



Influenza A H1N1 (Swine flu)

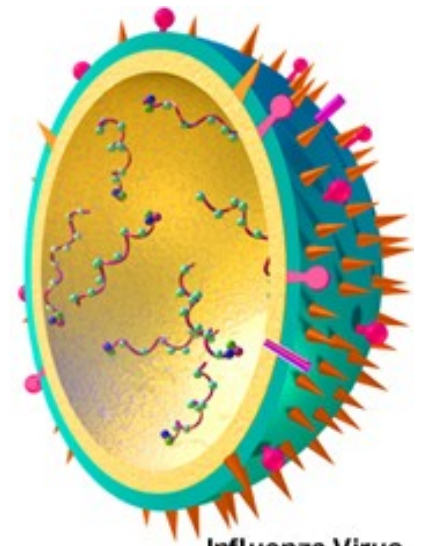
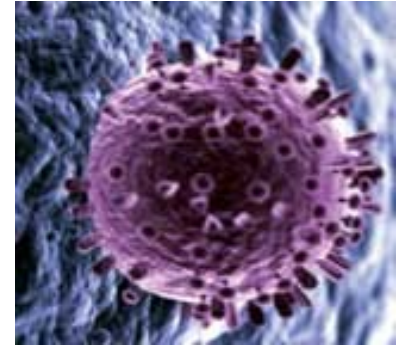
Virus, Disease, Epidemiology, Vaccination, Control

Dr. Noel McCarthy

Thames Valley Health Protection Unit – Oxfordshire

Virology

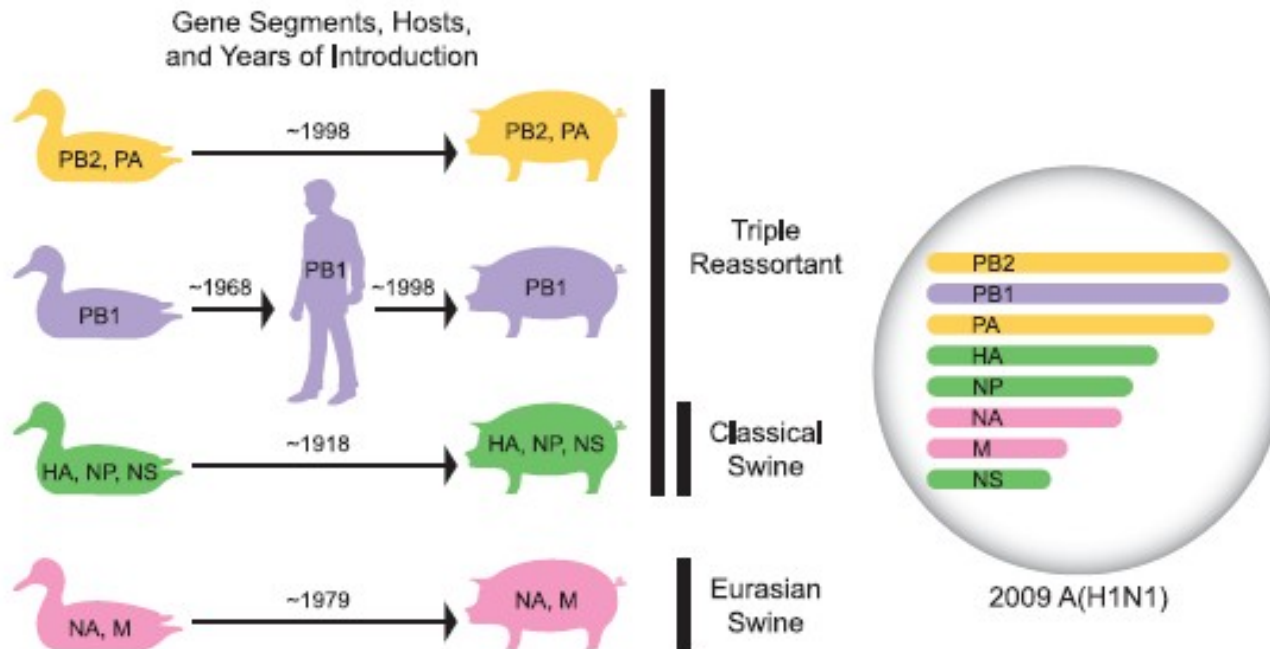
- **Influenza A**
 - **Haemagglutinin**
 - **Attachment of virus**
 - **Neuraminidase**
 - **Release and spread of virus**



Influenza Virus

Credit: NIAID

Current H1N1 (Swine)



Rebecca J. Garten, et al. Antigenic and Genetic Characteristics of Swine-Origin 2009 A(H1N1) Influenza Viruses Circulating in Humans. *Science* 325, 197 (2009).

Pandemic

- **“Antigenic shift”**
 - **New virus – to humans - for H and N parts**
- **Older humans?**
 - **Cross-reactive antibody**
 - **0% in children**
 - **6%--9% aged 18--64 years**
 - **33% aged >60 years.**
 - **Katz J et al. Serum Cross-Reactive Antibody Response to a Novel Influenza A (H1N1) Virus After Vaccination with Seasonal Influenza Vaccine. MMWR, May 22, 2009 / 58(19);521-524**

Influenza-typical symptoms

- **Rapid onset**
- **Fever**
- **Cough**

- **Malaise (80%)**
- **Headache (65%)**
- **Loss of appetite (60%)**
- **Coryza (60%)**
 - Runny nose
 - Sneezing
- **Muscle pains (53%)**
- **Sore throat (50%)**

Symptoms in UK students

FIGURE 3

Symptoms reported by confirmed cases of influenza A(H1N1)v by age group, boarding school South East England, May-June 2009 (n=63)

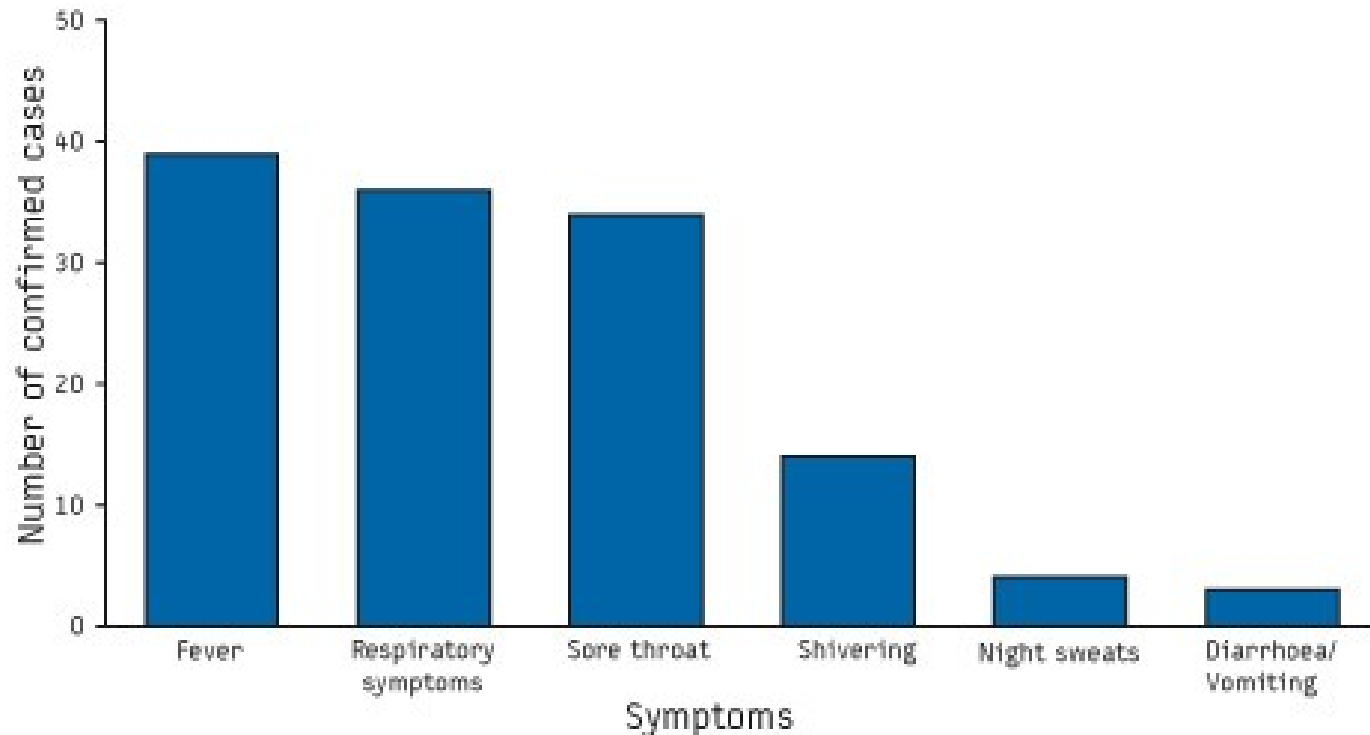


TABLE 2

Distribution of symptoms among cases of influenza A(H1N1)v infection, as of 8 June 2009, EU+3 countries (n=371)

	Number	Percentage
At least one symptom	344	93
GENERAL	317	85
Fever or history of fever	290	78
Headache	160	43
Muscle pain	145	39
Joint pain	79	21
RESPIRATORY	295	80
Dry cough	188	51
Productive cough	60	16
Sore throat	172	46
Runny nose	120	32
Sneezing	72	19
Shortness of breath	34	9
GASTRO INTESTINAL	34	24
Diarrhoea	45	12
Vomiting	49	13
Nausea	57	15
OTHERS	146	39
Conjunctivitis	21	6
Nose bleeding	9	2
Altered consciousness	2	1
others (various)	117	32

Symptoms across EU

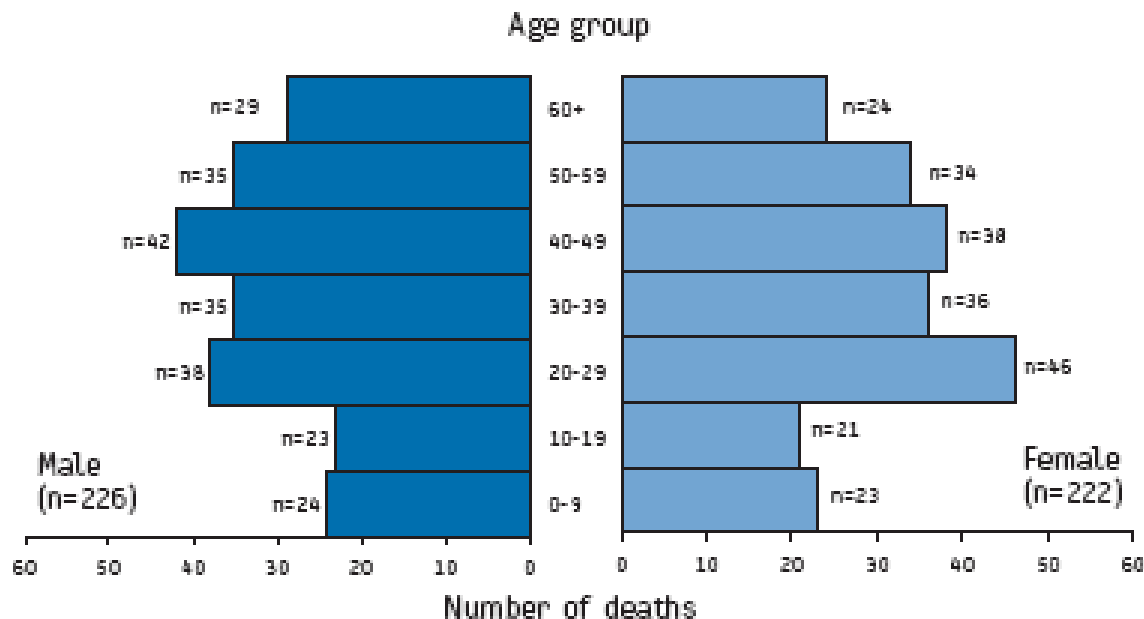
ECDC working group on influenza A(H1N1)v ■
 Preliminary analysis of influenza A(H1N1)v individual and aggregated case reports from EU and EFTA countries. Eurosurveillance, Volume 14, Issue 23, 11 June 2009

Greater severity

- **Usual risk factors**
- **Pregnancy seems important**
- **Older age good rather than bad?**
 - **Less marked in Australia and Canada**
- **No data on early clinical warning signs**
- **Why severe sometimes?**
 - **Unknown – severe influenza or secondary infections**
 -

Who dies (1)?

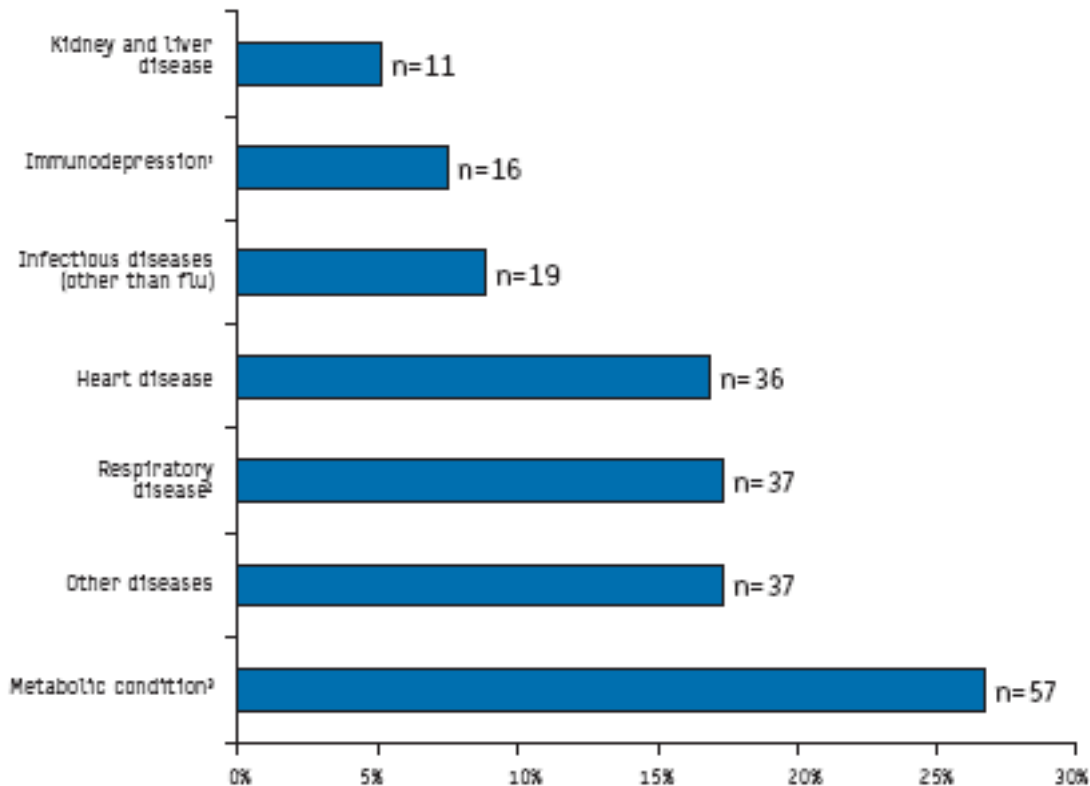
Deaths associated with pandemic H1N1 influenza worldwide by age and sex, as of 16 July 2009* (n=448)



* Individual data, except from Mexico where aggregated data originate from the Ministry of Health.

Who dies (2)?

Underlying diseases in pandemic H1N1 influenza
2009-associated deaths worldwide* as of 16 July 2009 (213
diseases documented in 193 fatal cases)



¹Including tumour (n=5), transplantation (n=2) and auto-immune disease (n=3)

²Including asthma (n=8)

³Including obesity (n=7), diabetes (n=5), obesity and diabetes (n=1) and obesity and/or diabetes (n=41 for whom only aggregated data were available)

Pregnancy

UK National guidance – uncertain.

USA – CDC – 8% of deaths in pregnant women (1% of population)

Conclude

Some increase

Especially third trimester

Perhaps 4-5 fold increased risk

L Vaillant. Epidemiology of fatal cases associated with pandemic H1N1 influenza 2009. Eurosurveillance. 20 August 2009.

* Individual data, except from Mexico where aggregated data originated from the Ministry of Health.

How many die (of those with flu)

- **New Zealand 1/20,000**

M G Baker. Pandemic influenza A(H1N1)v in New Zealand: the experience from April to August 2009. Eurosurveillance, Volume 14, Issue 34, 27 August 2009

- **International study 4/1,000**

- Probably an overestimate – deaths counted but recovered cases probably missed

L Vaillant. Epidemiology of fatal cases associated with pandemic H1N1 influenza 2009. Eurosurveillance. 20 August 2009.

Very rough estimate: 1/5,000 cases die

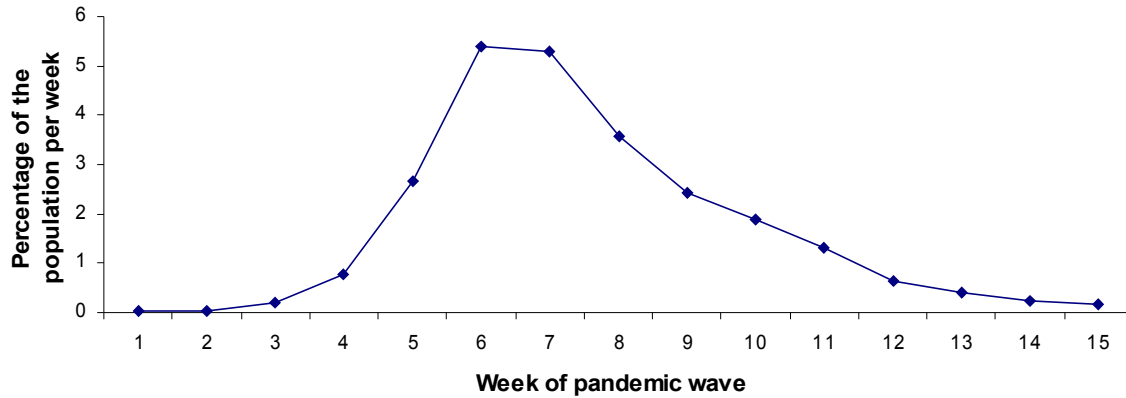
ECDC – UK planning assumptions < 1/1000

How much and when?

- **Models predicted in the order of 30% over a wave (i.e. over this winter)**
- **New Zealand 11% - in their winter**

M G Baker. Pandemic influenza A(H1N1)v in New Zealand: the experience from April to August 2009. *Eurosurveillance*, Volume 14, Issue 34, 27 August 2009
- **UK planning assumptions 20-30%**
 - **Probably < 20%**

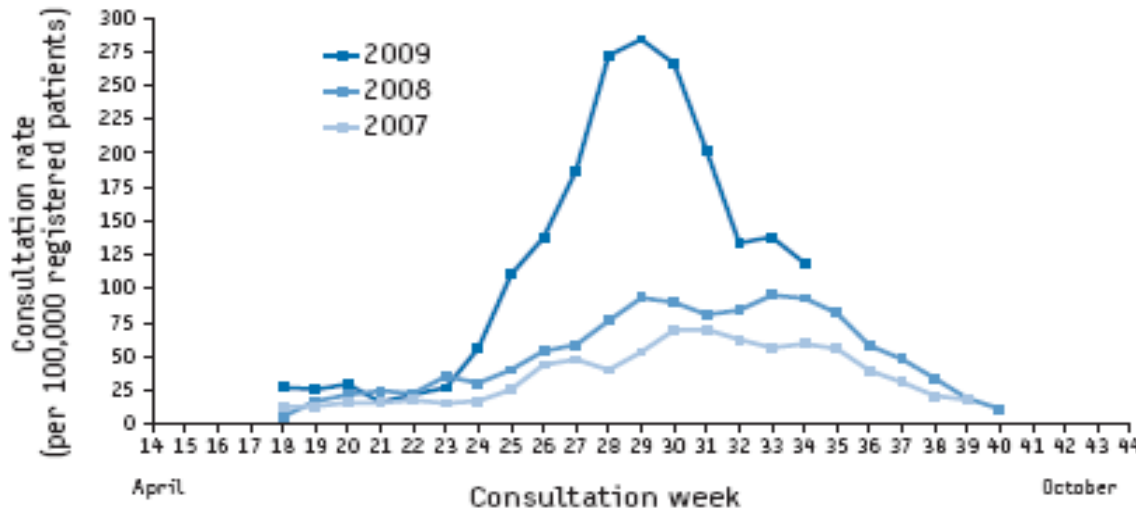
**Most rapid plausible time course for pandemic flu wave
(assuming it affects 25% overall)**



When?

Expect a main peak over about 3 months this winter.

Weekly rate of ILI per 100,000 registered population, all ages, New Zealand, 2007–2009



Possibly severe flu seasons for a few years

M G Baker. Pandemic influenza A(H1N1)v in New Zealand: the experience from April to August 2009. Eurosurveillance, Volume 14, Issue 34, 27 August 2009

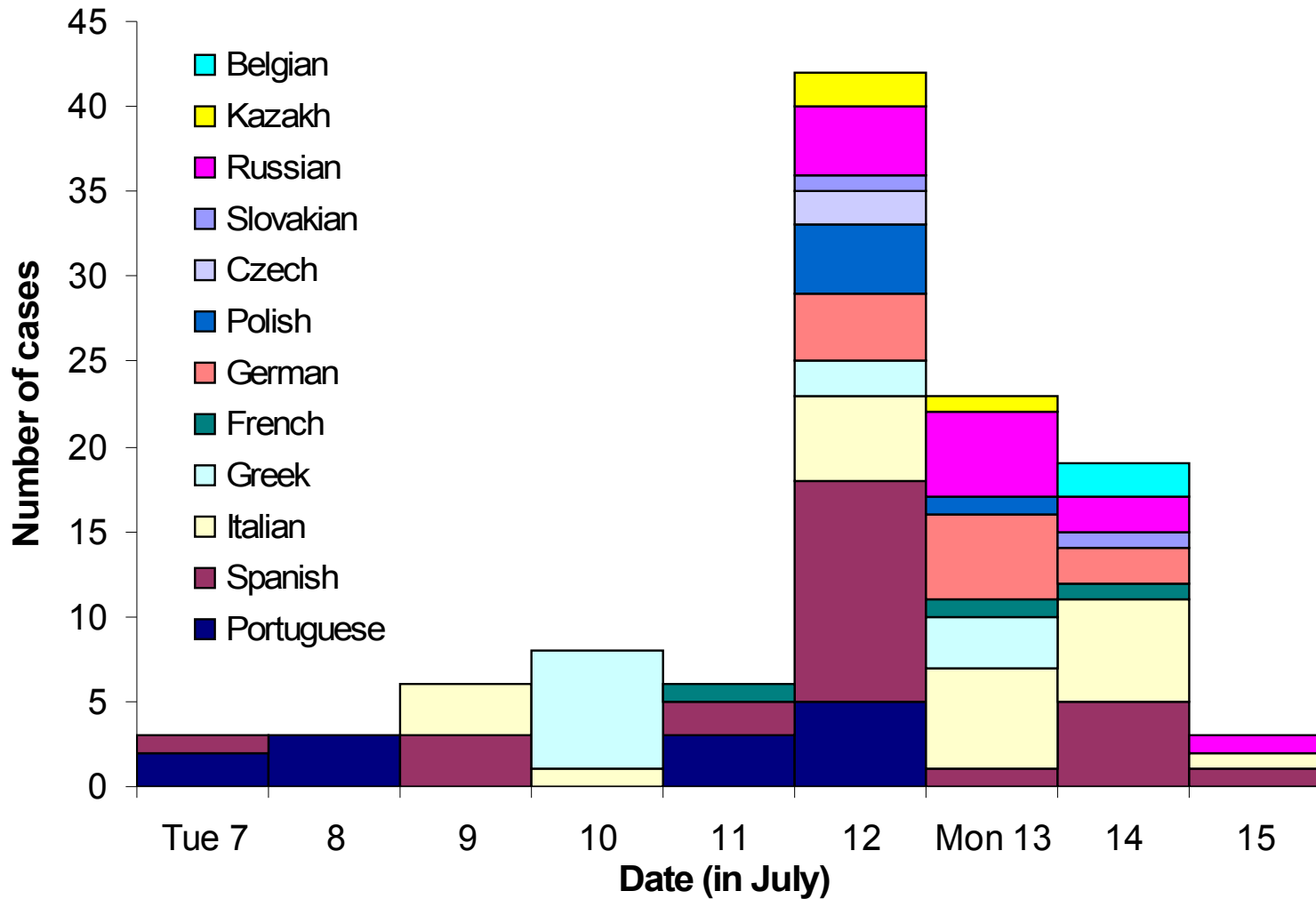
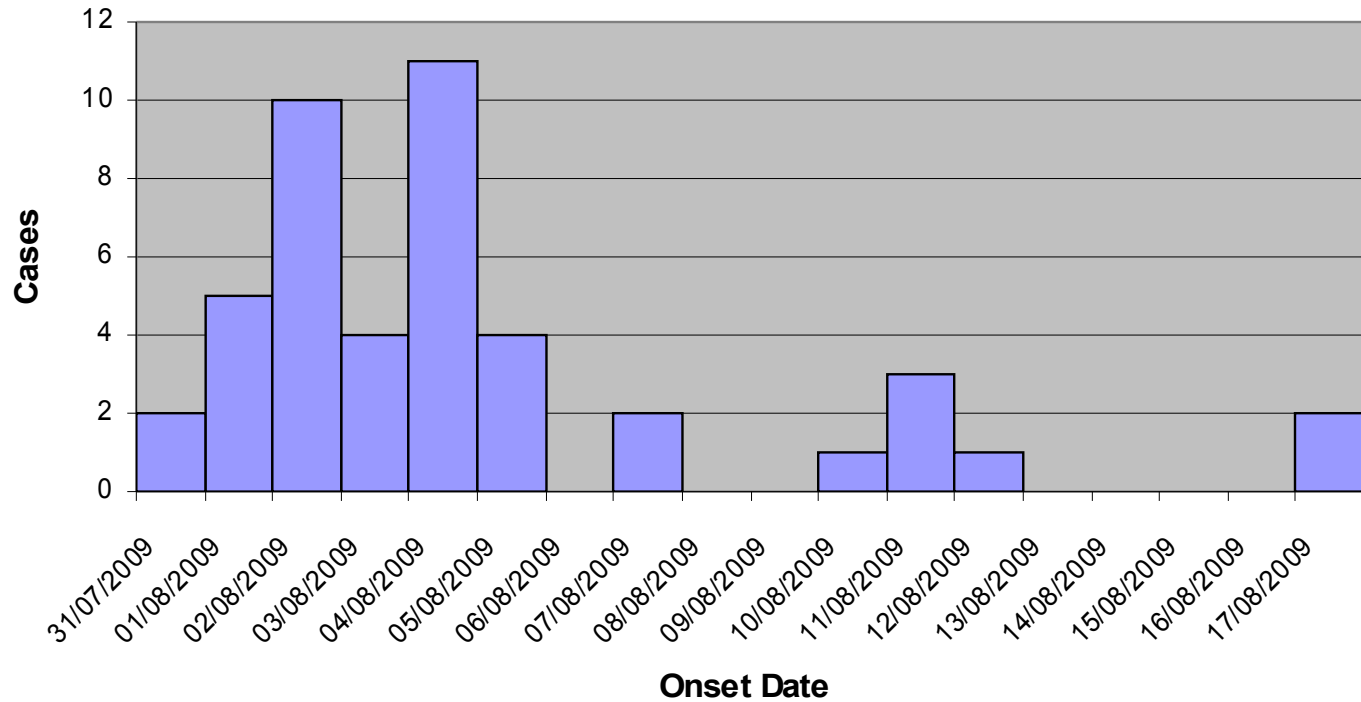


Figure. Date of diagnosis by nationality. Residential Language School, Oxford, 2009 (n=114).

Epidemic Curve of Swine Flu Second wave Language School Jul-Aug 2009



Risk factors

- **Residential more than educational**
- **“Transmitting events”**
 - **The bus trip to the cup final**
 - **Those whom we speak to on the bus**
 - **The social event after it**

H1N1 vaccines

Two H1N1 vaccines

Prepandrix (GSK)

- **Split virion**
- **Inactivated**
- **Egg based production**
- **Adjuvanted (AS03)**
- **Contains thiomersal**

**Multi dose vial 2.5ml suspension
and
2.5ml adjuvant – reconstitute to
5mls
0.5ml dose (3.75mcg)**

Celvapan (Baxter)

- **Whole virus vaccine**
- **Inactivated**
- **Vero cell production**
- **Not adjuvanted**

**Multi dose vials 5ml suspension
0.5ml dose (7.5mcg)**

Celvapan not licensed – name not confirmed
Prepandrix licensing report last week (23 Sept)

Prepandrix (GSK)

Each Prepandrix box contains

- **1 box (50 multidose vials) of vaccine antigen suspension**
- **2 boxes (25 vials each) of adjuvant**
- **Antigen & adjuvant must be mixed together before administration**
- **Each 5ml vial for administration contains 10 doses**
- **Each pack should provide 500 doses**
- **Pack size: 260mm x 113mm x 97mm**

Celvapan (Baxter)

Each box will contain 20 multidose vials

- **Each vial contains 10 doses of vaccine antigen suspension**
- **Celvapan does *not* require reconstitution**
- **Box size – 206mm x 166mm x 55mm**

Vaccine stability data

Prepandrix (GSK)

Once reconstituted the vaccine should be used within 24 hours

Celvapan (Baxter)

Vial to be used in one session or within 3 hours, whichever is less

Inactivated vaccines

Partially simulate immune aspects of infection

- **Don't cause a real infection**
- **Vaccine has sufficient antigen to produce a reaction**
- **Antibody levels and protection wane**
- **Repeated doses to compensate**
- **Boost antibody levels**
- **Provide more refined antibody response**
- **Enhance memory**

Adjuvants

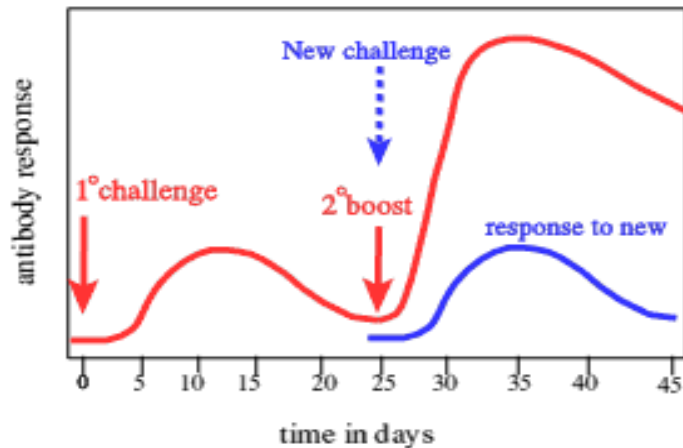
Prepandrix (GSK) uses an adjuvant (AS03)

The functions of adjuvants are:

- To improve immunogenicity
- To minimise the amount of antigen required
- **Trials with H5N1 and AS03**
 - Two doses – broad protection

Vaccine intervals

Specific memory is the hallmark of the adaptive immune response



With kind permission from Nick Holmes

- Primary immune response develops in the weeks following first exposure to an antigen
- Secondary immune response is faster and more powerful
- **Higher level of response**
- **More specific response**
- **More sustained memory**
- ***Possibly broader protection***

Other additives

- **Preservatives: prevent vaccines from contamination by bacteria and fungi**
Prepandrix contains a preservative - thiomersal

<http://www.immunisation.nhs.uk/files/thiomersalfsht.pdf>

Schedule

- **Expected to be administered as two doses with at least a 3 week interval**

Who should be immunised?

- **Persons at highest risk of severe illness**
- **Staff working with vulnerable groups**

Priority Groups

- 1. Individuals >6 months age up to 65 years in the current seasonal flu vaccine clinical at risk groups**
- 2. All pregnant women (subject to licensing conditions on trimesters)**
- 3. Household contacts of immunocompromised individuals**

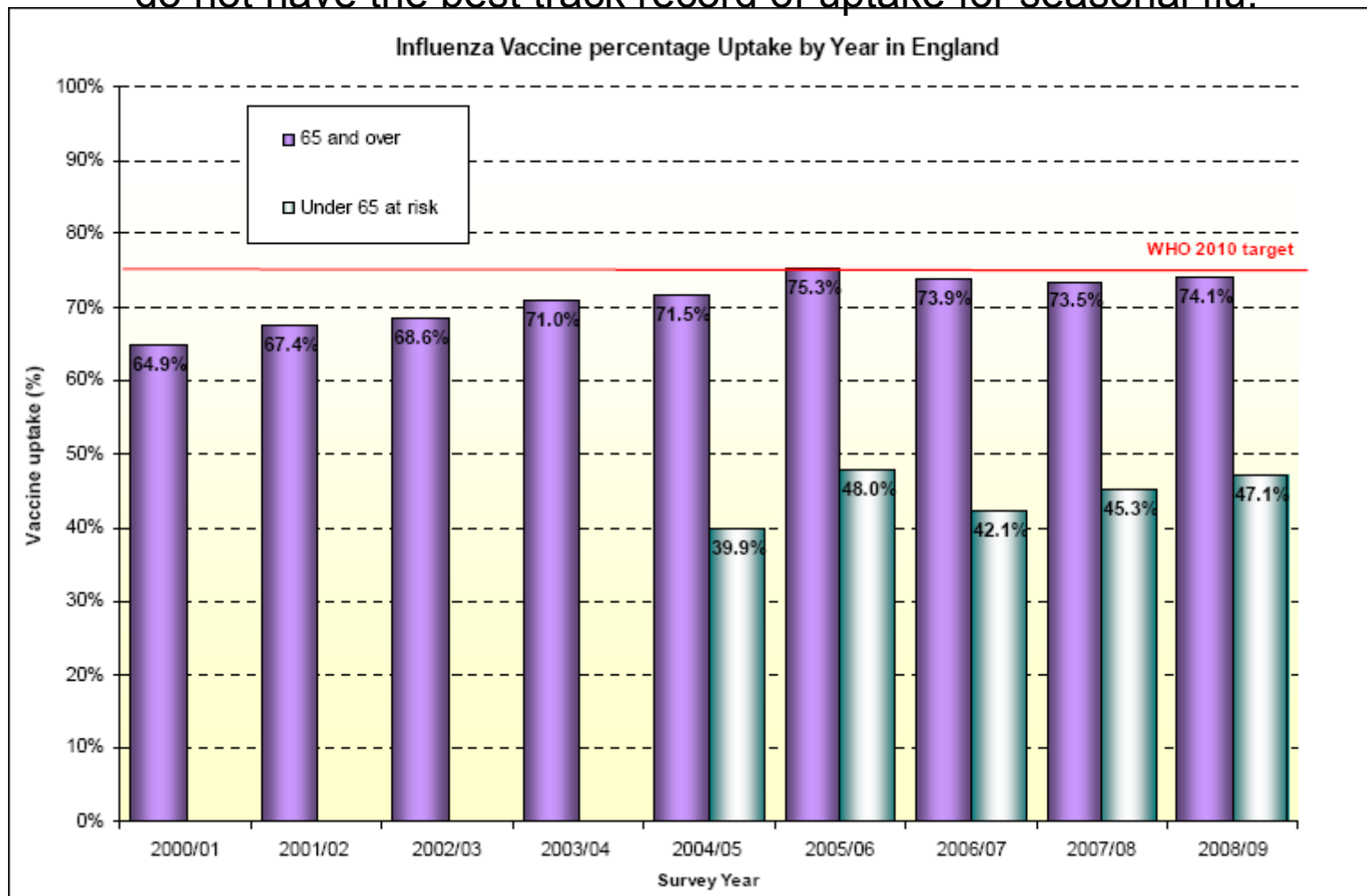
then

- 4. People age 65 years and over in the current seasonal flu vaccine clinical at risk groups**

Priority groups 1-3 may be vaccinated concurrently, rather than in priority order

Clinical risk groups under age 65

do not have the best track record of uptake for seasonal flu!



Frontline health and social care workers

**Offered vaccine at the same time as
the first clinical risk group.**

Control in institutional settings

Measures

- **Plan and infrastructure**
 - **Individual hygiene**
 - **Cleaning**
 - **Care of those ill**
- **Rapid diagnosis and isolation**
- **Avoid major transmissions events**

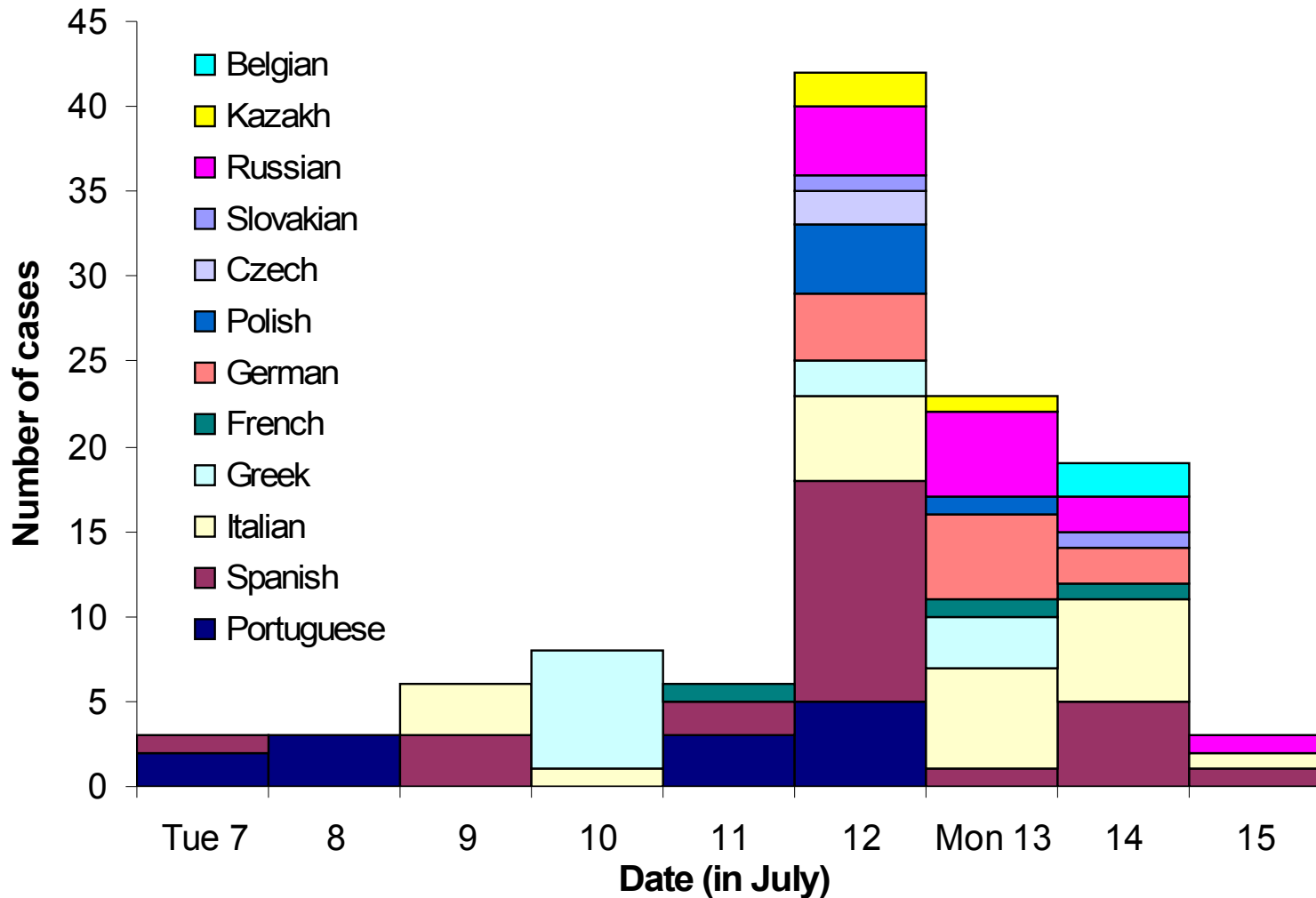
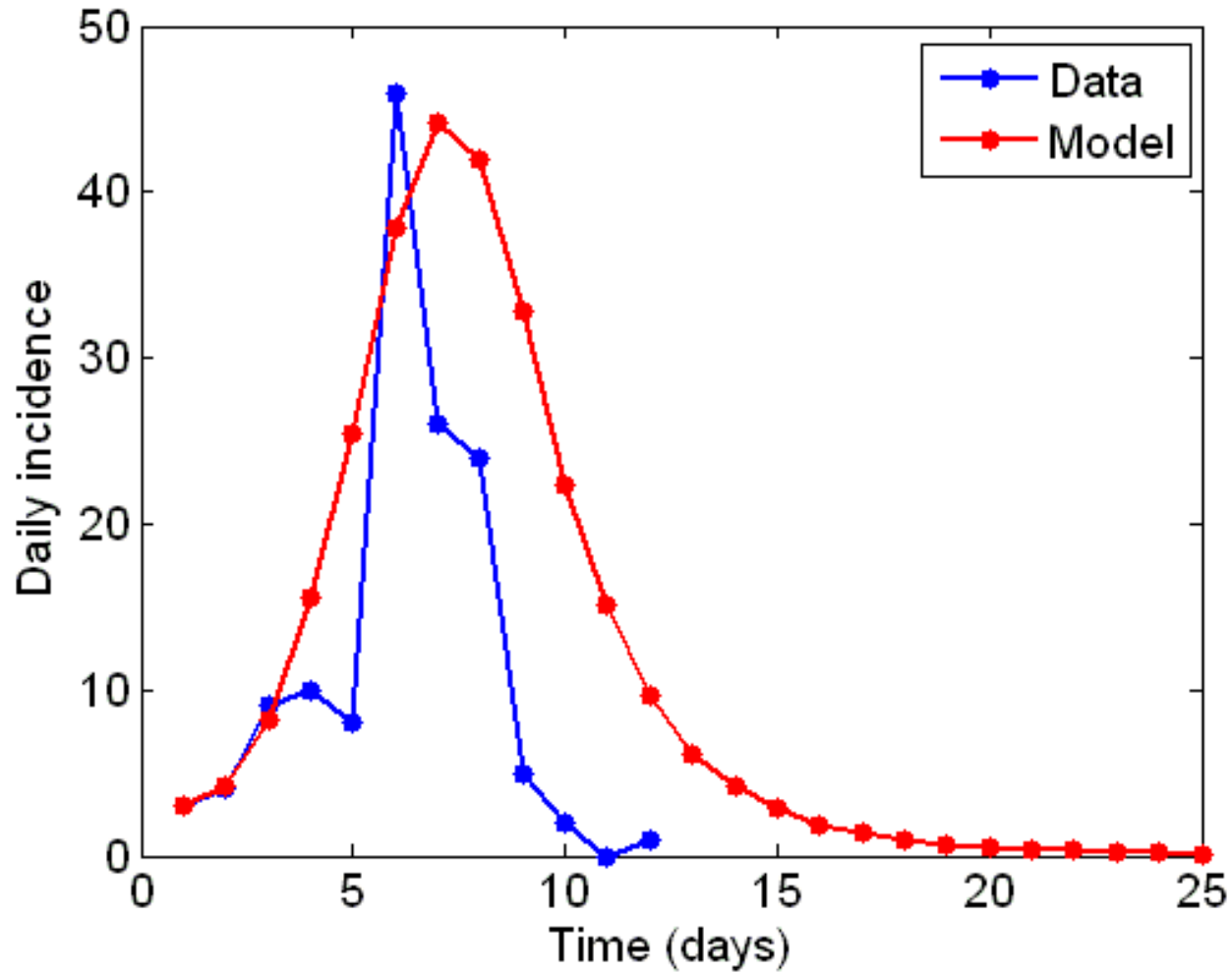


Figure. Date of diagnosis by nationality. Residential Language School, Oxford, 2009 (n=114).

Intervention and impact



Diagnosis

- **Clinical**
 - **Most cases**
 - **Past clinical swine flu does not rule out**
- **Laboratory**
 - **Institutions and other public health settings**