Modelling the impact of pandemic intervention strategies

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Outline

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- Pandemics
- Risk of a flu pandemic
- Emergence
- Containment
- Travel restrictions to slow international spread
- Impact of pandemic in Europe
- Mitigation – layered interventions
- Uncertainties
- Conclusions

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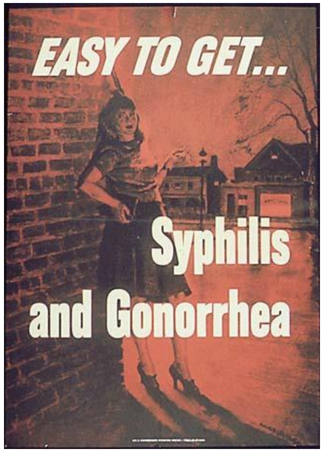
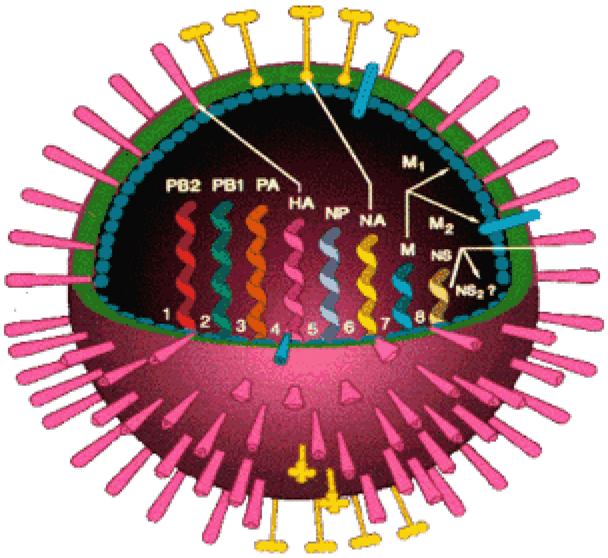
Pandemics

- Pandemic = global epidemic of a new disease.
- Starts with a *zoonosis* mutating to be transmissible.
  - Influenza and HIV/AIDS
  - Black Death and syphilis
  - SARS – might have caused a pandemic.
- Can profoundly affect society.



Influenza

- All flu starts as 'bird flu'.
- Very genetically diverse.
- Very common in birds.
- Most bird flu is non-lethal.
- Occasional outbreaks of highly lethal bird - the types we hear about.



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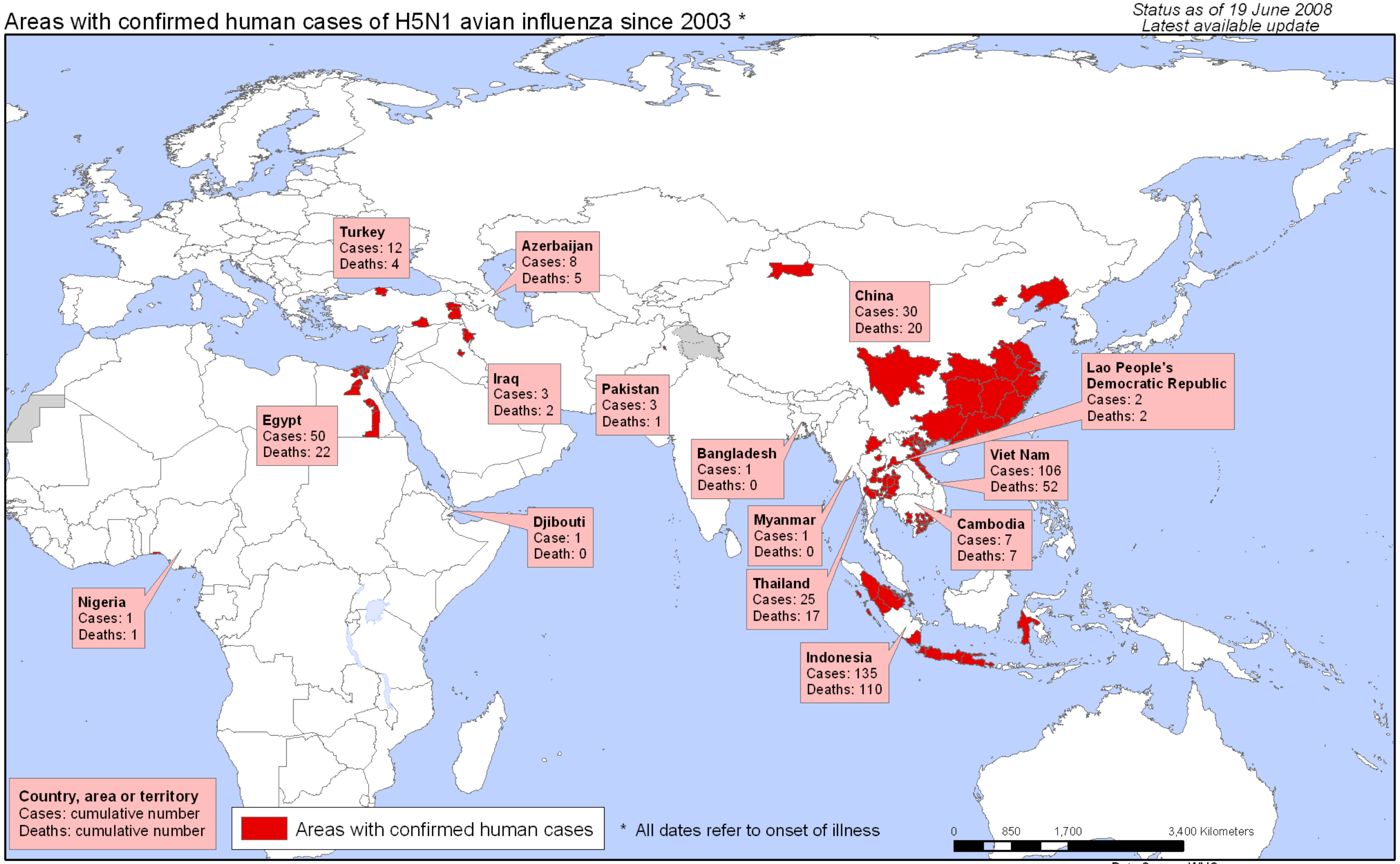
So why worry?

- People can also be infected with bird flu – with difficulty.
- Bird virus can mutate to be transmissible in people= 'human flu'.
- Every time this happens, can cause a pandemic - no immunity.
- Can't predict the next one – but we expect 3-4 per century.
- Top threat identified by UK Govt.

H5N1 'bird flu'

- H5N1 very unusual – v. lethal bird virus which has spread worldwide.
- 'Only' 385 people infected so far– but 243 died.



World Health Organization

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Data Source: WHO
Map Production: Public Health Information and GIS
World Health Organization

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Is a flu pandemic imminent?

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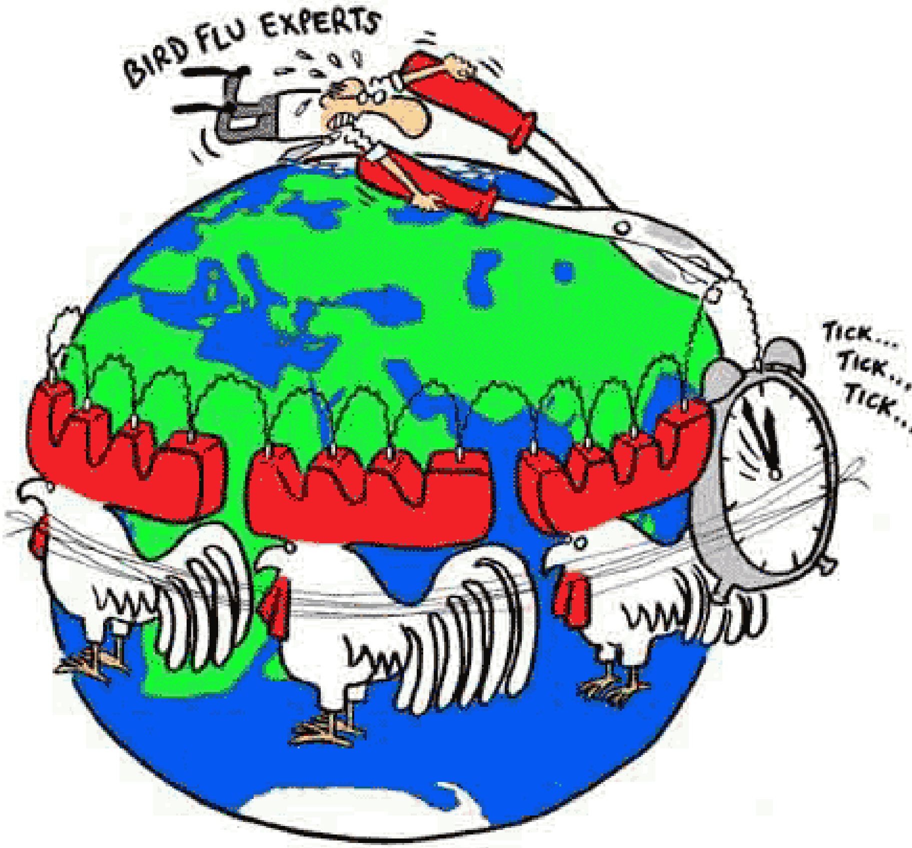
- Need to distinguish *probability* from *severity* in evaluating risk.
- Probability may not have increased – no more bird flu overall, but H5N1 more visible.
- BUT a H5N1 pandemic could be much worse than other strains, given >50% current mortality.
- We *do* need to be ready – but for low risk of catastrophic event.



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How a pandemic might start

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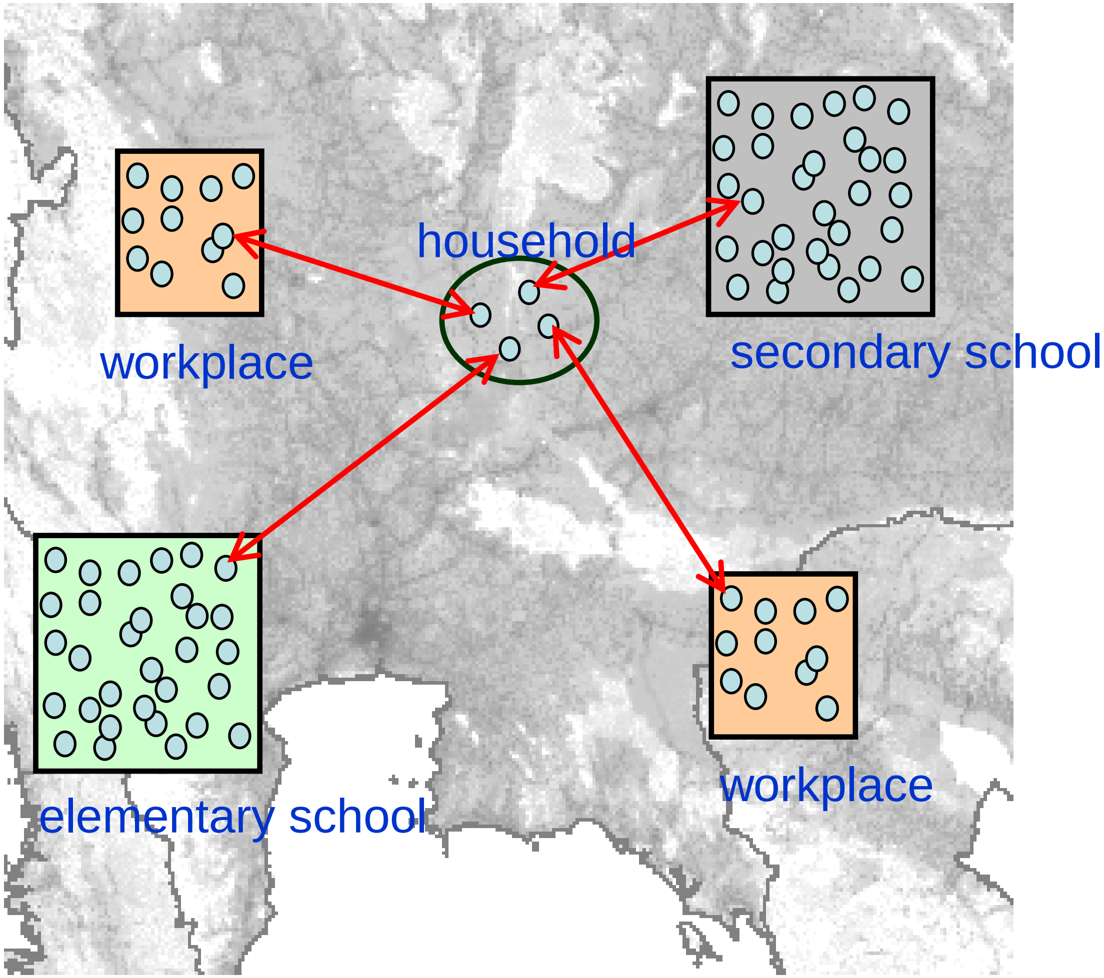
- Someone gets infected with bird flu.
- The virus in that person mutates and becomes transmissible.
- That person then infects people – mostly in the same household.
- Those people infect more people – mostly in same village…
- ... until people realise something is wrong – depends on lethality.

Simulating pandemics

- ‘Synthetic population’ in super-computer.
- People reside in **households**, but go to **school** or a **workplace** during the day.
- **Local movement/travel** plus **air travel** included.
- Disease spreads from **person to person** (spread in birds not included).
- Have modelled **Thailand, UK, US,** and now **EU and China.**
- **Need lots of data…**



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Simulated emergence in Anhui, China

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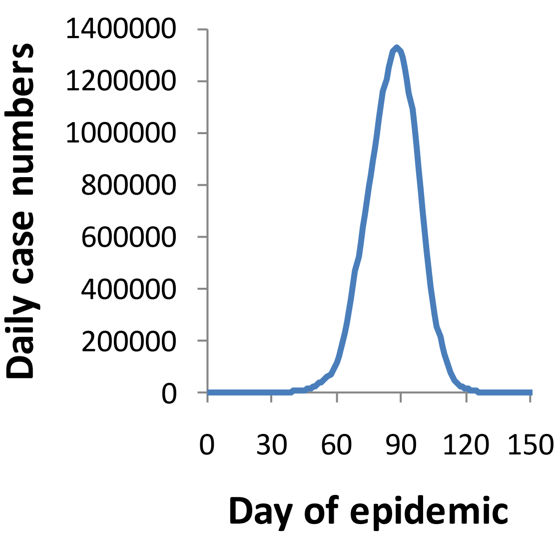
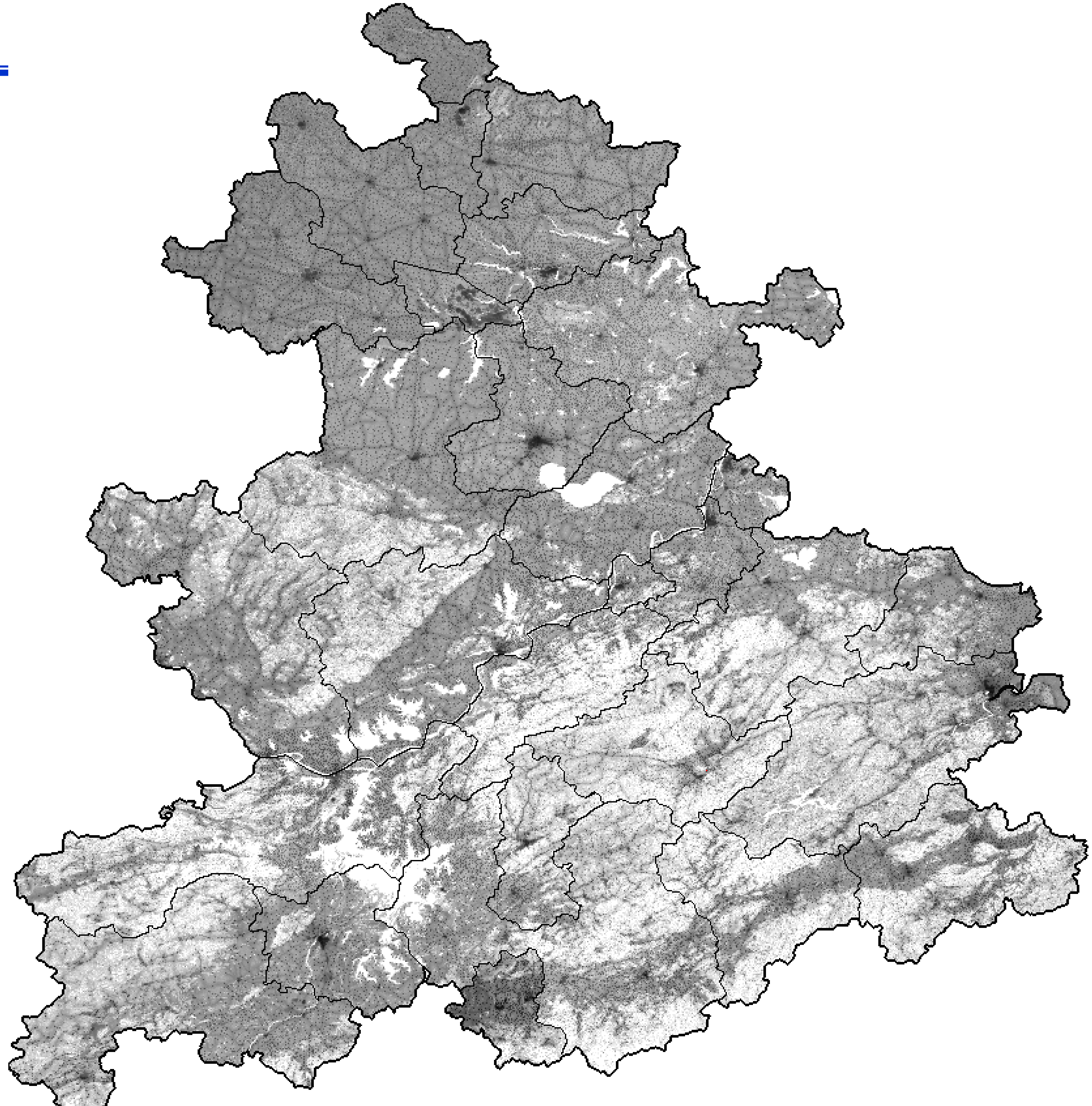
- 112 million people modelled (including border districts of neighbouring provinces).
- Locality of travel means wave-like spread and more irregular epidemic as new urban centres affected.

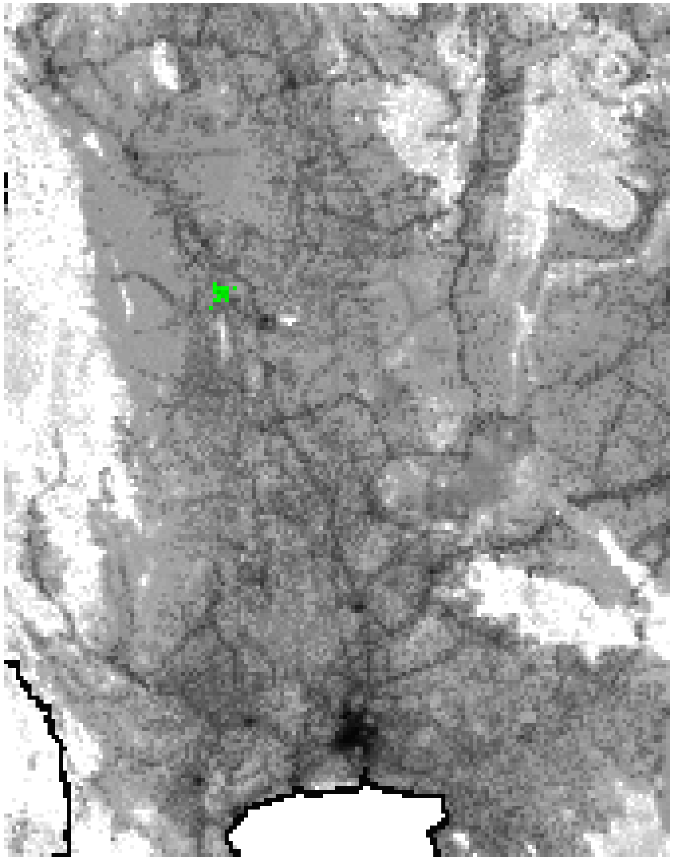


R_0=1.8



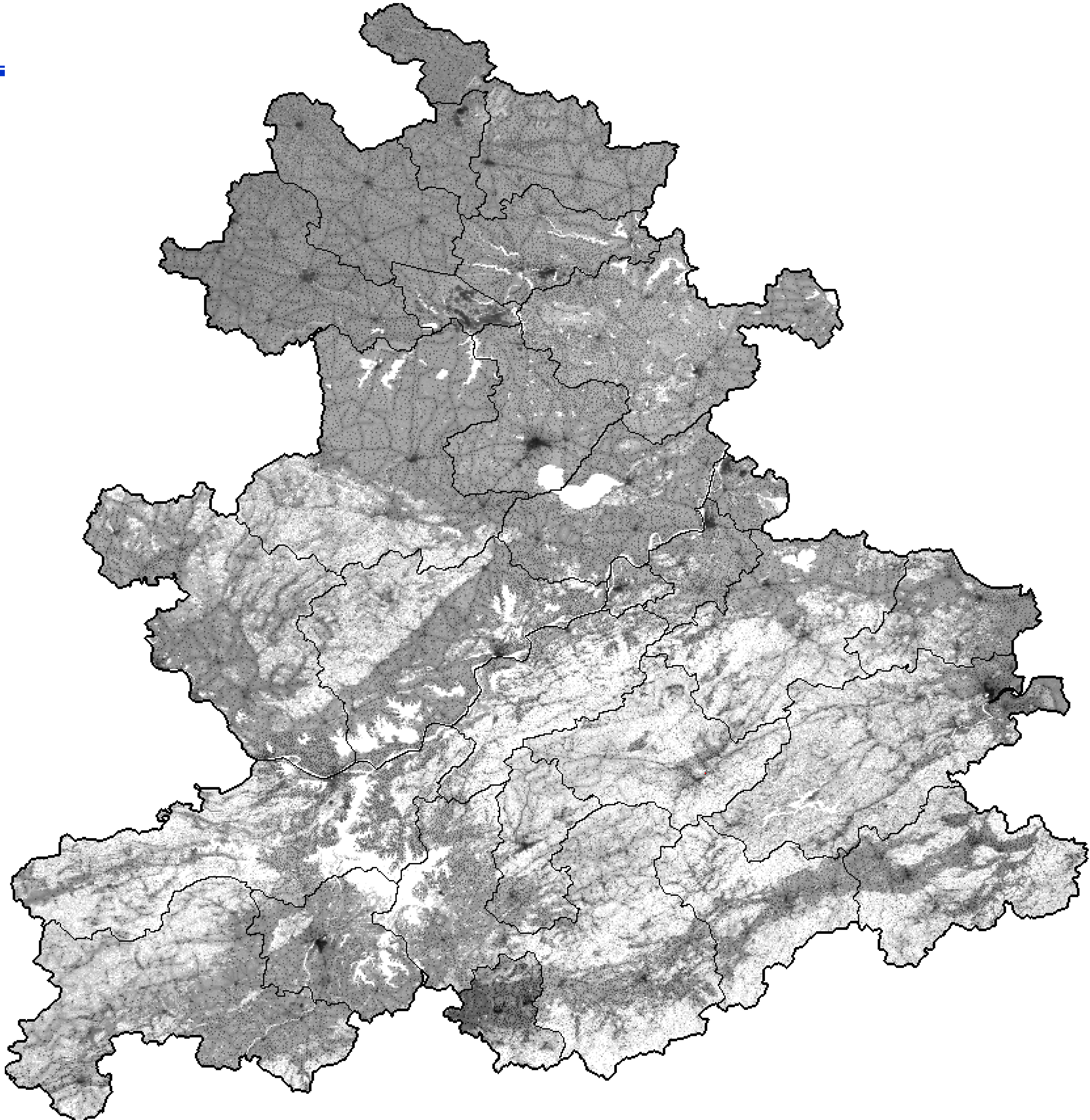
Can we contain a pandemic at source?

- Perhaps.
- BUT need to act fast (before 50 cases accumulate)
- and may need to use 3 million courses of antiviral drugs.
- Non-pharmaceutical interventions and vaccines will also play a role.
- The World Health Organisation and various governments are continuing to actively plan for containment operations.



Example of control in Anhui

- Containment by day 44, after 101 cases.
- 1.1 million courses of AV used.



R_0=1.8

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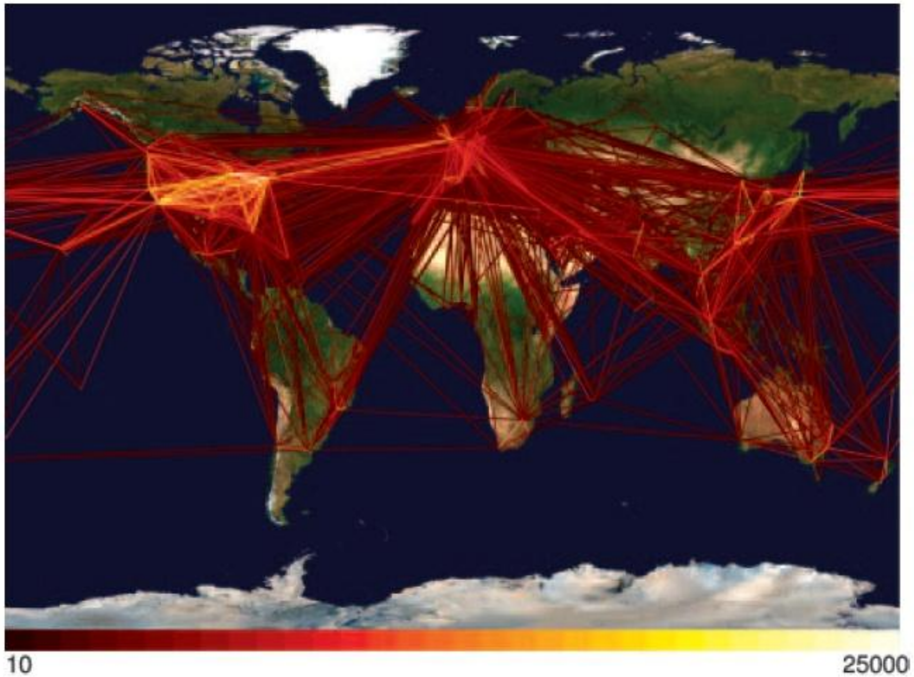
Will travel restrictions stop spread?

- 90% of international travel will probably cease anyway.
- Key problem – growth rate of flu pandemic – 10 fold in 7-14 days
- So stopping 90% of infections buys 1-2 weeks, 99% buys 2-4 weeks.
- V. difficult to reduce travel by >99%.
- Hence travel restrictions probably only useful while containment is attempted.



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A European pandemic

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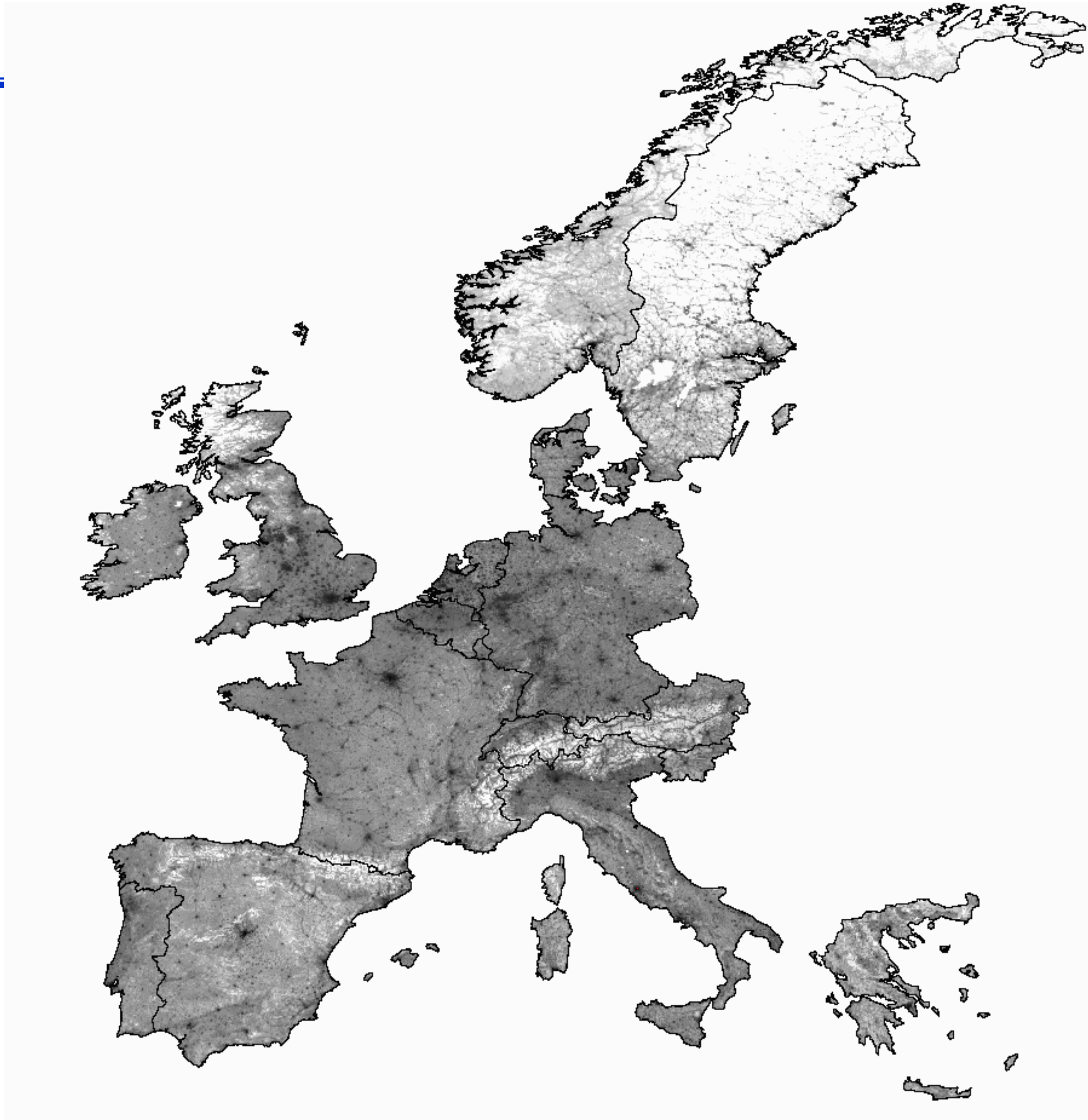
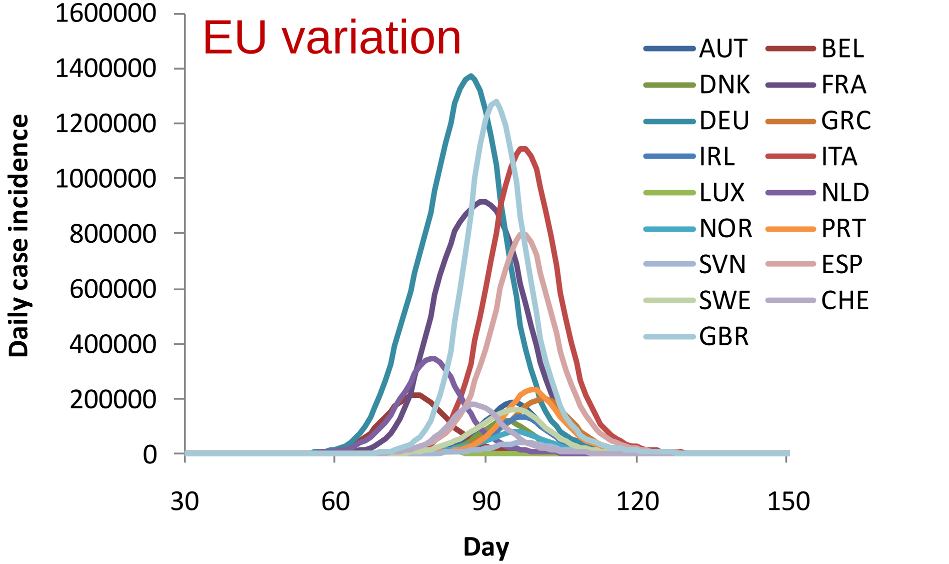
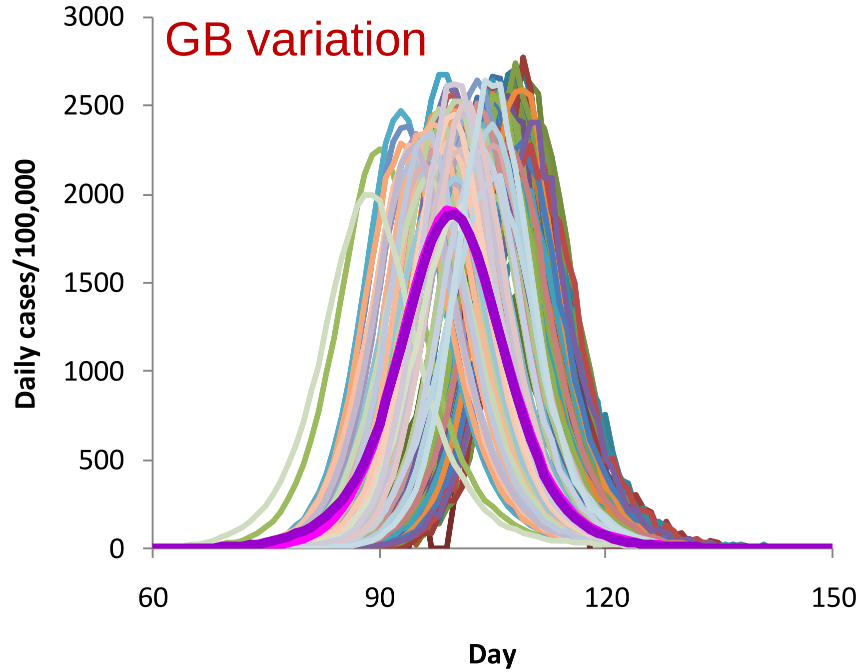
- Pandemic will take 1-4 months to reach EU from SE Asia
- For R_0=2, epidemic will peak 8-12 weeks after 1st case in EU.
- ~1/3 of people likely to be ill (from past pandemics).
- ~1700 cases per 100k on worst day at EU scale.



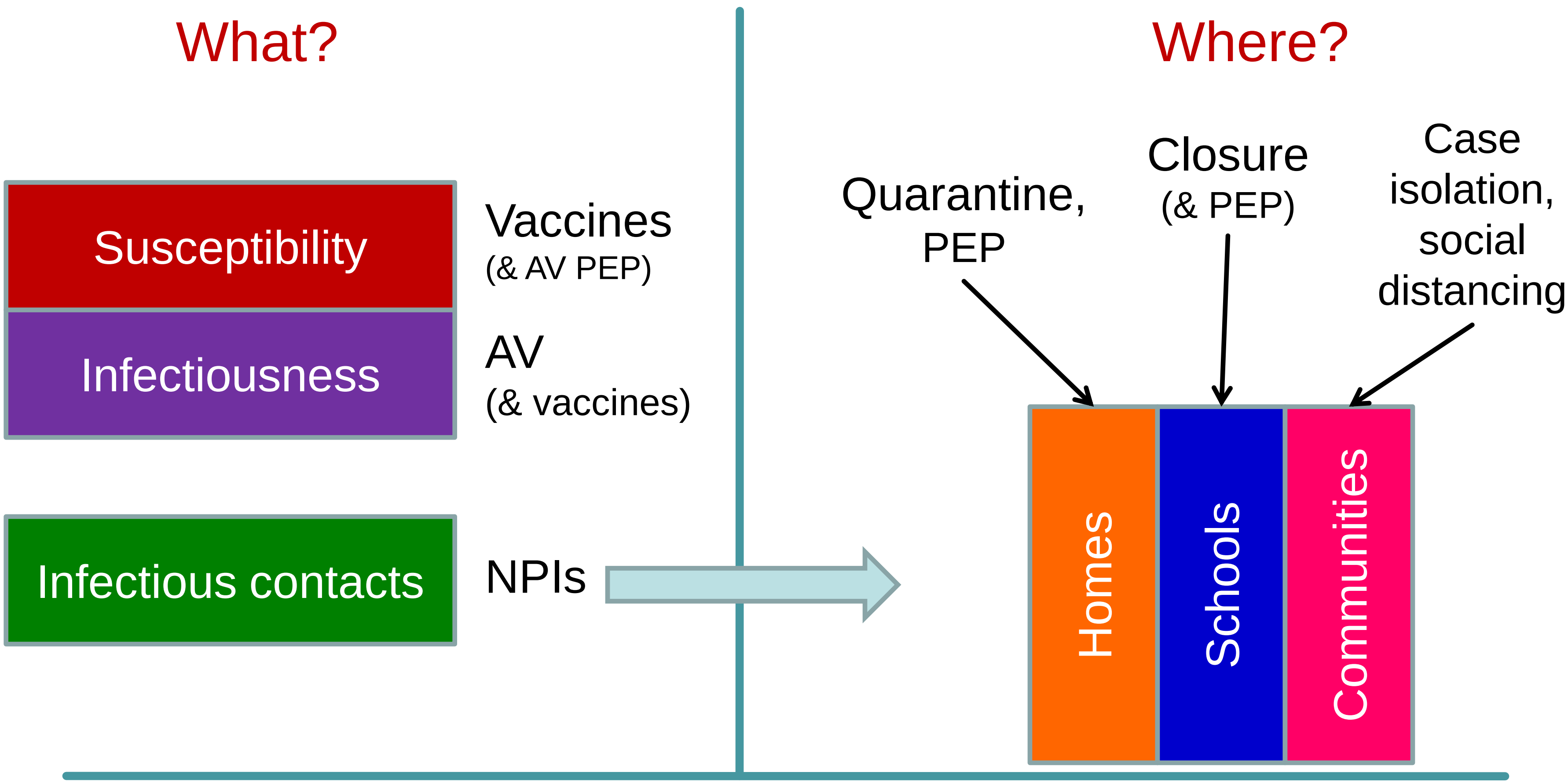
Local epidemics

- Pandemic will not be synchronized across Europe.
- Up to 4-5 week variation in the timing of the peak of the epidemic between countries.
- And also between regions in the same country.
- Peak daily case incidence of 1700/100k for EU, ~1900 for a large country, and ~2500 in a local district.
- = 15%+ local absenteeism in worst week.
- School closure would increase this to 25%+.





Intervention mechanisms



- Modelling can't predict impact of interventions without effectiveness data.
- But can extrapolate from study data to the population.

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Effectiveness of single interventions at reducing attack rates

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Treatment

If given with 24h of symptoms, can reduce transmission, and thus attack rates by ~1/8.

Prophylaxis

Household prophylaxis reduces attack rates by ~1/3, but need ~50% stockpile.

School closure

Reduce peak incidence by ~40%, but might also prevent 1/7 cases.

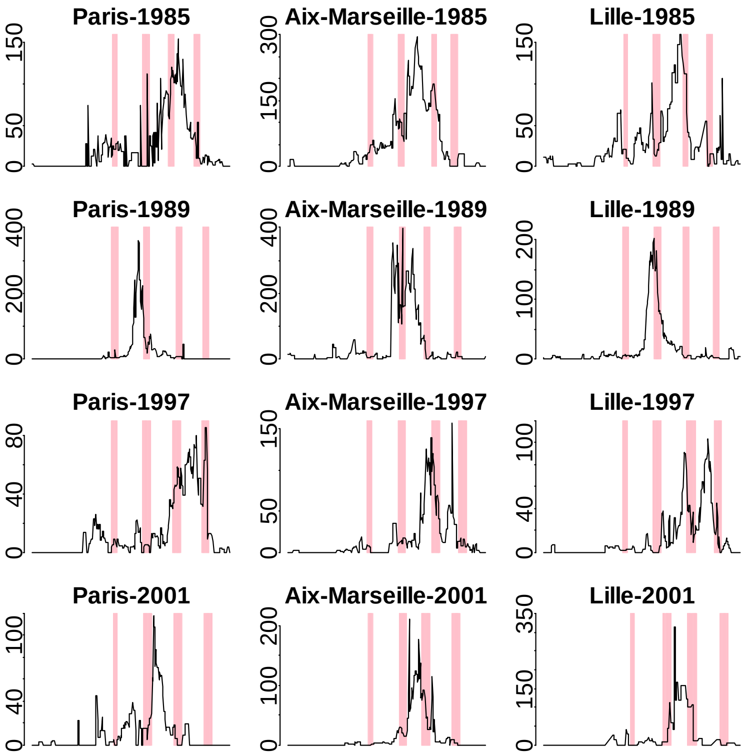
Vaccination

Difficult to predict efficacy – but 20% coverage of low efficacy vaccine might prevent 1/3 cases.

What is the impact of school closure?

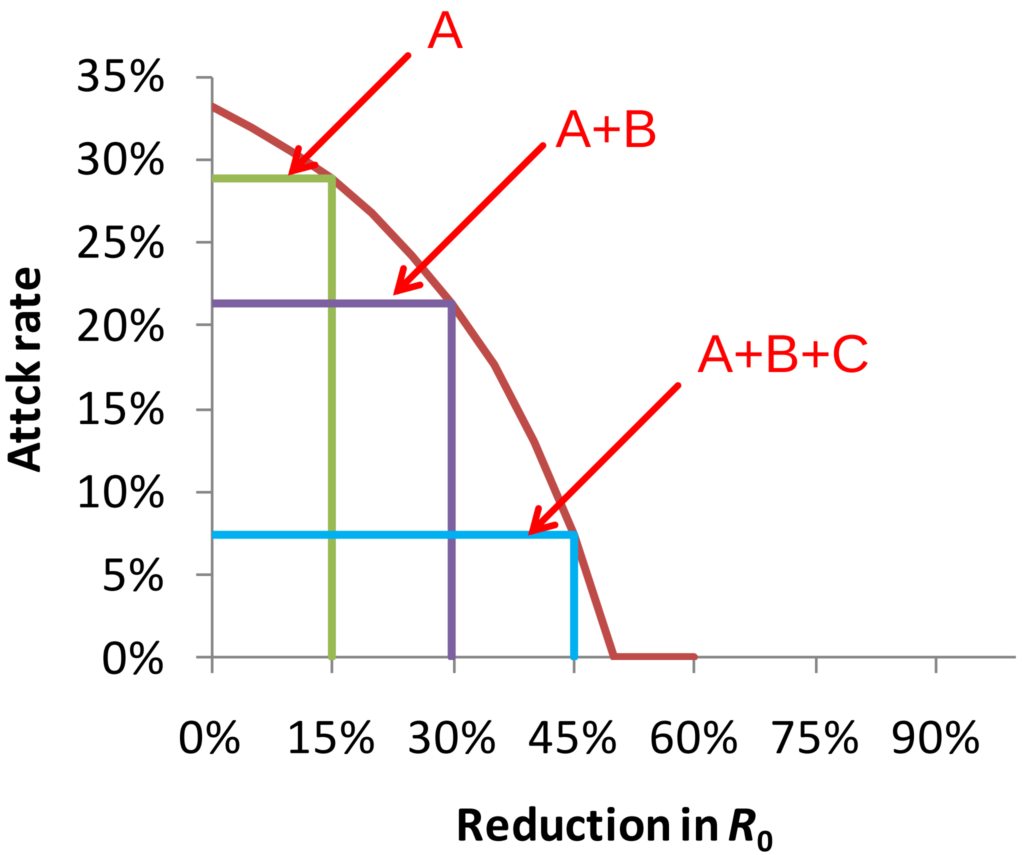
- No data until recently on transmission in schools .
- Have now used sentinel surveillance data on seasonal ILI incidence to estimate effect of school closures.
- Estimate that closure would prevent 1 in 7 cases (1 in 5 in children) in a pandemic...
- ... But this critically dependent on effect of compensatory behaviours.

(Cauchemez et al, Nature 2008)



The benefits of combining interventions

- If A, B & C each block 15% of transmission, 2 or 3 together give much more than 30% or 45% drop in attack rate.
- *e.g.* reducing transmission by 45% might reduce attack rates by 80%.
- But only if interventions do not 'overlap'.



for R_0=2

Combining interventions: example results for R_0=2

- Results are indicative of magnitude of effect, not precise predictions (too many uncertainties).
- Some interventions reduce *peak* attack rates better than others.
- Vaccine has both protective and therapeutic efficacy.

AV treatment	PEP	School closure	Vaccination coverage	Vaccine efficacy	Min AV stockpile	% drop in attack rate	% drop in peak daily attack rate
+	-	-	-	-	20%	4%	5%
+	+	-	-	-	59%	32%	44%
+	-	+	-	-	25%	[illegible]	[illegible]
+	+	+	-	-	47%	45%	67%
+	-	-	20%	45%	24%	21%	31%
+	-	+	20%	45%	21%	[illegible]	[illegible]
+	-	+	20%	70%	19%	[illegible]	[illegible]
+	+	+	20%	45%	40%	52%	71%

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Need for a failsafe policy

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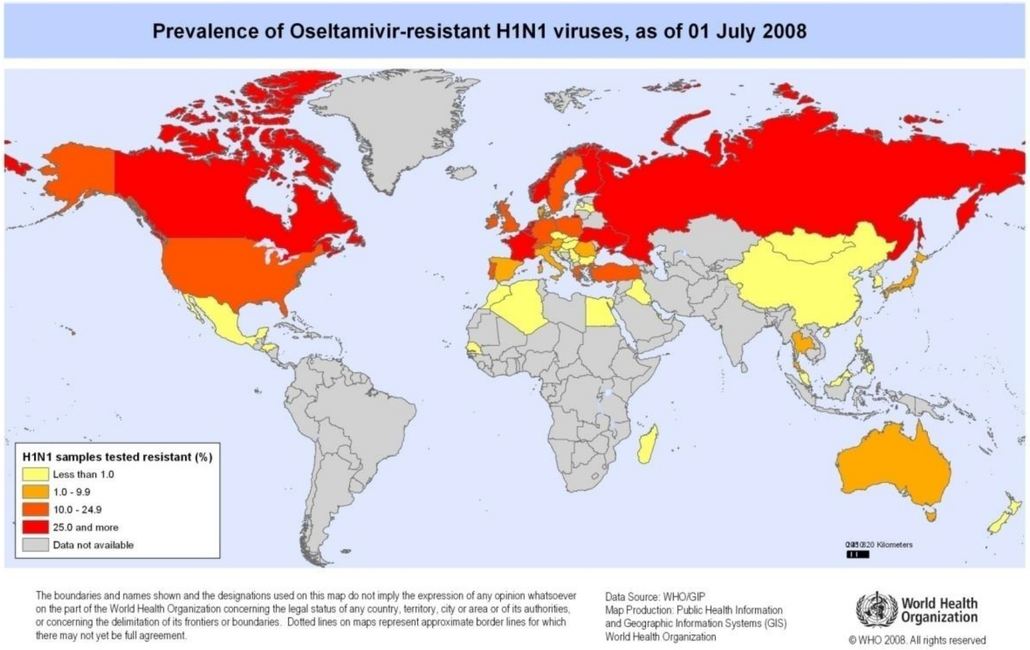
- New antiviral-resistant strains of H1N1 seasonal flu have spread round the world very rapidly in the last 18 months – hence diversified stockpile.

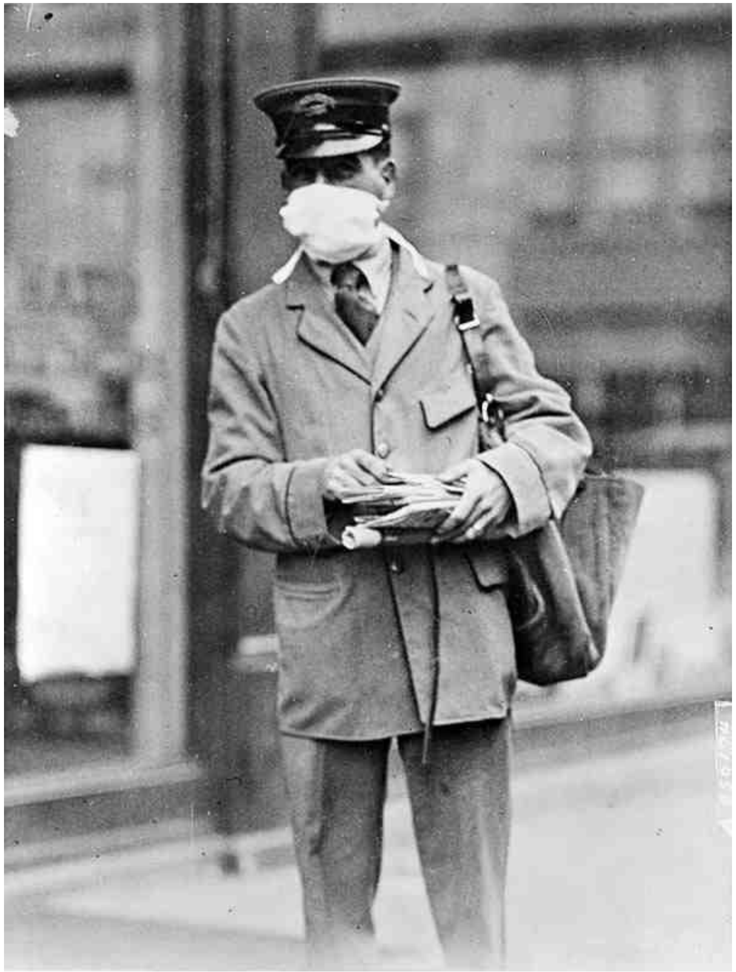
- If we stockpile H5N1, the pandemic may be caused by H7N2.

- Population compliance with public health measures uncertain.



Uncertainties

- Effectiveness of non-pharmaceutical interventions (e.g. masks) – ongoing studies and analysis of historical epidemics.
- Better estimates of AV and vaccine efficacy.
- Better understanding of transmission.
- Lethality of the next pandemic.
- ...



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Summary

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- Containment at source requires early detection of a cluster, very rapid and intense response.
- Travel restrictions need to stop 99%+ of travel to have substantial effect.
- Can expect 1/3 of population or more to become sick over 8-12 weeks of a pandemic.
- Local epidemics more ‘peaky’ that national averages – absenteeism might reach 15% in worst week (more with school closure).
- Combining non-overlapping interventions has a higher impact than the sum of the individual impacts.
- Layering multiple interventions also gives highest impact, most failsafe policy.
- Still many uncertainties – may be reduced with new analyses/studies, but will still need rapid data collection and analysis in a pandemic.