 2013/14. Of the 906 hospitalised cases reported, 243 were in children under 17 years of age.



Seasonal and pandemic influenza: Weekly GP consultations for influenza-like illness

RCGP Index for Influenza & Influenza-like Illness, 1966 and 2003
(Year marked at start of season i.e. Week 40 (October))





Public Health
England

PANDEMIC INFLUENZA

***"Most experts believe that
it is a matter of when,
not whether,
another influenza pandemic
will strike"***



Pandemic flu

- Virus mutates markedly ('Antigenic shift')
- Large proportion of the population is susceptible.
- Often created by the strain "jumping" from another species e.g. Flu virus found in ducks, chickens, horses, pigs, whales, seals...



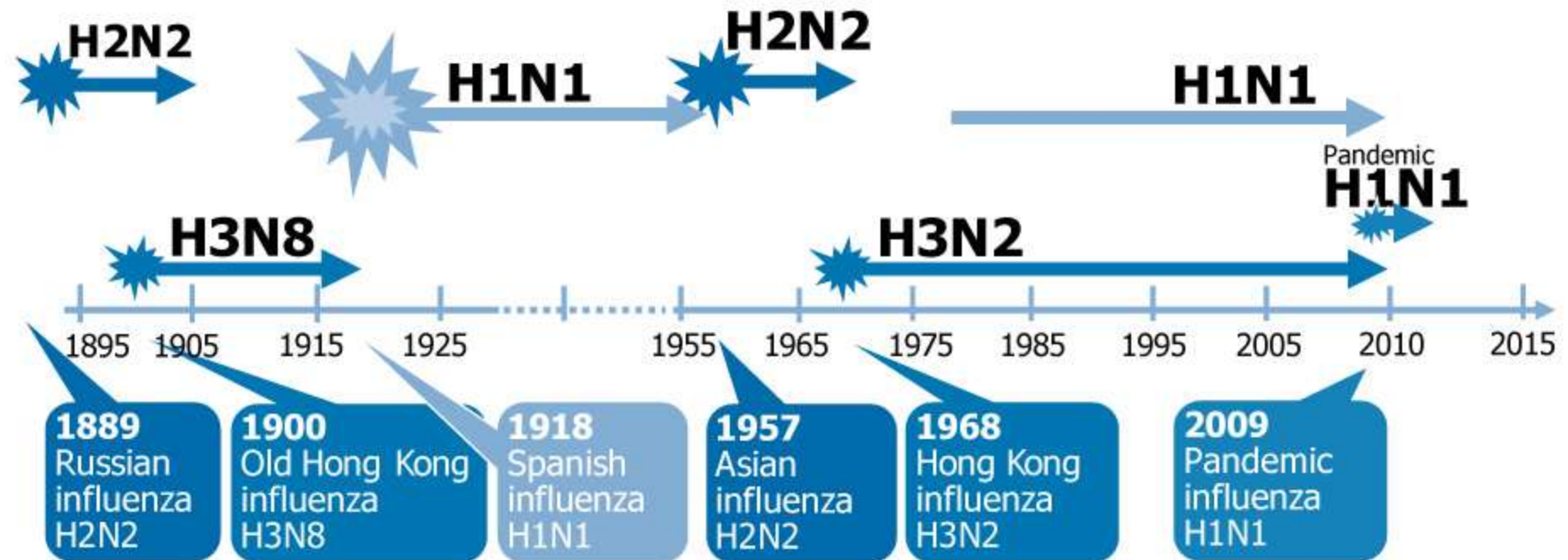
Pandemic Flu Will Cause:

- High morbidity
- Excess mortality
- Social disruption
- Economic disruption

Previous pandemics: 1918, 1957, 1968

FIGURE

Recorded human pandemic influenzas since 1885 (early sub-types inferred)

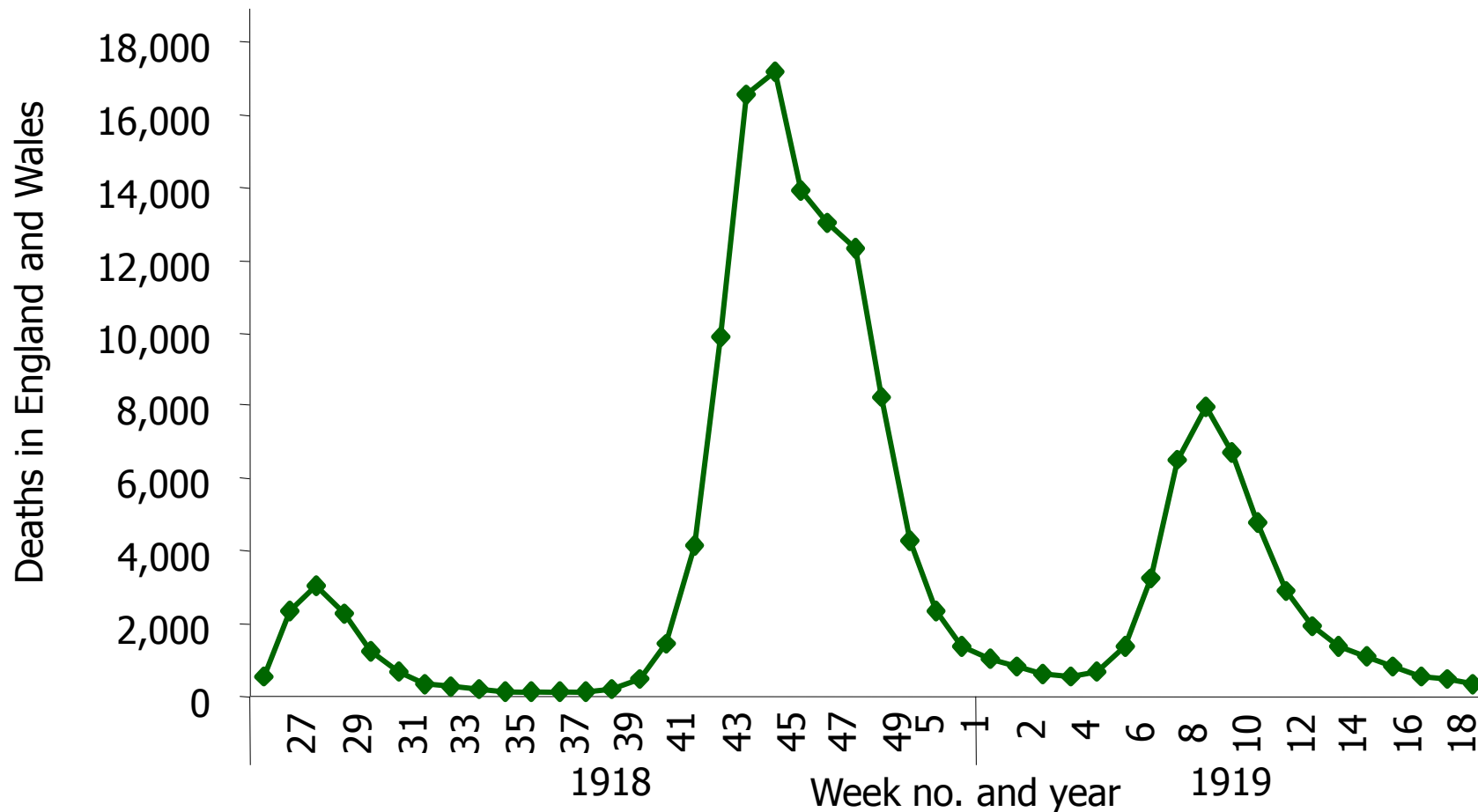


Source: European Centre for Disease Prevention and Control (ECDC) 2009

Reproduced and adapted (2009) with permission of Dr Masato Tashiro, Director, Center for Influenza Virus Research, National Institute of Infectious Diseases (NIID), Japan.



Previous Pandemics: 1918/19 – H1N1



1918/19: 'Influenza deaths', England and Wales.

The pandemic affected young adults, the very young and older age groups.



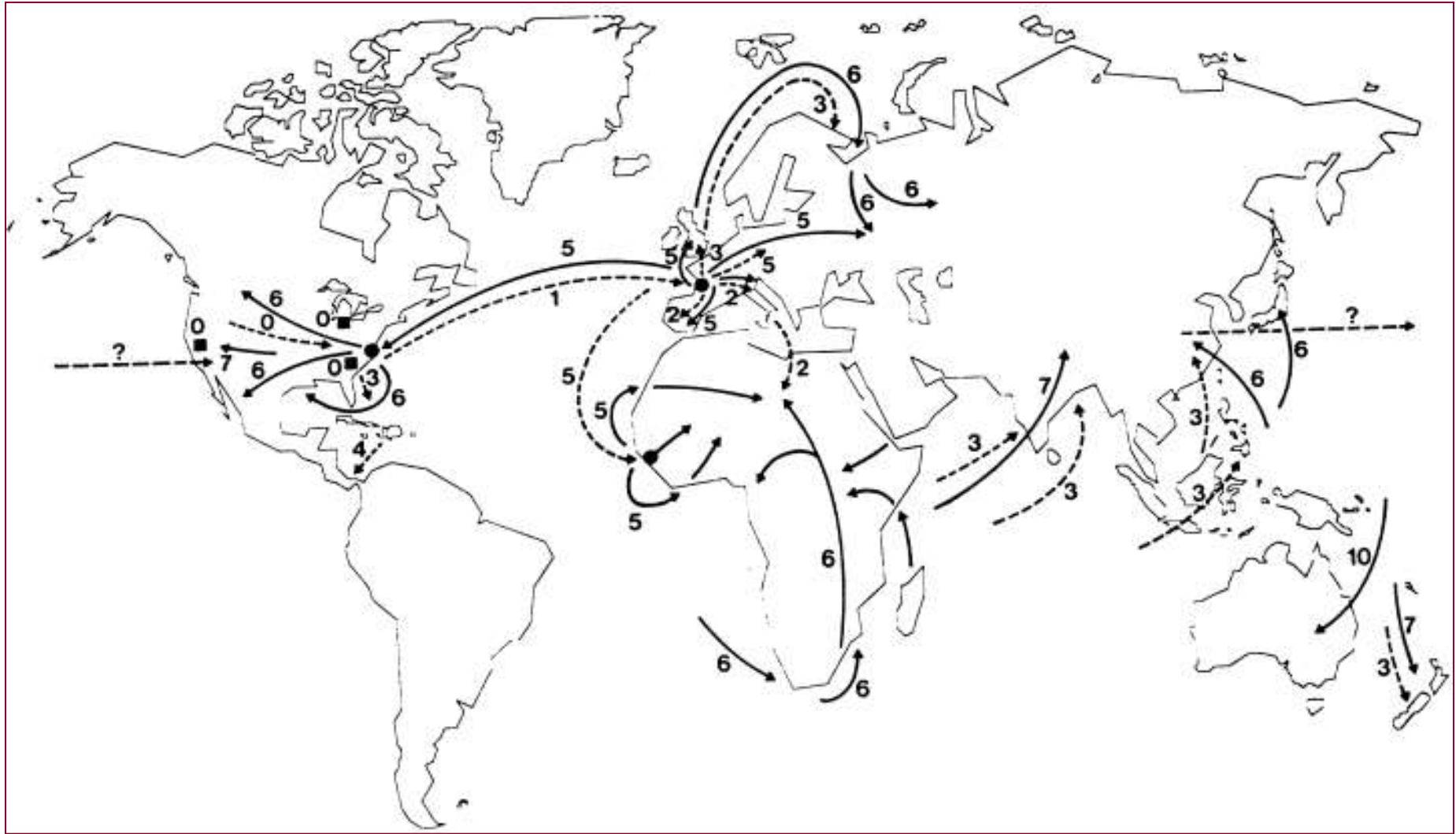
The Spanish flu of 1918/19

- H1N1 flu subtype, derived from an avian source
- Killed between 50 and 100 million people worldwide, with about 40% of the world's population becoming ill.
- Of those who died, many felt ill in the morning and were dead by nightfall. It killed more people than WWI.
- Believed that the movement of soldiers helped to spread the virus further afield.
- It killed mostly young people (between 20 and 40 years) impacting greatly on future generations because these were the people of working (tax-paying) and child-bearing age.



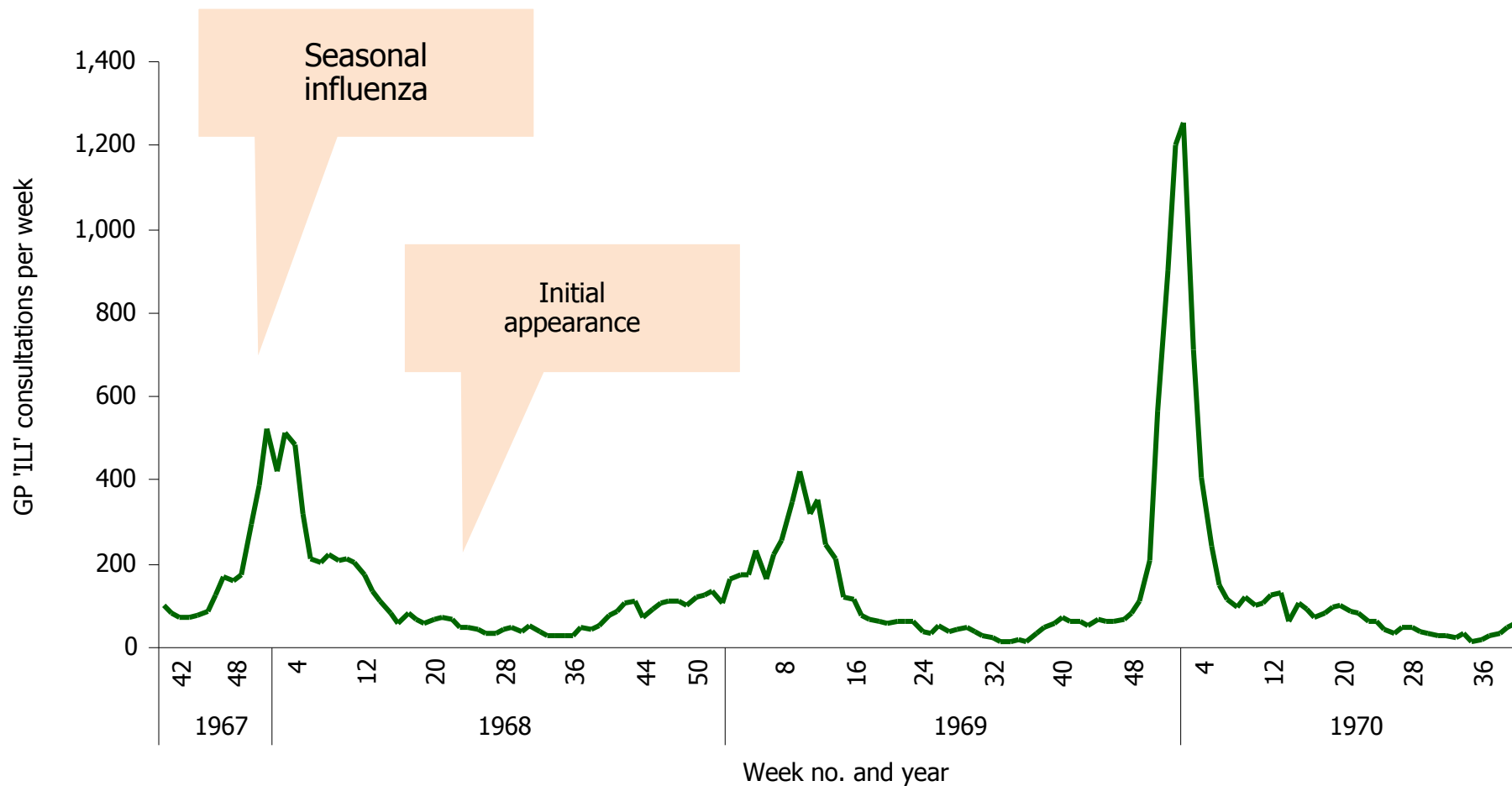
The influenza pandemic of 1918-20.

Source: C.W. Potter, Journal of Applied Microbiology





Previous Pandemics: 1968/69 – H3N2



1968/69: ILI.

The pandemic affected all age groups.



What might we expect from Pandemic Flu?

- Incubation period 1-4 days
- Infectious from onset of symptoms to 4-5 days after,
- 10% infectious before symptom onset.
- Warning? 2-4 weeks from first case to first introduction to UK??
- First wave last 3-5 months. Subsequent waves may be worse
- What age groups will be affected?
- Will take 4 – 6 months (or more) before vaccine available
- Effectiveness of anti-virals??

Possible impact of pandemic influenza on Leeds

Overall case fatality rate	Clinical attack rate		
	<i>10%</i>	<i>25%</i>	<i>50%</i>
0.37%	265	662	1,323
1%	715	1,789	3,577
2.5%	1,789	4,471	8,943
5%	3,577	8,943	17,885
10%	7,154	17,885	35,770
25%	17,885	44,713	89,425
50%	35,770	89,425	178,850



Will we get more pandemics?

- More travel
- More people
- Intensive farming
 - More animal contacts with people
 - Factory farming breeding grounds for viruses
- BUT on the plus side
 - Better nutrition, overall healthier population
 - Better supportive care options
 - Vaccination
 - Antivirals?



Avian Flu (H5N1)

- Before 1997, H5N1 flu virus started circulating in SE Asia
- Mild disease in birds (ruffled feathers and depression)
- Mutation to highly pathogenic form → 100% mortality
- First human cases: Hong Kong 1997
- December 2003: outbreak in poultry in Korea
- 2005: avian flu spreads westwards with bird migration
- Jan 2006: Human cases in Turkey
- March 2007: Turkeys in Suffolk
- December 2008 Swans in Portland

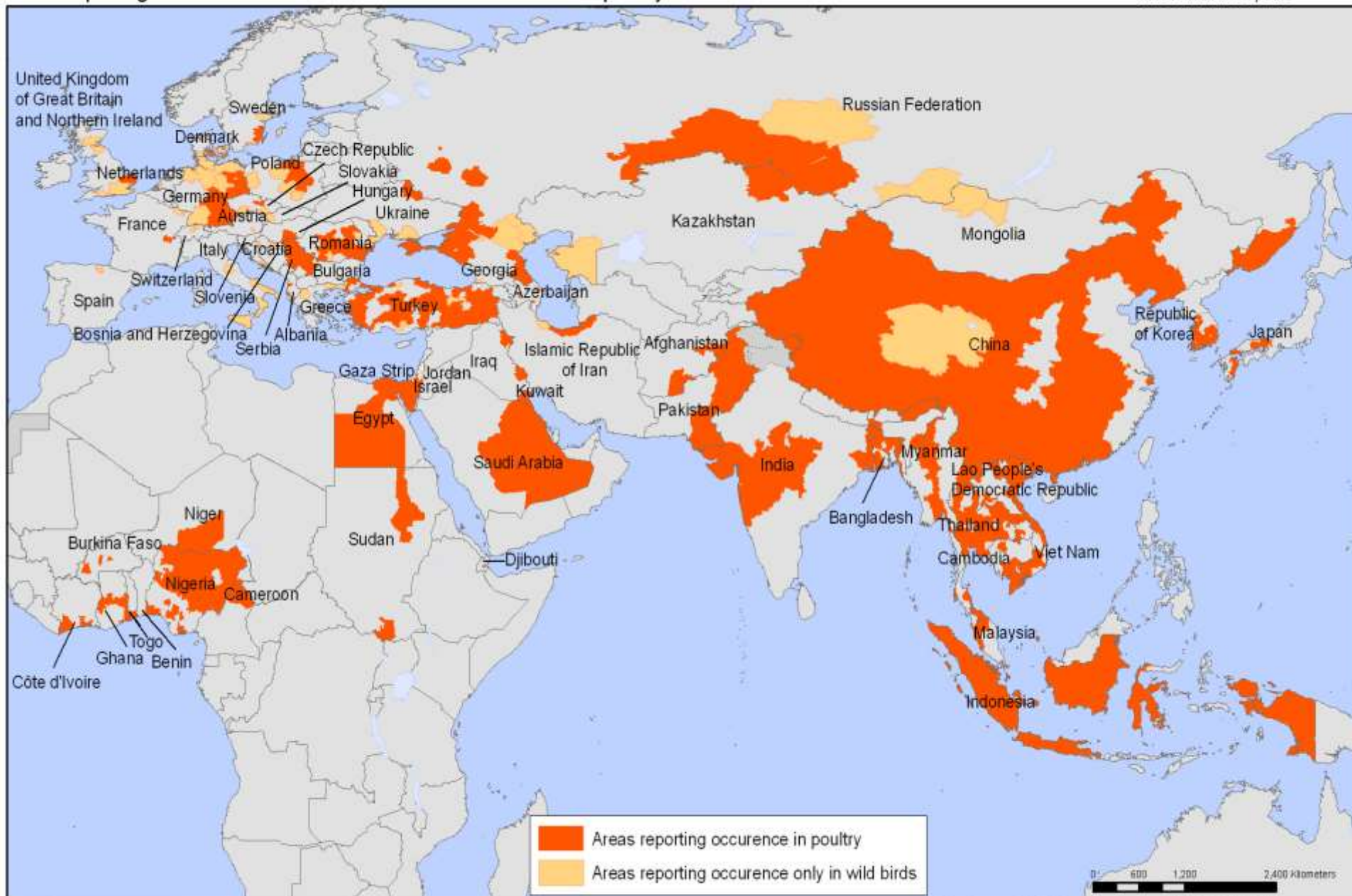


Avian Flu (H5N1)

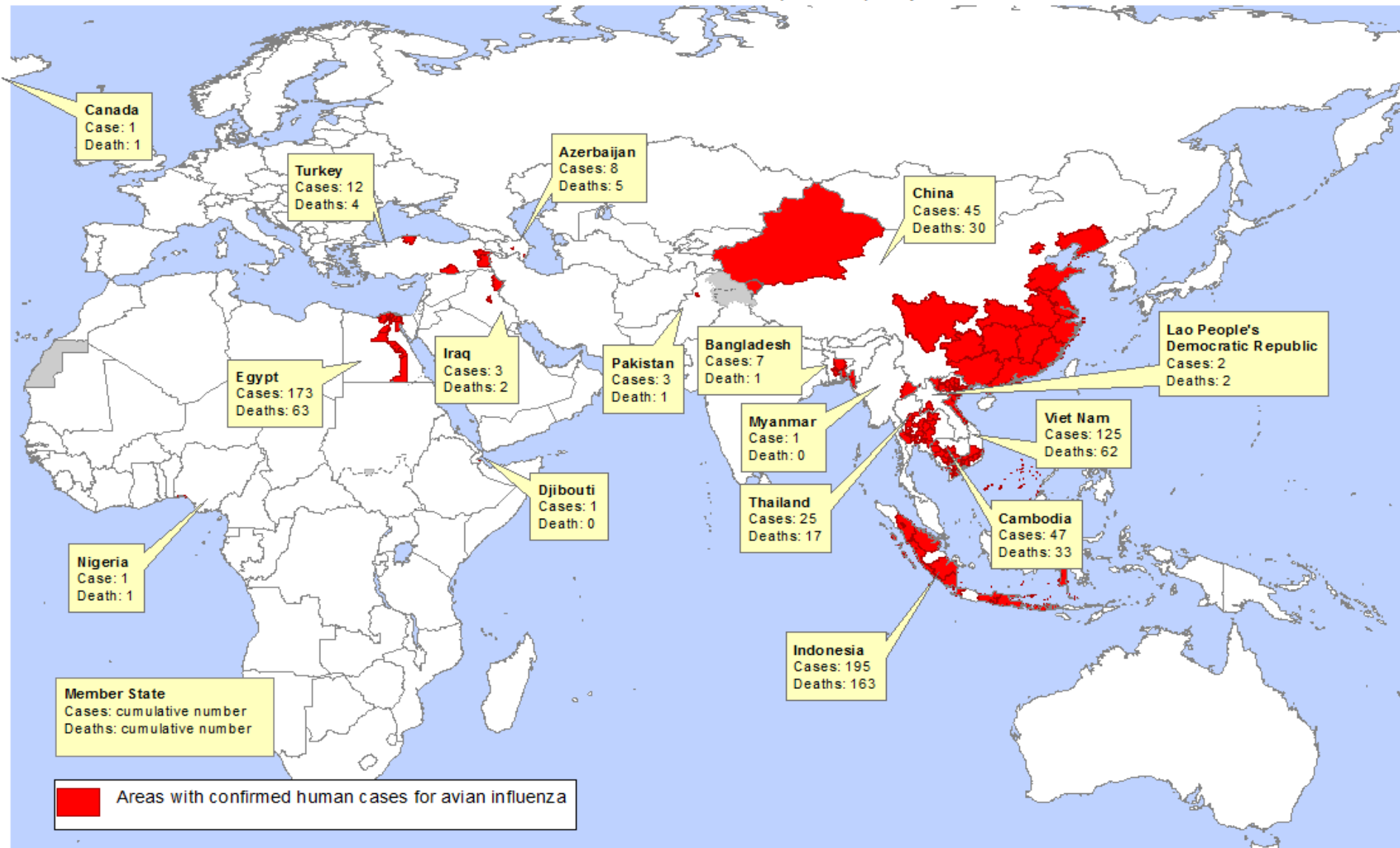
- Strictly an avian pathogen but has the documented ability to pass from birds to humans
- Why SE Asia?
 - Close proximity of poultry and people.
 - 50 – 80% of poultry in small rural households
- Most seasonal influenza get secondary bacterial pneumonia, whereas H5N1 causes a primary viral pneumonia



Areas reporting confirmed occurrence of H5N1 avian influenza in poultry and wild birds since 2003



Areas with confirmed human cases for avian influenza A(H5N1) reported to WHO, 2003-2013*



*All dates refer to onset of illness
Data as of 24 January 2014
Source: WHO/GIP

The designations employed and the presentation of the material in this publication do not imply the expression of any opinion whatsoever on the part of the World Health Organization concerning the legal status of any country, territory, city or area or of its authorities, or concerning the delimitation of its frontiers or boundaries. Dotted and dashed lines on maps represent approximate border lines for which there may not be full agreement.
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Incidence of Avian Flu (H5N1) in Humans

2003 – 1st April 2011 (WHO)



Country	2003		2004		2005		2006		2007		2008		2009		2010		2011		Total	
	cases	deaths	cases	deaths	cases	deaths	cases	deaths	cases	deaths	2008 cases	2008 deaths	2009 cases	2009 deaths	2010 cases	2010 deaths	2011 cases	2011 deaths	cases	deaths
Azerbaijan	0	0	0	0	0	0	8	5	0	0	0	0	0	0	0	0	0	0	8	5
Bangladesh	0	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0	1	0	2	0
Cambodia	0	0	0	0	4	4	2	2	1	1	1	0	1	0	1	1	3	3	13	11
China	1	1	0	0	8	5	13	8	5	3	4	4	7	4	2	1	0	0	40	26
Djibouti	0	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0	1	0
Egypt	0	0	0	0	0	0	18	10	25	9	8	4	39	4	29	13	14	5	133	45
Indonesia	0	0	0	0	2	0	55	4	15	1	24	2	20	1	9	7	5	4	176	145
Iraq	0	0	0	0	0	0	3	2	0	0	0	0	0	0	0	0	0	0	3	2
Lao People's Democratic Republic	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	2	2
Myanmar	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0	1	0
Nigeria	0	0	0	0	0	0	0	0	1	1	1	0	0	0	0	0	0	0	1	1
Pakistan	0	0	0	0	0	0	0	0	3	1	0	0	0	0	0	0	0	0	3	1
Thailand	0	0	17	12	5	2	3	3	0	0	0	0	0	0	0	0	0	0	25	17
Turkey	0	0	0	0	0	0	12	4	0	0	0	0	0	0	0	0	0	0	12	4
Viet Nam	3	3	29	20	61	19	0	0	8	5	6	5	5	5	7	2	0	0	119	59
Total	4	4	46	32	98	43	115	79	88	59	44	33	73	32	48	24	23	12	539	318

Case Fatality Rate
59%



Controlling Avian Flu

- Cull affected birds
- Biosecurity and quarantine
- Disinfecting farms
- Control poultry movement
- Vaccinate workers – seasonal influenza vaccine
- Antivirals for poultry workers
- Personal Protective Equipment (PPE)
- Try to reduce chance of co-infection



Public Health
England

H1N1 Influenza (Swine Flu)



Public Health
England

Prior to the Pandemic

- International surveillance
- Virus research
- Vaccine research
- Stock piling of drugs
 - 30 million courses of Oseltamivir
- Plans written – strategic
- Preparation of information – public and professional





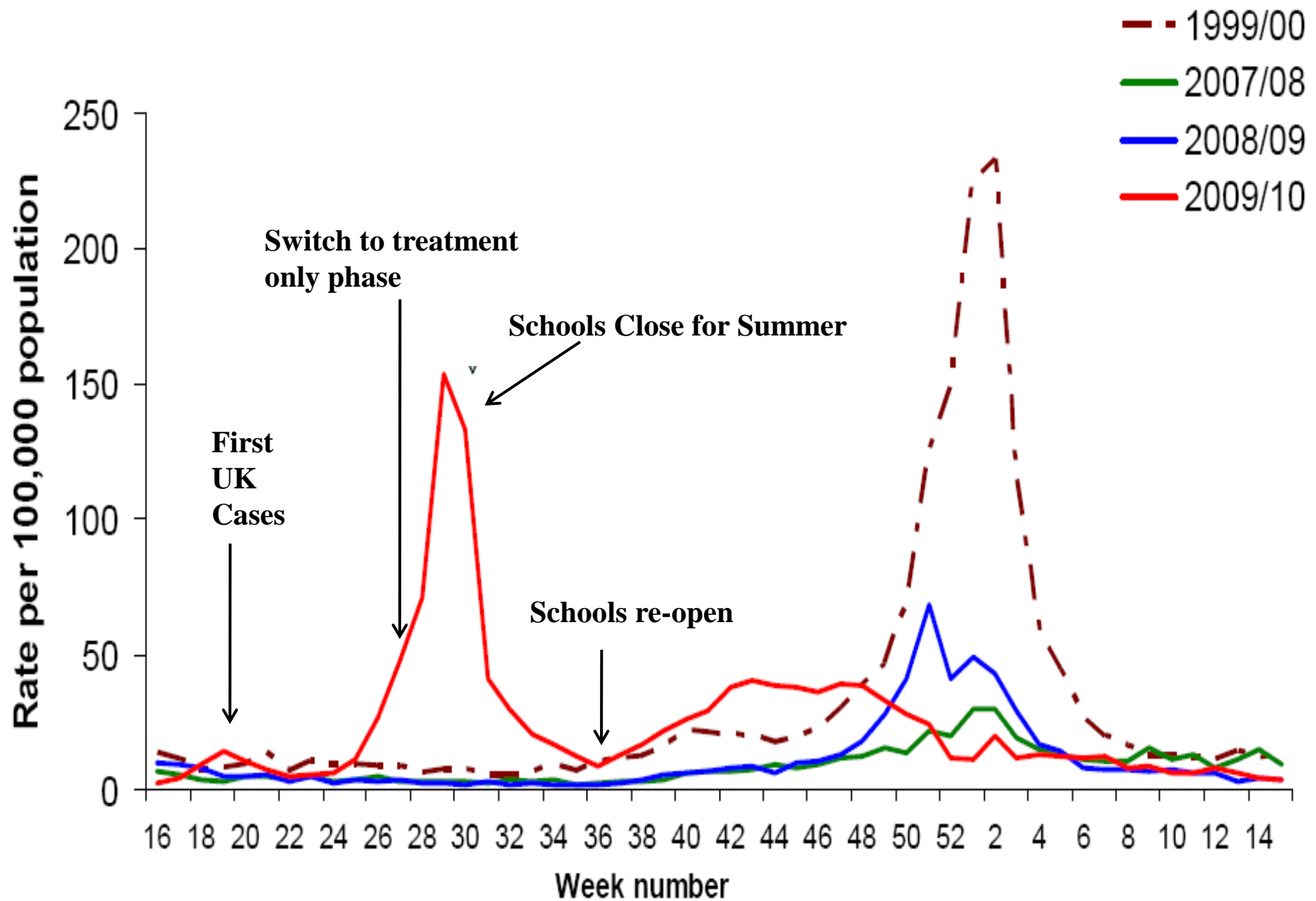
H1N1 – Swine Flu

- Reassortment of swine, avian and human flu virus
- Novel virus substantially different from human H1N1 virus; many people susceptible
- Human to human transmission
- Sensitive to Oseltamivir and Zanamivir (at the moment)
- Seasonal influenza vaccine not effective
- People over 40 year have some immunity



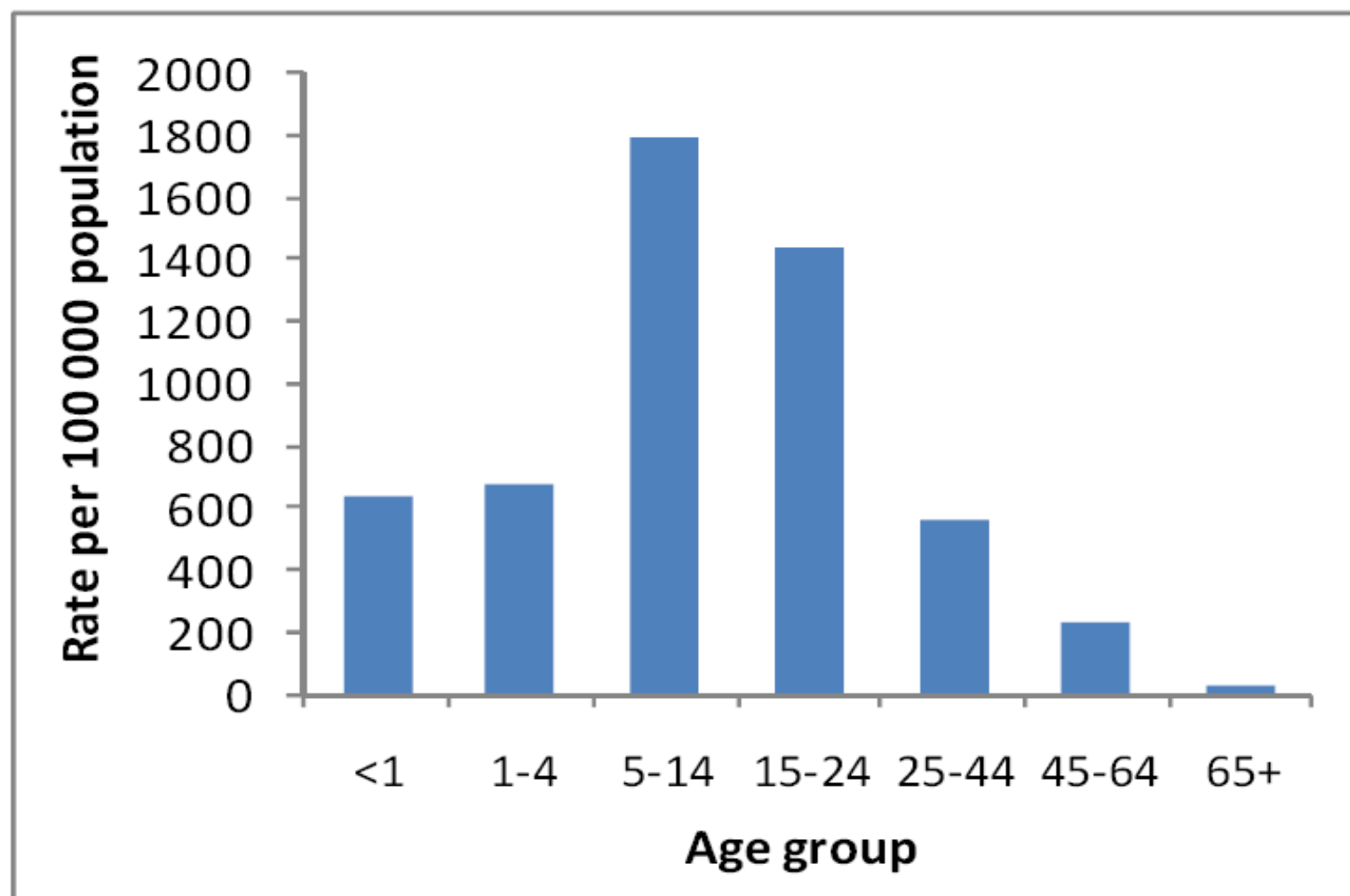
Managing the Early Stages

- **Containment Phase**
 - Identification of cases – swabs (couriers),
 - Treatment of cases
 - Contact tracing – family, airline passengers
 - Large scale prophylaxis
- **Treatment Phase**
 - Treat cases only
 - National Flu Pandemic Service



Week ending 11 April 2010: **3.7 consultations per 100,000 population**

Figure 3: Estimated rate, per 100,000 population, of clinical cases of pandemic H1N1 2009, by age group, England to 27 September 2009*



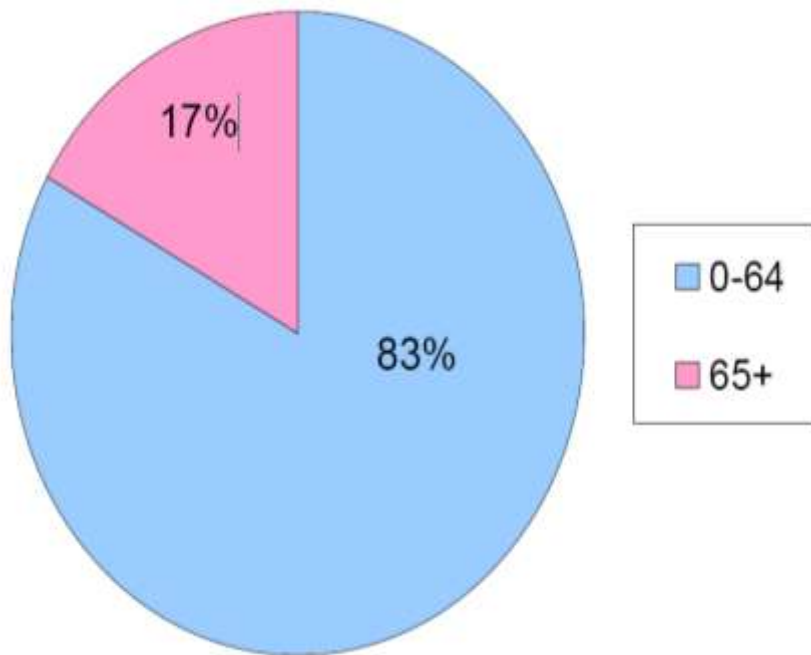
** Estimated number of cases to 27 September using data reported on 28 October 2009*



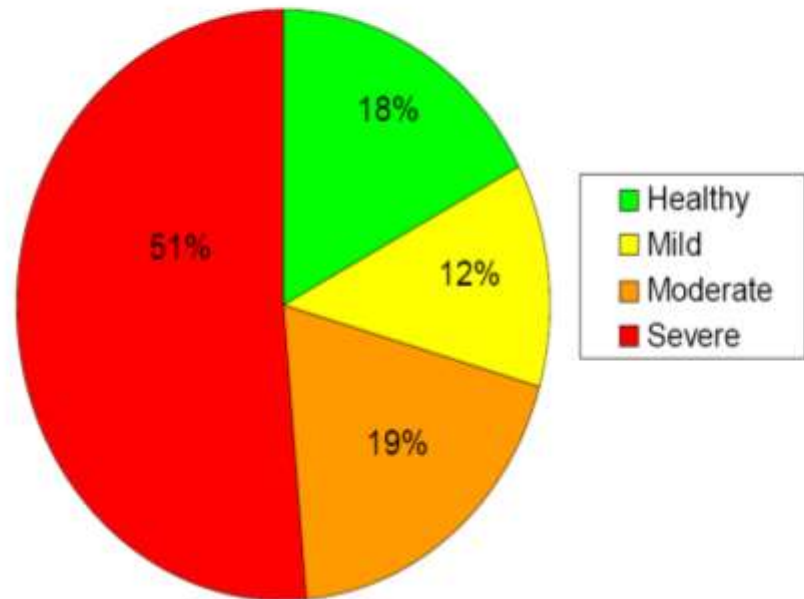
Deaths from Swine Flu

- 474 confirmed swine flu deaths in the UK

Age distribution of deaths



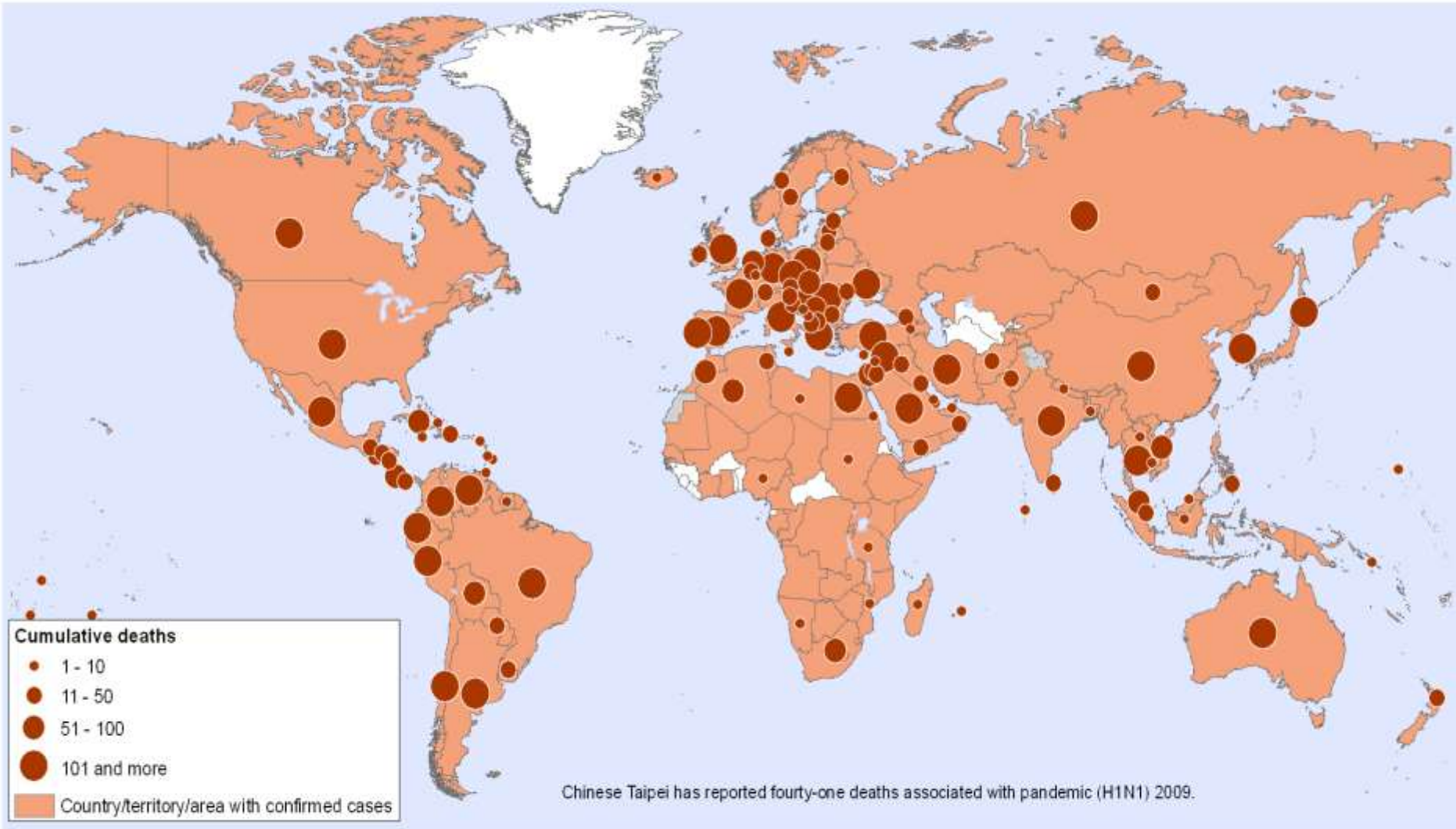
Underlying conditions for fully investigated deaths related to pandemic H1N1 (2009) influenza



Pandemic (H1N1) 2009

Status as of 28 March 2010

Countries, territories and areas with lab confirmed cases and number of deaths as reported to WHO



The boundaries and names shown and the designations used on this map do not imply the expression of any opinion whatsoever on the part of the World Health Organization concerning the legal status of any country, territory, city or area or of its authorities, or concerning the delimitation of its frontiers or boundaries. Dotted lines on maps represent approximate border lines for which there may not yet be full agreement.

Map produced: 01 April 2010, 05:30 GMT

Data Source: World Health Organization
Map Production: Public Health Information
and Geographic Information Systems (GIS)
World Health Organization



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Public Health
England

Infection Control

- Hand hygiene, cough etiquette
- Universal precautions and PPE (mask, apron, gown, gloves)
- Surgical masks OK for non aerosol generating procedures
- Segregation of patients
- Reduce social contact
- Flu surgeries
- Environmental cleaning

CATCH IT

Germs spread easily. Always carry tissues and use them to catch your cough or sneeze.



BIN IT

Germs can live for several hours on tissues. Dispose of your tissue as soon as possible.



KILL IT

Hands can transfer germs to every surface you touch. Clean your hands as soon as you can.



NHS

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Managing cases

- Call centres
- Non medical staff manage cases according to an algorithm
- Patient or relative collects antivirals
- Home delivery of anti virals for some
- Clinical staff free to treat high risk and severely ill people
- Hospital admission criteria

Antiviral drugs

- UK stockpiled 30 million courses
- Would cover a 50% attack rate
- Mostly Tamiflu, with some Relenza
- Tamiflu needs to be given with 24-48 hours of contact to have maximum effect
- Evidence from seasonal flu is that it reduces hospitalisation by 50% and duration of disease by approximately 24hours (drug company studies...)
- Issues:
 - What happens if the virus develops resistance?
 - What about side effects?
 - Who do we give them to?
 - How do we distribute them?



Limited role of face masks

Close contact – 1 metre

Fit tested respirators for high risk procedures only

Only useful if:

- Worn correctly
- Changed frequently
- Removed properly
- Disposed of safely
- Used in combination with good universal hygiene practice

But:

- How many do you need per day?
- What will you say when the masks run out?



STAFF ISSUES

- Anxiety/unwilling to work
- Adequate protection
- Access to antivirals
- Risk to family
- Child care
- Segregation of staff
- Redeployment of staff
- Recycling of staff
- Organisations sharing staff



Impact on schools and services

- Likely to spread rapidly in schools and other closed communities
- What happens to NHS staffing levels if schools close down?
- Impact on all services including police, fire, the military, fuel supply, food production, distribution and transport, prisons, education and business



Vaccines

- Developed in the past but not used
 - capacity issues and too late
- Could take 6 -10 months, hopefully quicker
- When to switch from producing normal seasonal flu vaccine to the pandemic strain?
- Capacity:
 - will take time to manufacture
 - who do you allocate it to first?
- Two doses for at risk groups



Possible population-wide interventions

- Travel restrictions
- Restrictions of mass public gatherings
- Schools closure
- Voluntary home isolation of cases
- Voluntary quarantine of contacts of known cases
- Screening of people entering UK ports



CDC website:

- <http://www.cdc.gov/flu/about/viruses/>

HPA website:

- <http://webarchive.nationalarchives.gov.uk/20140722091854/http://www.hpa.org.uk/Topics/InfectiousDiseases/InfectionsAZ/SeasonalInfluenza/>

PHE Guidance

- <https://www.gov.uk/government/collections/seasonal-influenza-guidance-data-and-analysis>

Patient.co.uk resource for doctors:

- <http://www.patient.co.uk/doctor/influenza>