Modelling Infectious Diseases to Inform Health Policy

Peter G Grove

Department of Health

The impact of infectious diseases is of major importance for the work of the Department of Health.

DH Department of Health

"Plague" by Arnold Böcklin.

Including...

Immunisation

&

Pandemic influenza.

Immunisation

NHS

Vaccines used in the routine immunisation schedule 2013/14

When to immunise	Diseases protected against	Product reference	Vaccine given
Two months old	Diphtheria, tetanus, pertussis (whooping cough), polio and *Haemophilus influenzae* type b (Hib)		**Pediacel** (DTaP/IPV/Hib)
	Pneumococcal disease		**Prevenar 13** (PCV)
	Rotavirus		**Rotarix** (Rotavirus)
Three months old	Diphtheria, tetanus, pertussis, polio and Hib		**Pediacel** (DTaP/IPV/Hib)
	Meningococcal group C disease (MenC)		**NeisVac-C** or **Menjugate** (Men C)
	Rotavirus		**Rotarix** (Rotavirus)
Four months old	Diphtheria, tetanus, pertussis, polio and Hib		**Pediacel** (DTaP/IPV/Hib)
	Pneumococcal disease		**Prevenar 13** (PCV)
Between 12 and 13 months old – within a month of the first birthday	Hib/MenC		**Menitorix** (Hib/MenC)
	Pneumococcal disease		**Prevenar 13** (PCV)
	Measles, mumps and rubella (German measles)		**Priorix** or **MMR VaxPRO** (MMR)
Two and three years old	Influenza		**Fluenz** (Flu nasal spray) (annual) (if Fluenz unsuitable, use inactivated flu vaccine)
Three years four months old or soon after	Diphtheria, tetanus, pertussis and polio		**Repevax** (dTaP/IPV) or **Infanrix-IPV** (DTaP/IPV)
	Measles, mumps and rubella		**Priorix** or **MMR VaxPRO** (MMR) (check first dose has been given)
Girls aged 12 to 13 years old	Cervical cancer caused by human papillomavirus types 16 and 18 (and genital warts caused by types 6 and 11)		**Gardasil** (HPV)
Around 14 years old	Tetanus, diphtheria and polio		**Revaxis** (Td/IPV), and check MMR status
	MenC		**Meningitec**, **Menjugate** or **NeisVac-C** (MenC)
65 years old	Pneumococcal disease		**Pneumovax II** (PPV Pneumococcal polysaccharide vaccine)
65 years of age and older	Influenza		Flu injection (annual)
70 years old	Shingles		**Zostavax** (Shingles)


Pediacel


Prevenar 13

Rotarix


Menjugate*


NeisVac-C*


Menitorix


Priorix*


MMR VaxPRO*


Repevax*


Infanrix-IPV*


Gardasil


Revaxis


Fluenz


Zostavax

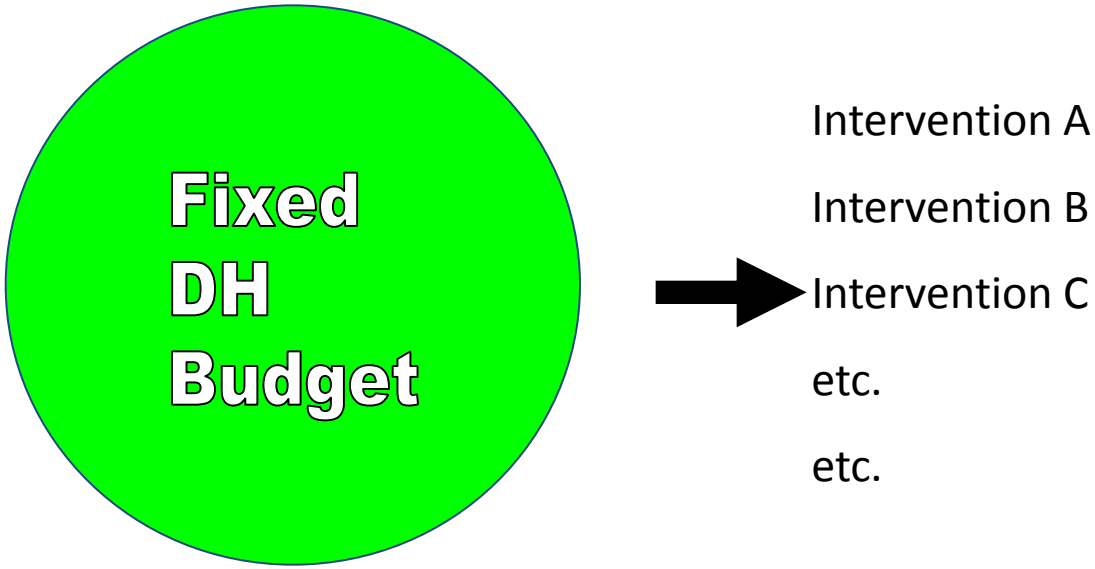
*NB Where a vaccine is manufactured by more than one supplier, it may, on occasion be necessary to substitute an alternative brand.

Influenza vaccine is only free to children aged two and three years. Hep B and PPV are also chargeable.
All other vaccines listed above are available free of charge at **www.ImmForm.dh.gov.uk**

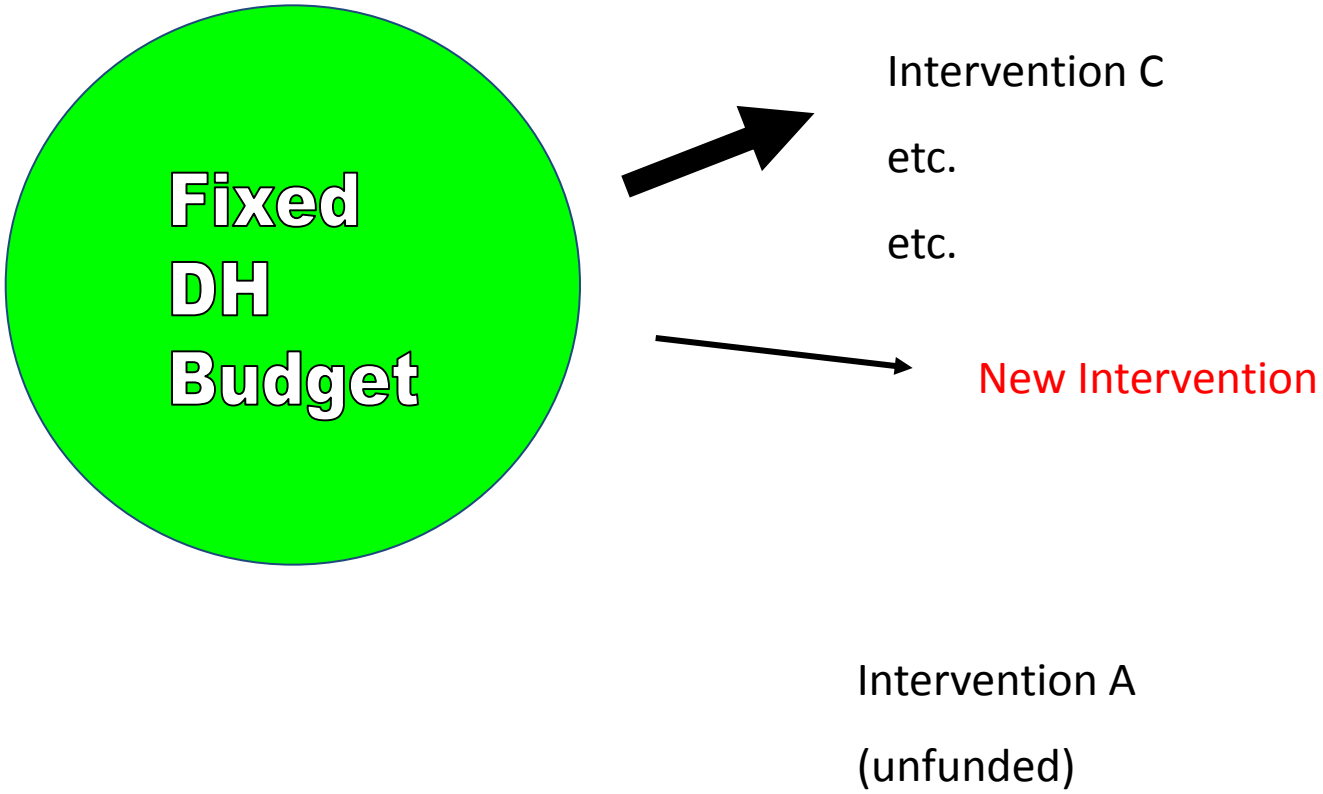
immunisation
The safest way to protect children and adults

NHS
Immunisation Information

Displacement



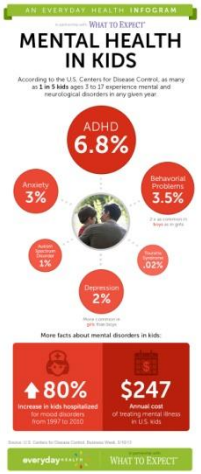
Displacement



Increasing Health Benefit

- New intervention must produce more health benefit than old per £ spent.
- NICE have evolved criteria of £20,000 per QALY.
- If the new intervention costs more than this the displaced treatment would probably have produced more QALYS per £ of NHS funding.
- Hence the displacement would have reduced the Health of the population (measured in QALYs).

It matters! - Men B ~ £5 per dose



In principle easy...

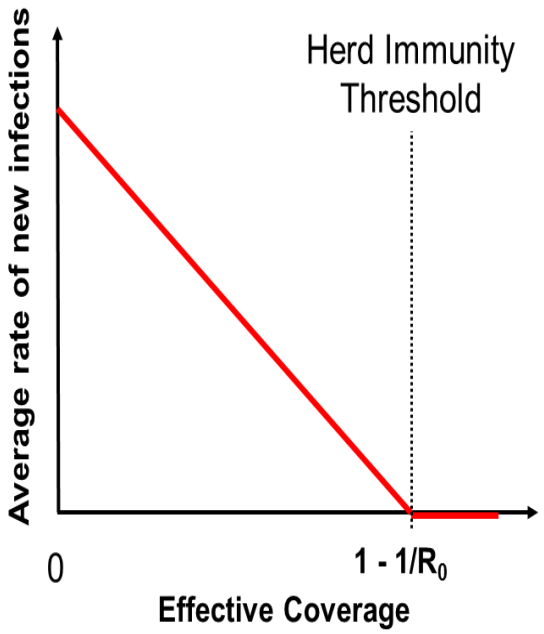
- Calculate impact of immunisation in ‘natural units’ e.g. lives saved.
- Calculate QALY gain
- Calculate cost
- Does it cost more than £20,000 per QALY.
- If so increases Net Health Benefit.

Modelling

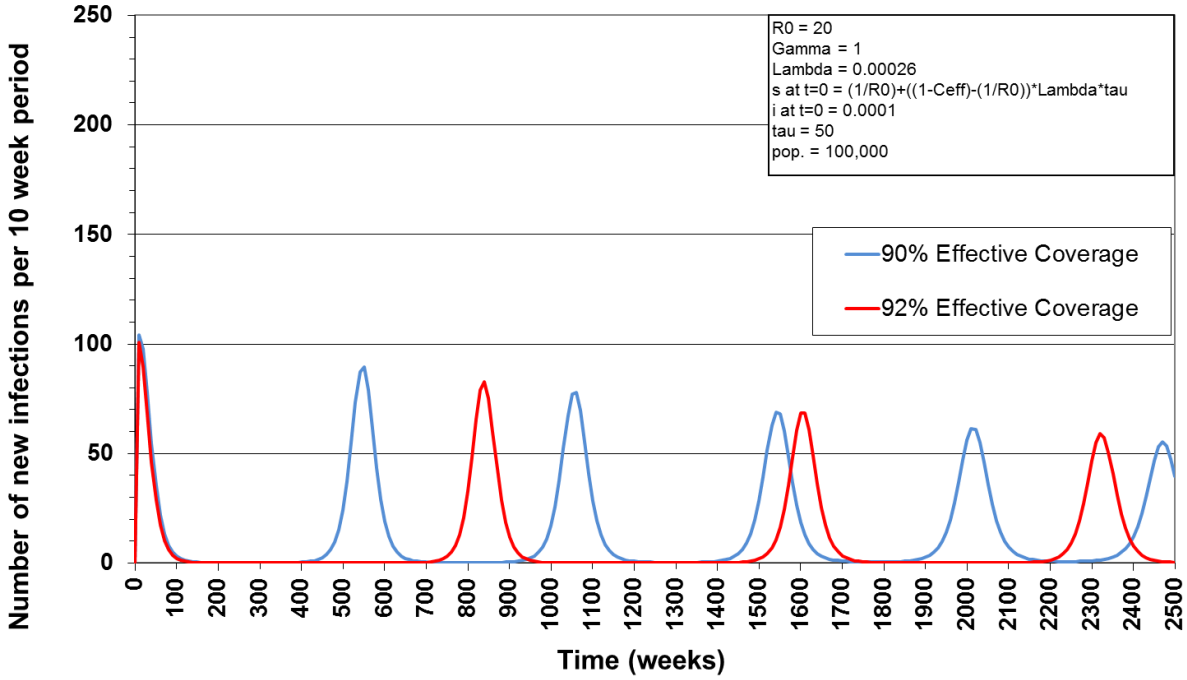
- Many infectious diseases have complicated behaviours in the community.
- Impact and cost-effectiveness of immunisation require sophisticated dynamical modelling.
- Difficult as non-linear, potentially chaotic systems.

Non-linearity – non-equilibrium important

On Average

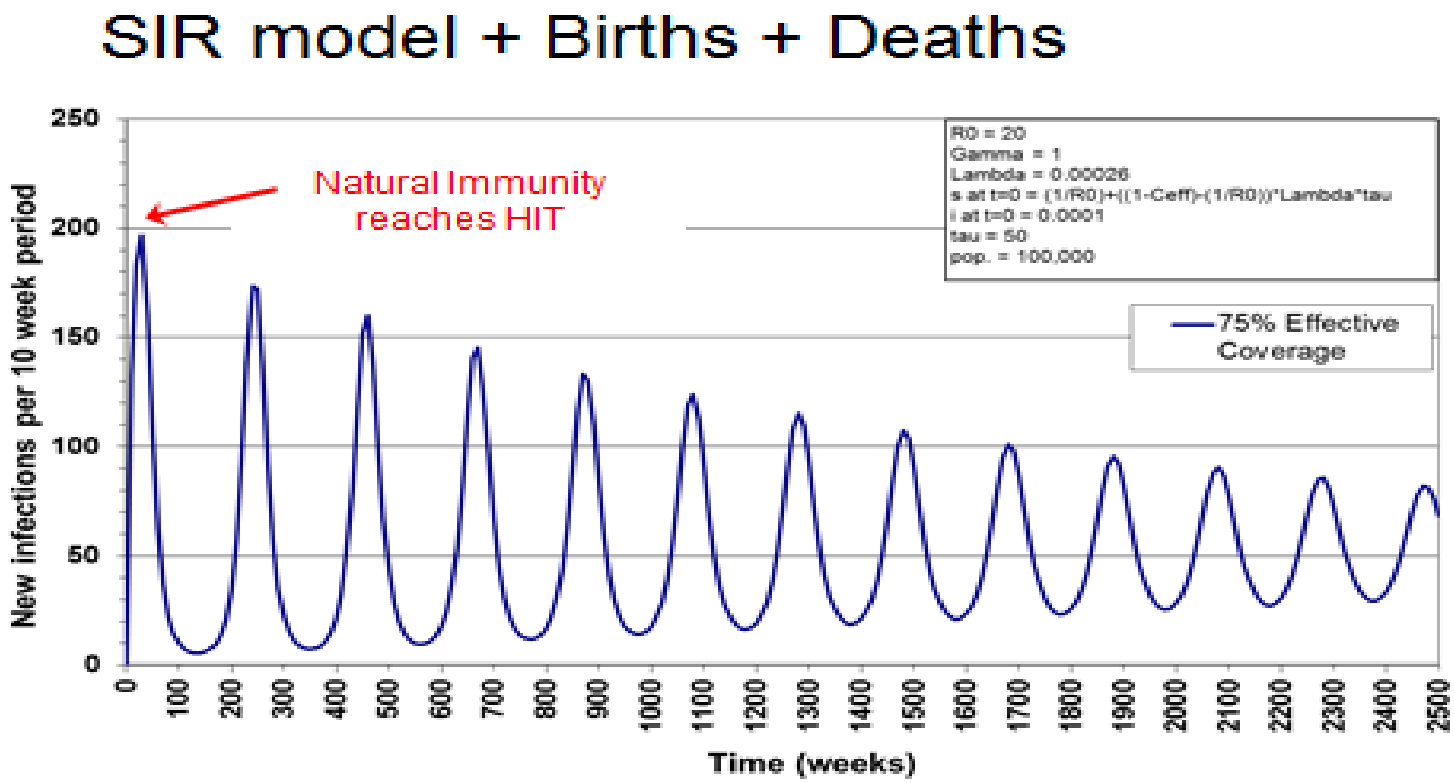


Real world



Even if approximately linear unlikely to be at equilibrium

(-until it gets another random kick.)



Mumps

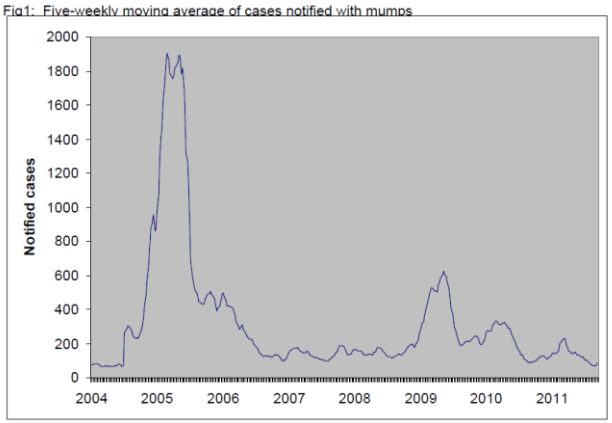
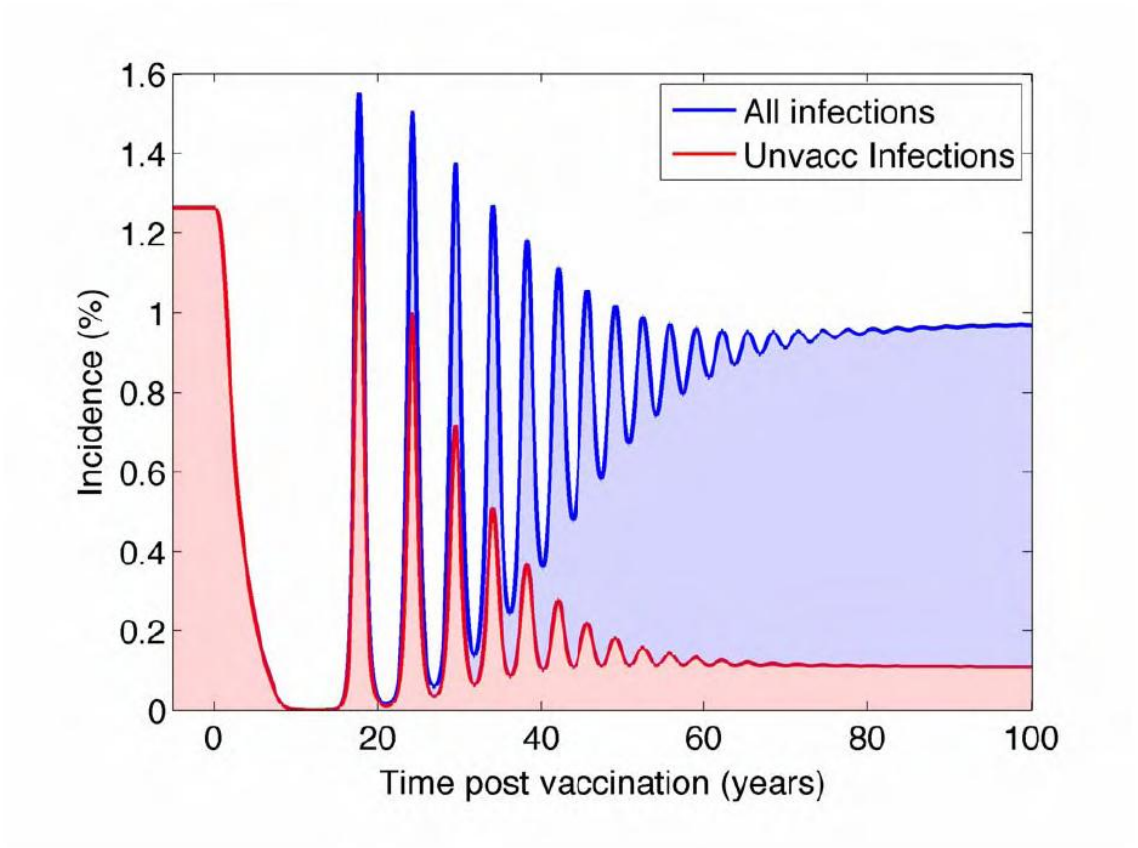
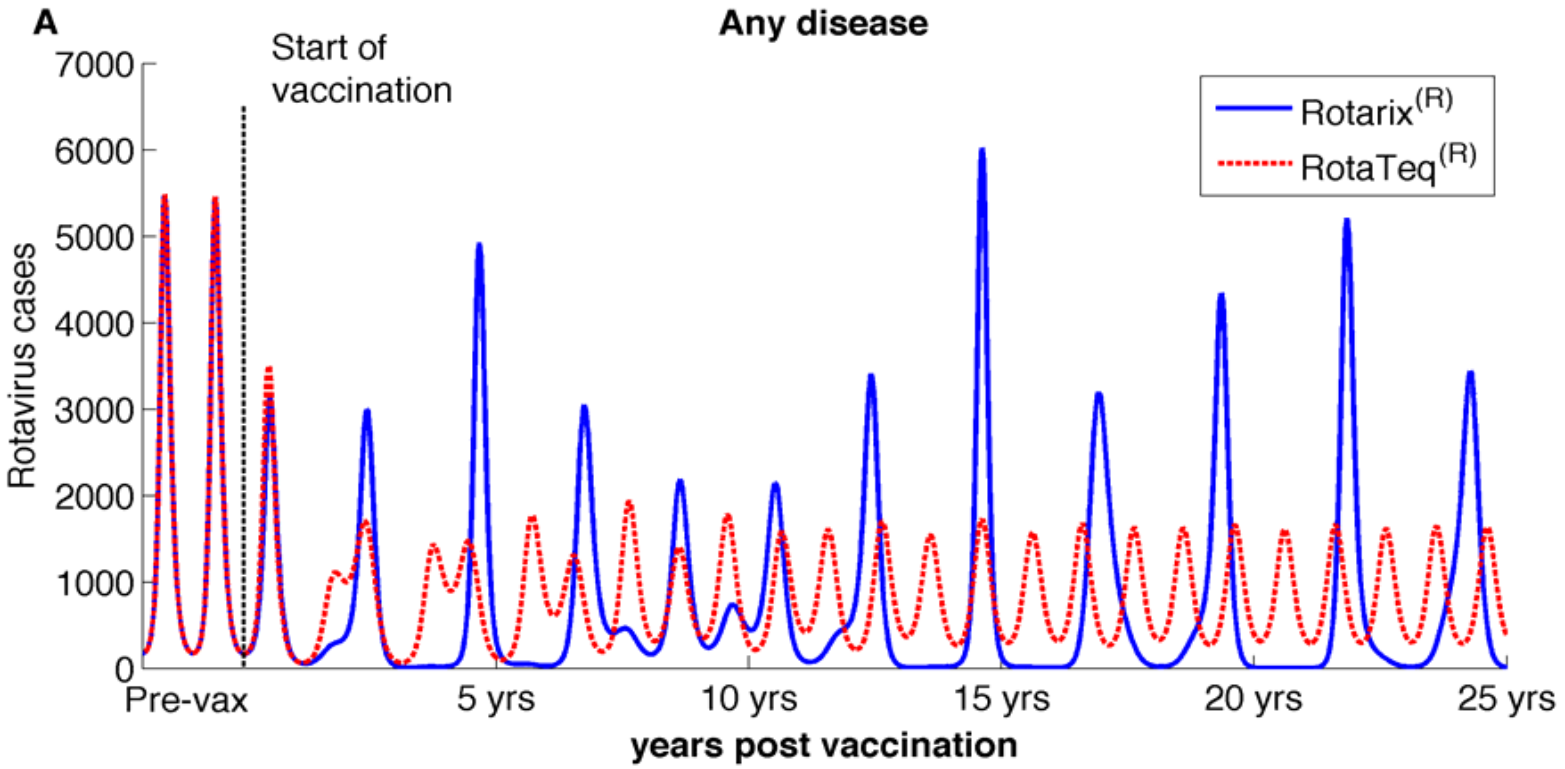


Fig1: Five-weekly moving average of cases notified with mumps
Notified cases
2000
1800
1600
1400
1200
1000
800
600
400
200
0
2004
2005
2006
2007
2008
2009
2010
2011

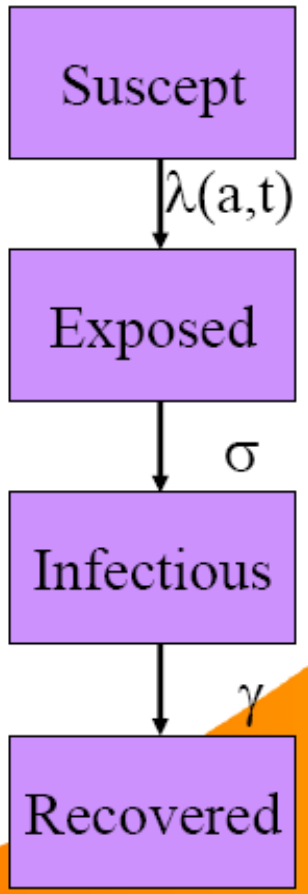

All infections
Unvacc Infections
Incidence (%)
1.6
1.4
1.2
1
0.8
0.6
0.4
0.2
0
0
20
40
60
80
100
Time post vaccination (years)

Rotavirus


A
Any disease
Start of vaccination
Rotarix(R)
RotaTeq(R)
Rotavirus cases
7000
6000
5000
4000
3000
2000
1000
0
Pre-vax
5 yrs
10 yrs
15 yrs
20 yrs
25 yrs
years post vaccination

Methods:
model structure

- **Age-structured transmission dynamic model**
- **Single-place or 'patch'**
- **Matrix SEIR**
- **Deterministic or Stochastic**



$SEIR$ model

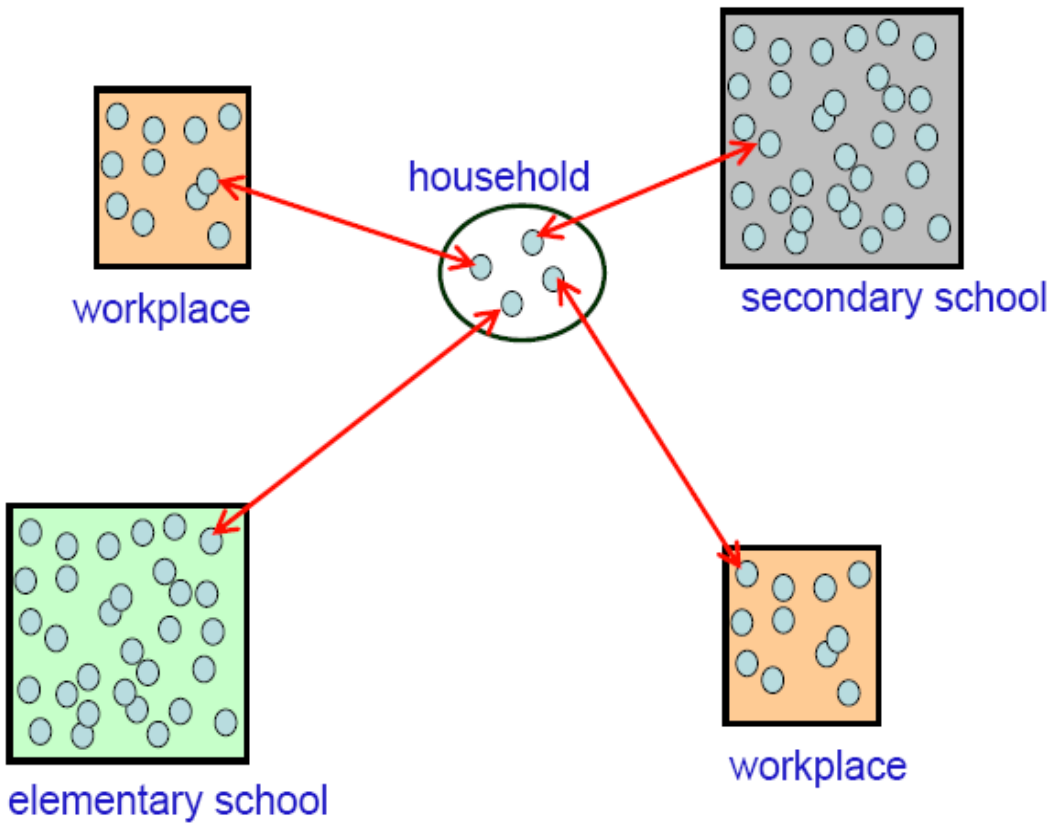
$$\begin{aligned}
\frac{dS}{dt} &= \mu(N[1-p]-S) - \frac{\beta IS}{N} \\
\frac{dE}{dt} &= \frac{\beta IS}{N} - (\mu+\sigma)E \\
\frac{dI}{dt} &= \sigma E - (\mu+\gamma)I \\
\frac{dR}{dt} &= \gamma I - \mu R,
\end{aligned}$$

$$\lambda(a,t) = \int \beta(a,a')\, I(a',t)\, da'$$

$$\lambda_i(t) = \sum_j \beta_{ij}\, I_j(t)$$

Imperial College London

‘Place’ model



Typical Problems

- Naive averages not meaningful.
- Complicated - coding errors inevitable
- Extreme sensitivity to initial conditions.
- Extreme sensitivity to parameters.
- Extreme sensitivity to structural assumptions.
- Limited horizon for simulation.

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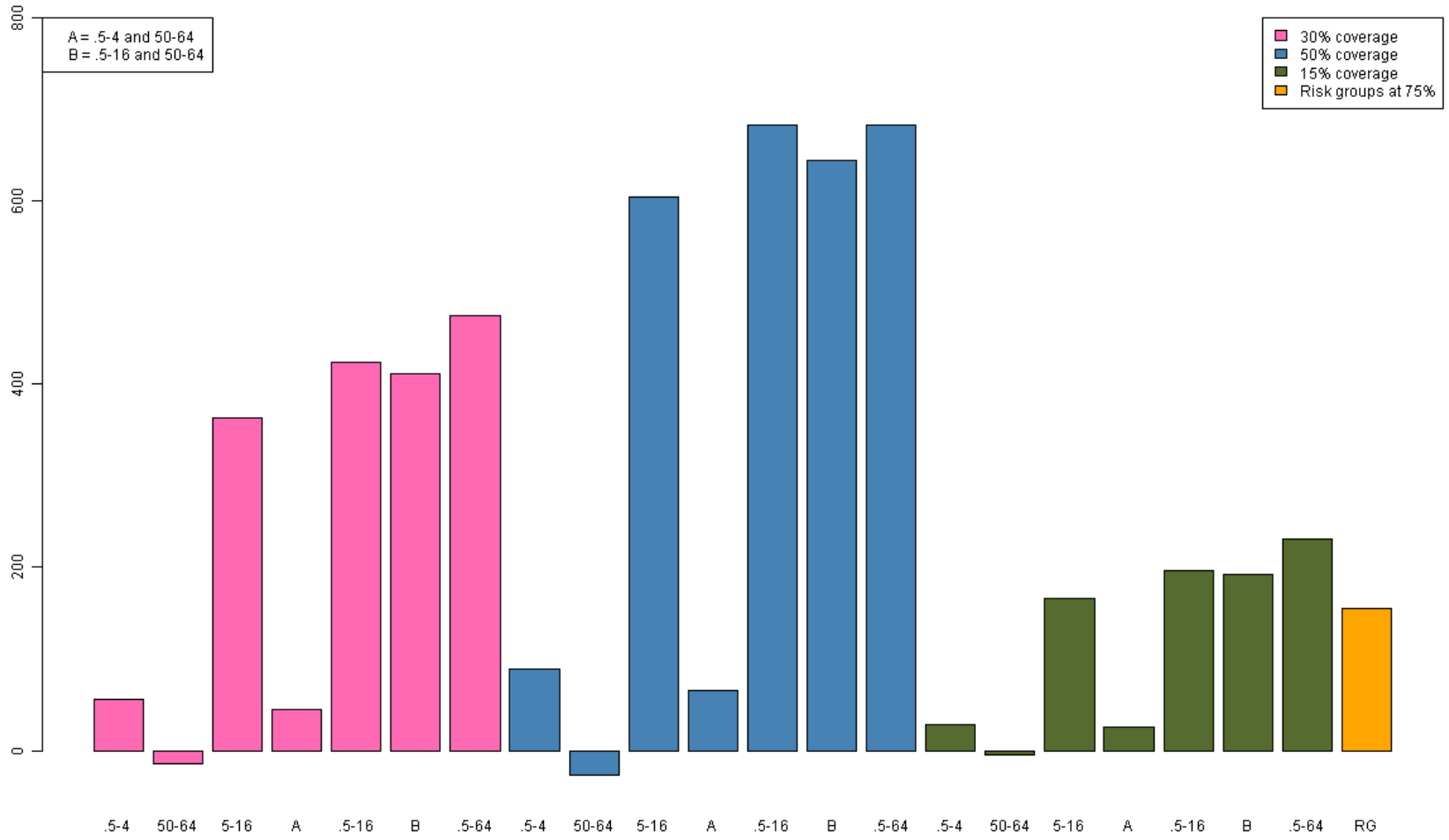
Not enough! – So need…

- Multiple models – different structures, different approaches.
- More than one group.
- At least ‘official view’ and ‘official opposition’.
- Method of defining and communication of both consensus *and* disagreement.

Immunisation

- First opinion from PHE.
- Second opinion from University of Warwick.
- Manufacturers models
- Considered by JCVI

Estimated net benefit (£m) of extending vaccination to different low-risk age groups (each bar), by differing levels of coverage in the low risk groups (different colours).



Recent Programmes

- HPV
- Zoster
- Rotavirus
- PCV13
- Childhood Influenza

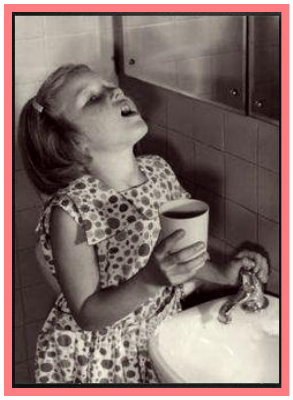
Pandemic Preparedness

Influenza is mainly a disease of birds

Which sometimes crosses over into humans…

Directly or Indirectly….

Circulating influenza strains in humans and pandemics in 20th Century



1918: "Spanish Flu"

40-50 million deaths

1957: "Asian Flu"

1 million deaths

1968: "Hong Kong Flu"

1 million deaths

H3N2

H2N2

H1N1

H1N1

1920 **1940** **1960** **1980** **2000**

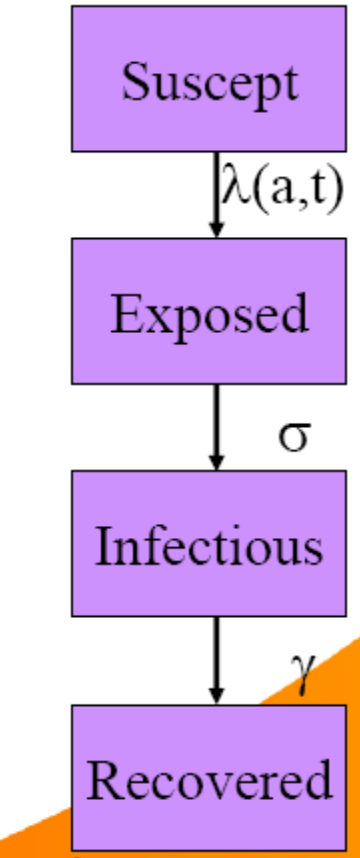
Nick Phin - HPA

Pandemic Preparedness

The pre-pandemic role of modelling is to map out the range of possible risks and to suggest which responses are robust over the range of uncertainty.

Methods:
model structure

- **Age-structured transmission dynamic model**
- **Population-based**
- **Deterministic or Stochastic**
- **Matrix SEIR**



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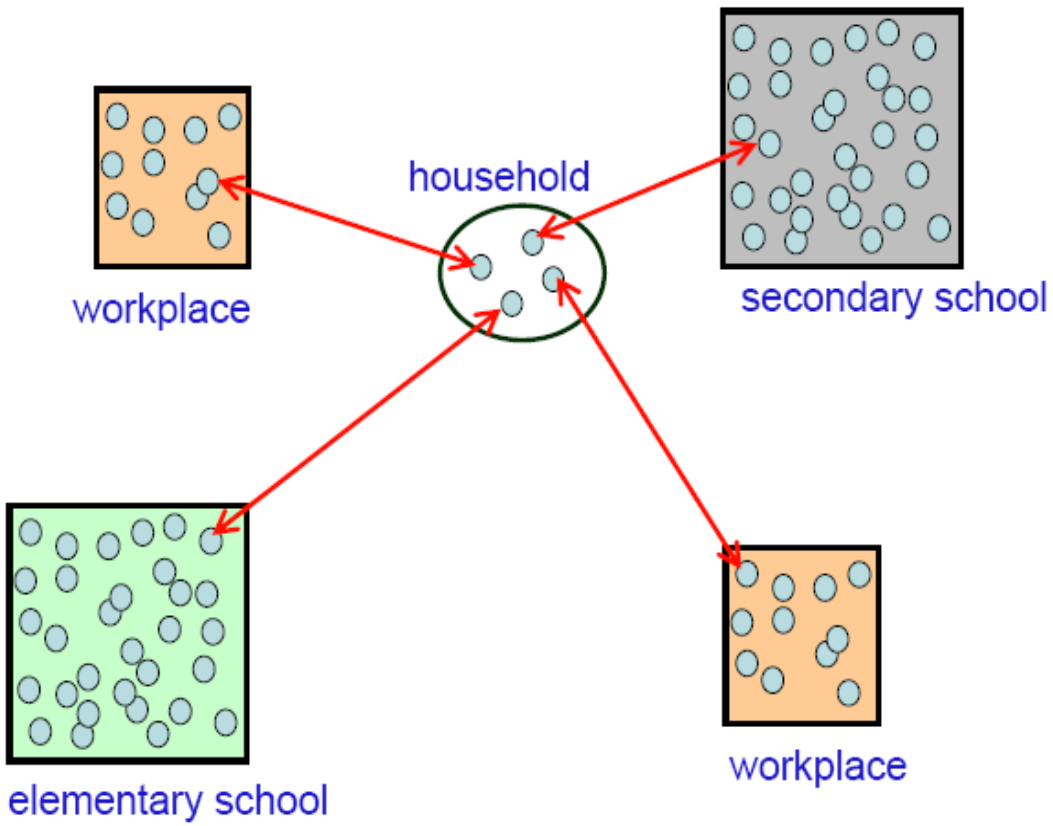


UK Advised Planning Assumptions

- Up to 50% of the population ill (with serological rates up to 80-85%).
- Of which, from 10% up to 25% are expected to have complications, half of these bateriological. (With possibly as little a 35% overlap between the 'at risk groups' and those who actually get complications.)
- Peak illness rates of 10 - 12% (in new cases per week - of the population) in the peak fortnight.
- Absences rates for illness reach 15-20% in the peak weeks (at a 50% overall attack rate, assuming an average 7 working day absence for those without complications, 10 for those with, and some allowance for those at home caring for children.)
- Case hospitalisation demand rates in the range 0.55% to 4% with an average six day length of stay.
  - but, of which 25% would, if the capacity existed, require intensive care for 10 days.
- Case fatality rates in the range 0.4% to 2.5%.

- Antiviral Stockpile: Two different antivirals ~50% population coverage.
- Antibiotic reserve.
- H5N1 pre-pandemic vaccine.
- Advanced purchase agreement for Pandemic Vaccine.

Real Time Modelling

Role of modelling

- How bad is it going to be?
  - Cases
  - Hospitalisations
  - Deaths
- When?
  - Peak demand
  - logistics
- Changing policy
  - Restricting antiviral usage
  - Closing schools.

Pandemic Influenza Scientific Advisory Group(SPI): Subgroup on Modelling

‘SPI-M’

Pandemic Groups

- Public Health England (HPA)
  - Infectious Disease Modelling (Dr Peter White).
  - Centre for Emergency Preparedness and Response (Professor Steve Leach)
- MRC Centre for Outbreak Analysis and Modelling, Imperial College London

  (Professor Neil Ferguson)
- LSHTM (Professor John Edmunds)
- University of Warwick (Professor Matt Keeling)
- HPAT Analytical Team
- Others (ICS)

Pandemic Influenza Scientific Advisory Group(SPI): Subgroup on Modelling

Modelling Summary

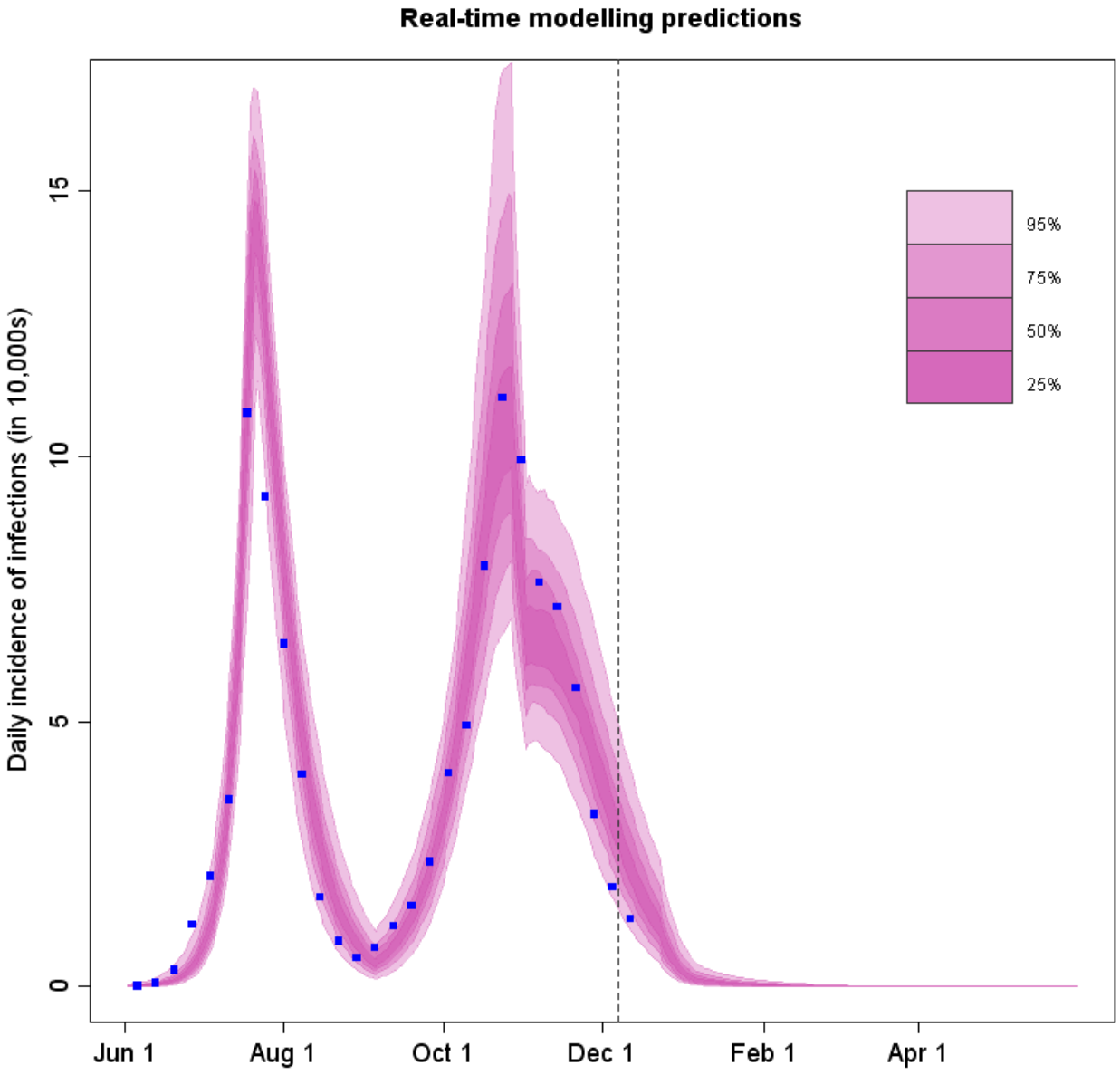
https://www.gov.uk/government/publications/spi-m-publish-updated-modelling-summary

RTM Discussion (2009)

- SPI-M-O
  - Met every week
  - Modelling carried out at HPA/Imperial College/DH
  - External review from LSHTM/Warwick University
- SAGE
- COBR

2009 Pandemic
Second Wave Forecasts
(mid September)

Predicted 2nd Wave Estimates vs Actual Counts (England)						
	Predicted 2nd Wave Lower Estimate	**Predicted 2nd Wave Higher Estimate**	**Predicted 2nd Wave Reasonable Worst Case**	**Actual 2nd Wave**		**Total:- 1st and 2nd Waves**
GP Consultations	270,000	800,000	1,300,000	299,081		687,147
Hospitalisations	5,900	16,800	29,300	17,390		
Critical Care Admissions	900	2,500	4,400	1,857		
Deaths	70	420	840	242		309



Source – HPA CfI

But…

- We were lucky. Many had some immunity, in most the disease was asymptomatic or very mild.

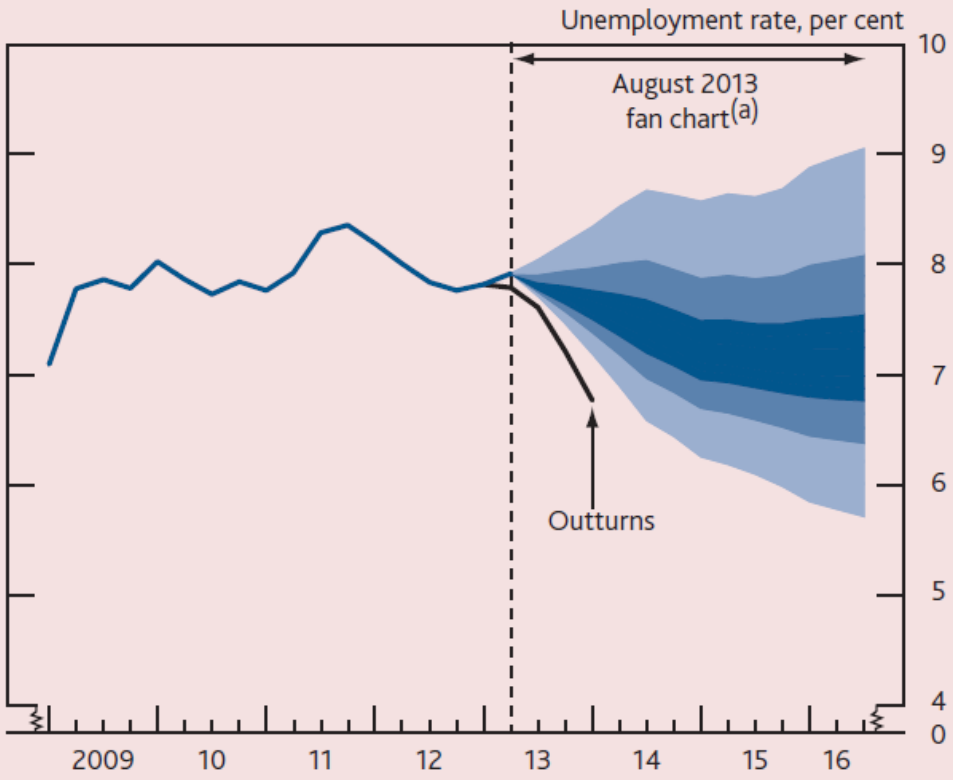
- Chance of a 20th Century style pandemic still ~ 1-3% per year. 25-50% people ill with 0.5% to 2.5% of those fatally so.

Conclusion

- Dynamical complex system modelling is essential to inform policy development in the Department of Health.
- Need for multiple views.
- Need to develop improved health economics approach to these complex systems and their complicated behaviours.
- Need to use complex system modelling more widely elsewhere in Government (note need for multiple views).

Chart C Unemployment has fallen far more quickly than expected

LFS unemployment rate outturn and projection in the August 2013 *Report*



(a) Based on constant interest rates of 0.5% and the assumption that the stock of purchased assets remained at £375 billion throughout the forecast period. See footnote to Chart 5.10 in the August 2013 *Report* for information on how to interpret the fan chart.

Lord Gus O'Donnell
Chairman, Frontier Economics
Former UK Cabinet Secretary

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