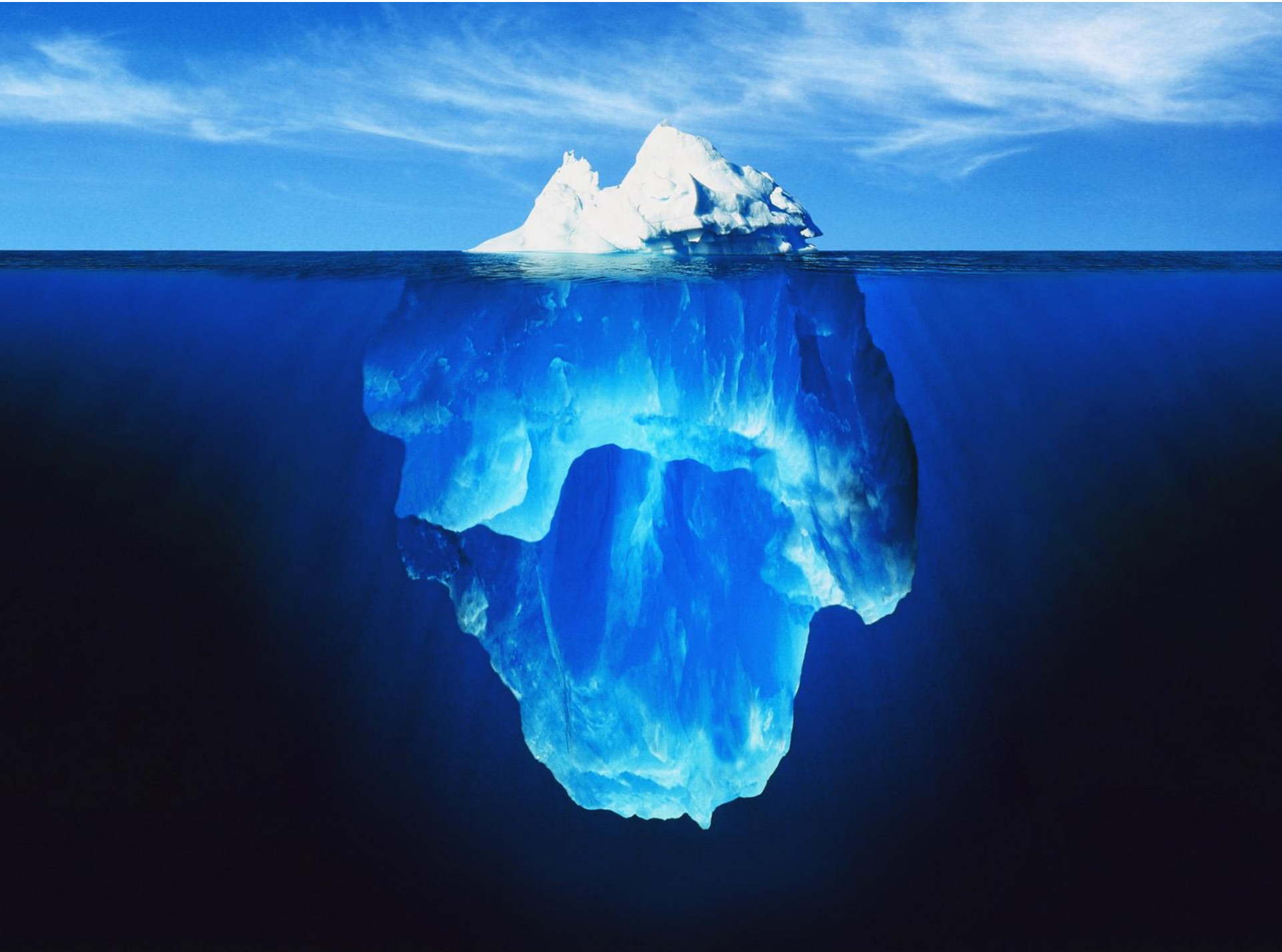
Public Health England

Right tools, Right application, Right answer

Maria Zambon
Public Health England



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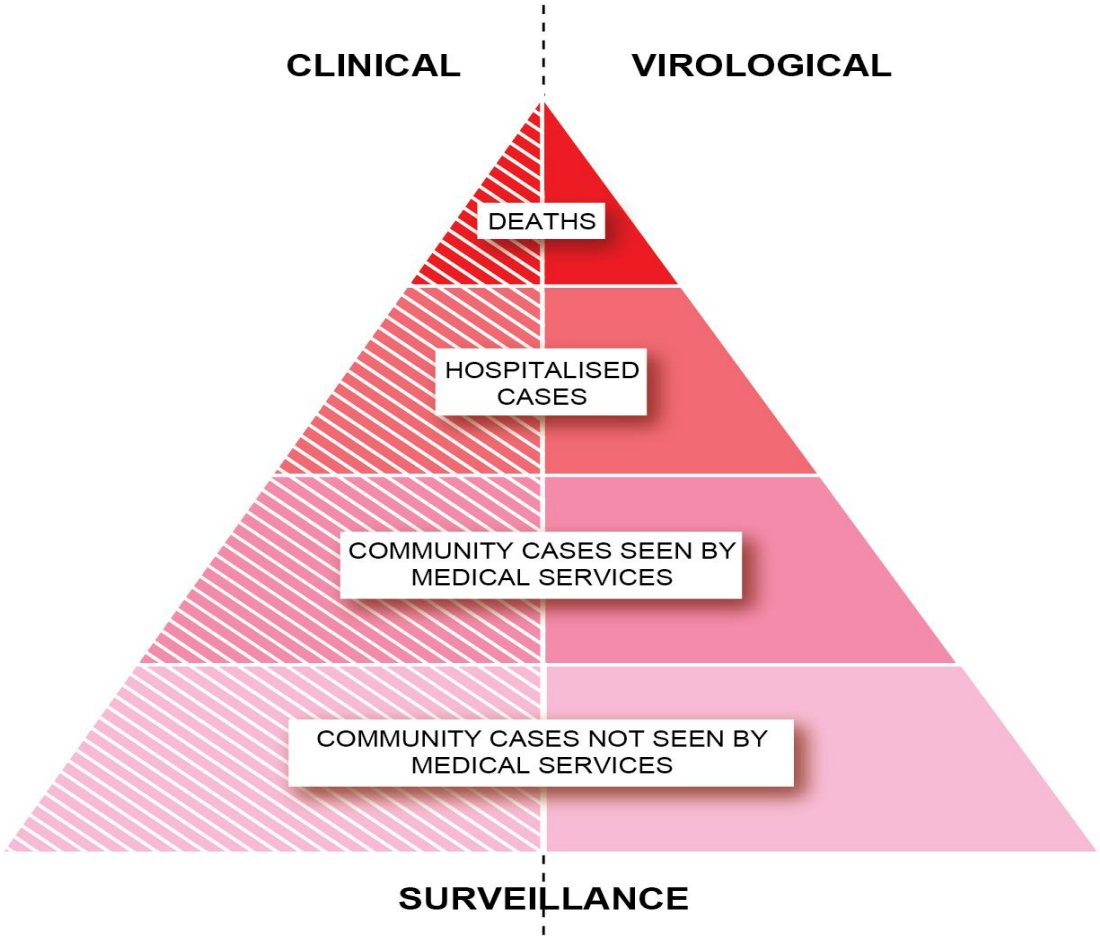
Tools for Assessment of Disease Burden



Changes in Diagnostic tools & capability

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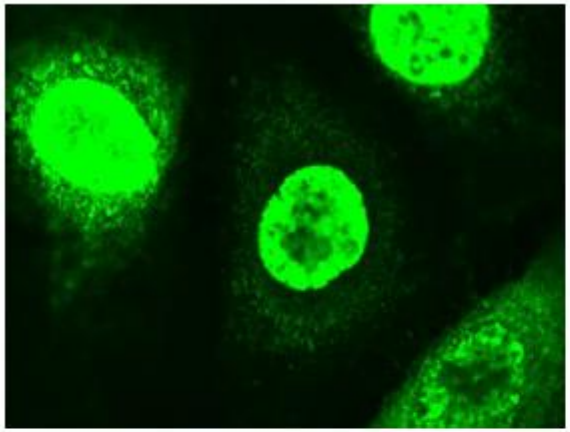
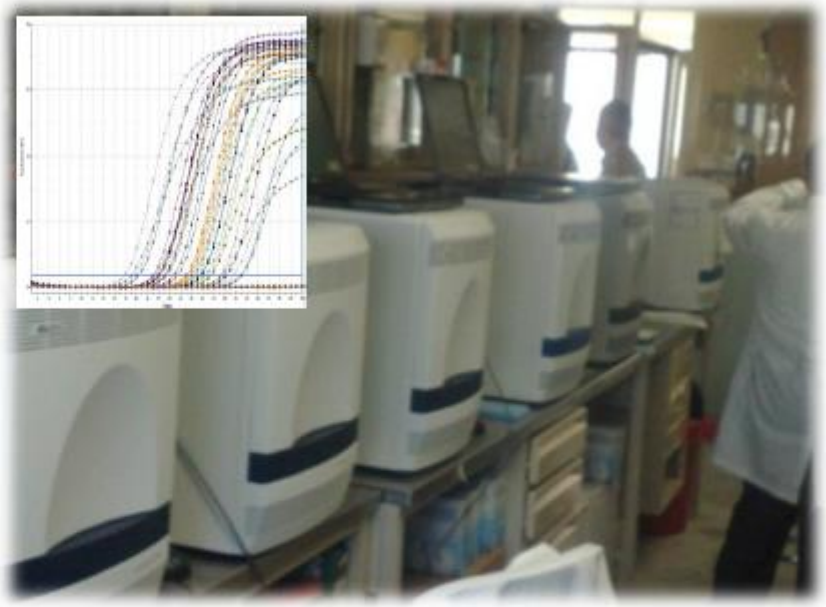


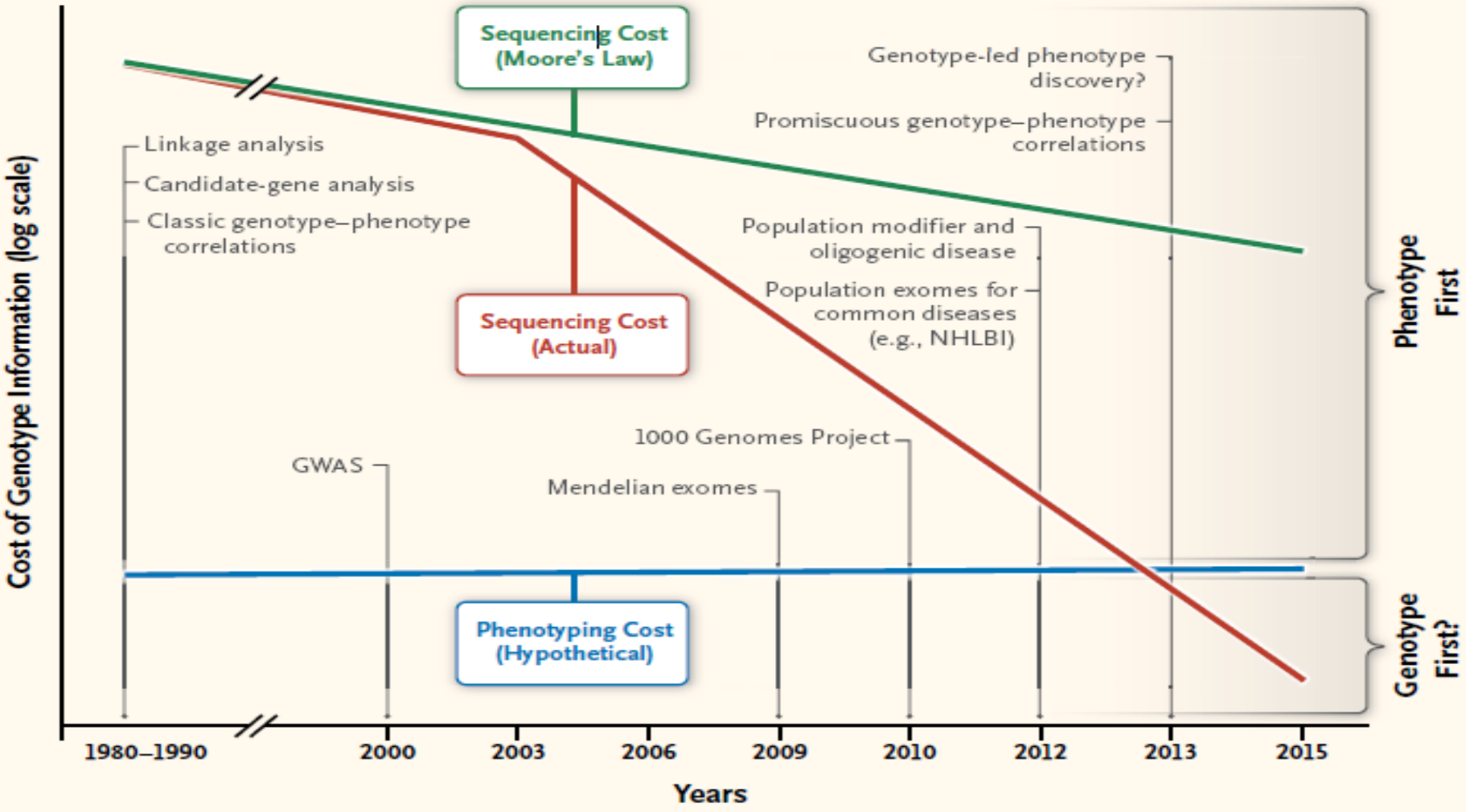
From: Immune-fluorescence



To: Real-time PCR

To Rapid near-patient tests (clinical)

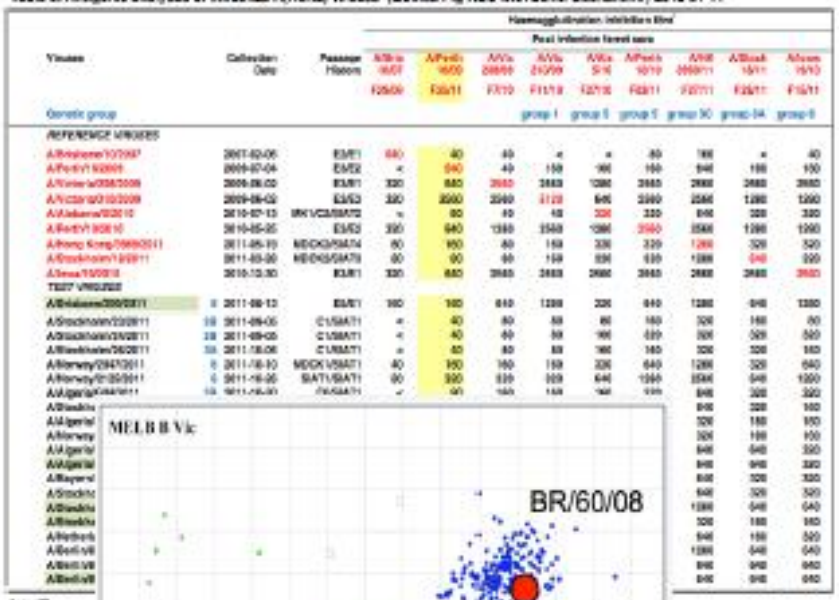
Public Health England

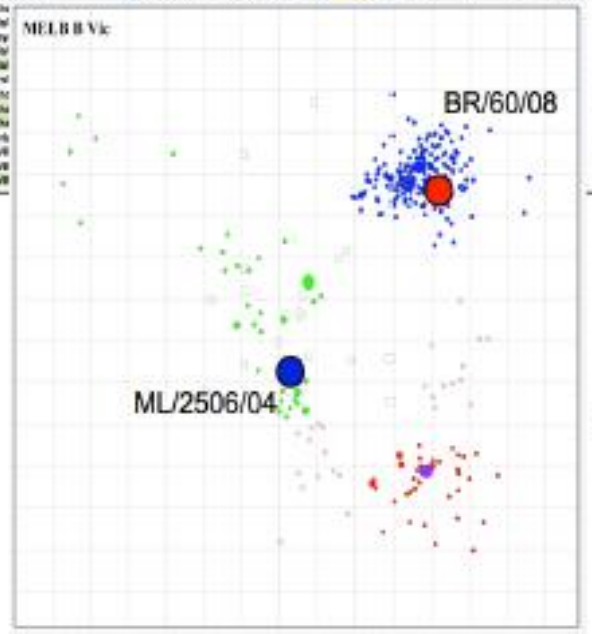


5 The Decreasing Cost of Genotype Information

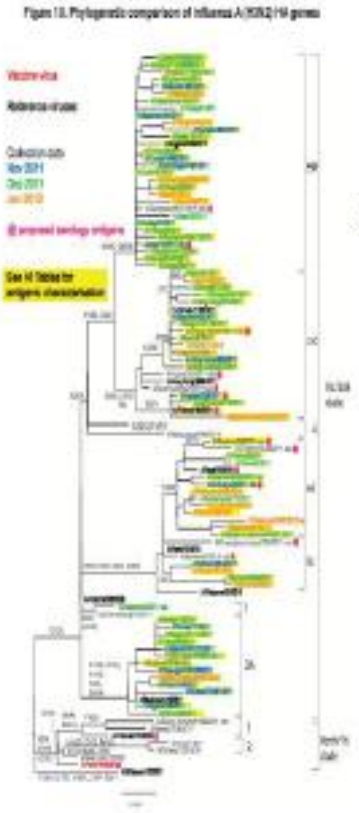
Improving Information for Interventions

HI (and neutralisation) data)

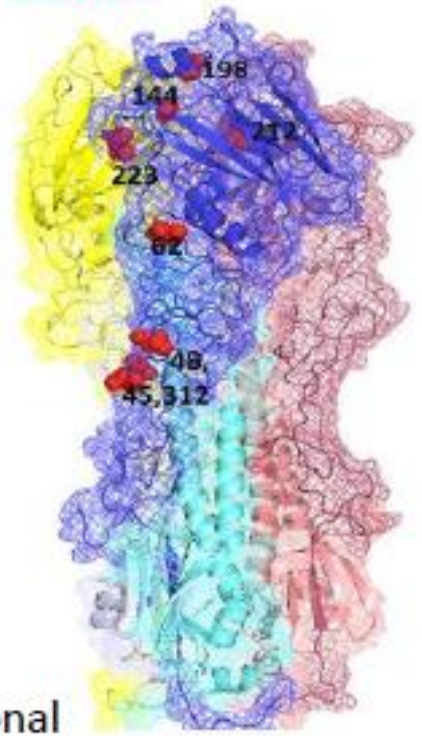




Antigenic cartography



Sequence analysis



Structural/functional significance of mutations

Introduction of New technologies

Top of the pyramid

Case studies

Public Health England

Paediatric Fatal Cases 2003-2004

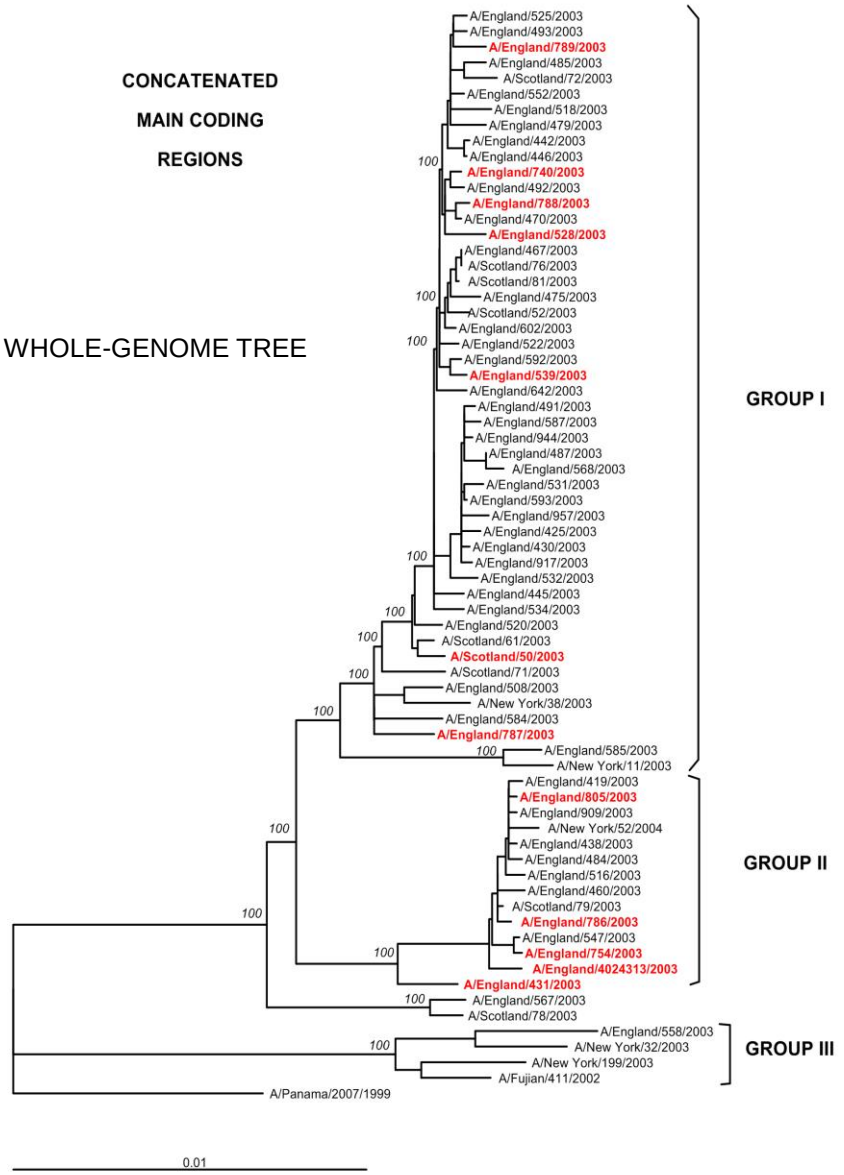
- Winter 2003-2004 : emergence antigenic variant

A/Fujian/411/2002-like viruses

- Poor vaccine match
- Unusual high number of influenza fatalities in children:

Sept -Dec 2003 in the UK

- No pre-existing risk factors
- None vaccinated
- Bacterial coinfection only in 3/17 (18%) cases
- WGS of all fatal cases & matched controls (1:3)



Galiano et al. PLoS One, 2012

Public Health England

Findings

- Fatal Cases distributed along all genetic lineages
- Several additional changes in internal genes & reassortment events noted
- **No genetic changes associated with fatal outcome**
- **Host-related susceptibility → naïve unvaccinated children undergoing first influenza infection**

Fatal cases , A(H1N1) pandemic 2009 viruses

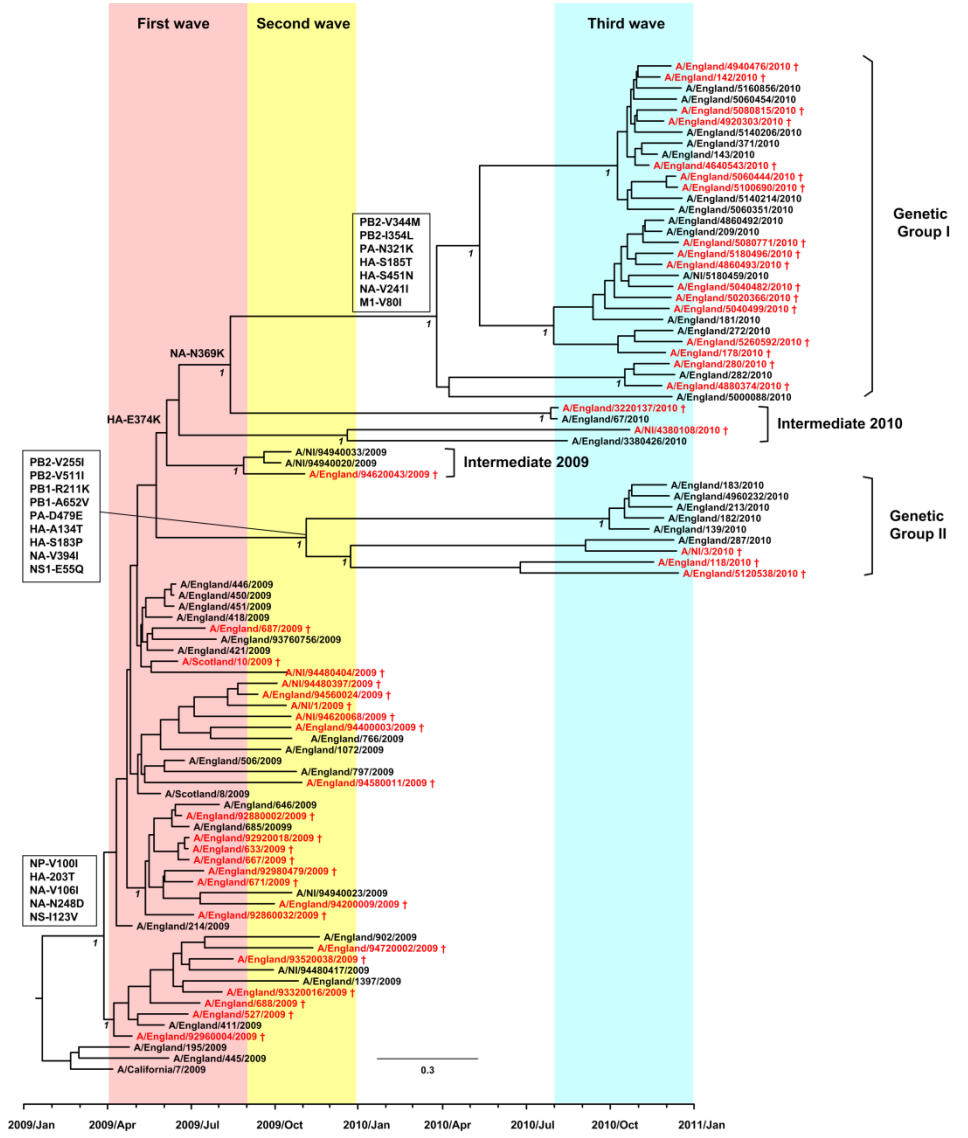
Public Health England

- WGS comparison of viruses isolated from fatal and 'control' mild cases from first, second and third wave of pandemics in the UK

No genetic differences between viruses from fatal and mild cases

Third wave viruses: Several signature changes

Ongoing adaptation to host?
Enhanced fitness?
New virulence factors?



Public Health England

Key findings

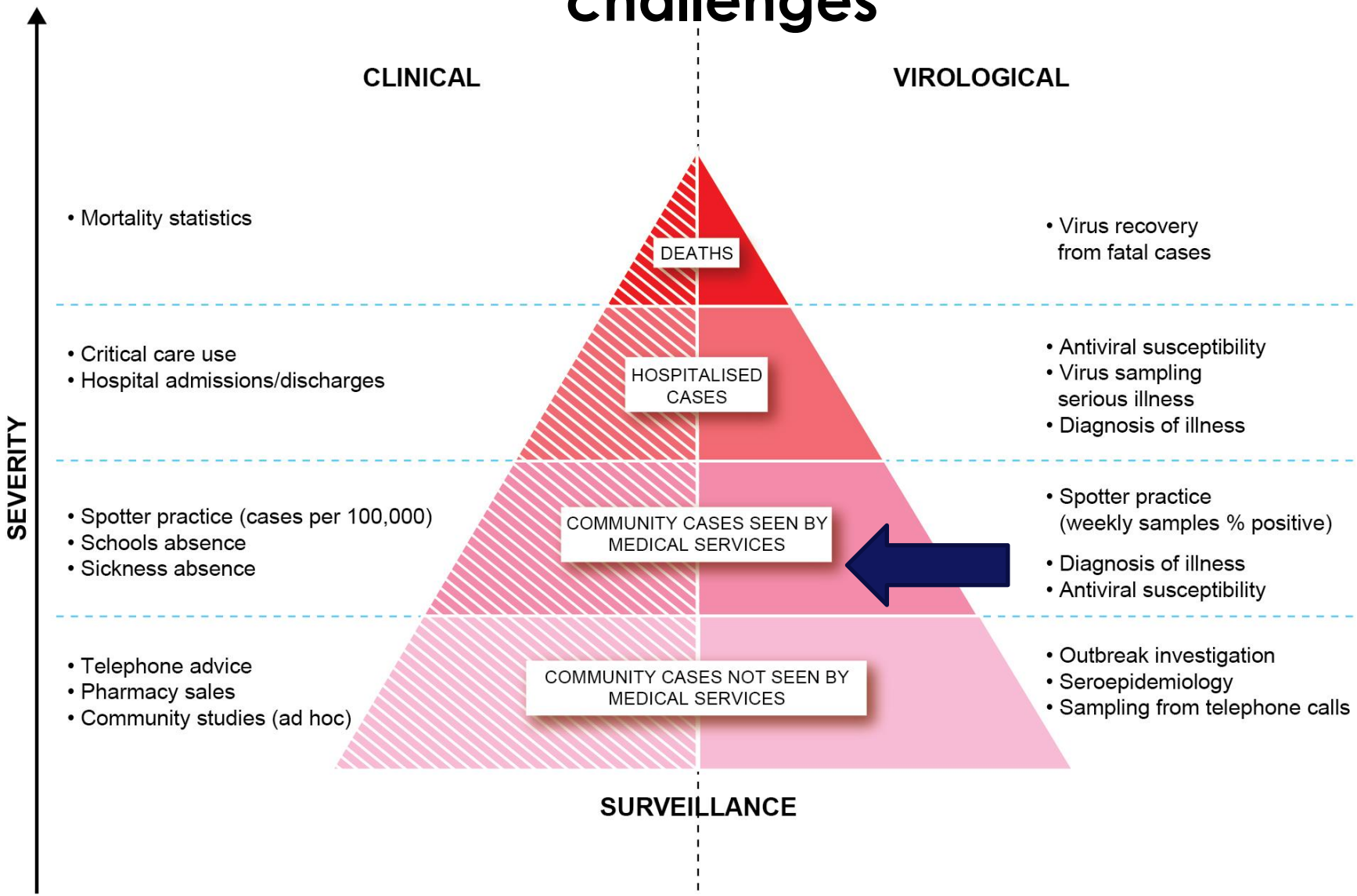
- WGS fatal vs. non-fatal ….no specific genetic changes associated with a fatal outcome,

(HA- D222G → not enough evidence)

- Variation observed in replication kinetics between viral strains in different waves
- Variation observed within and between waves

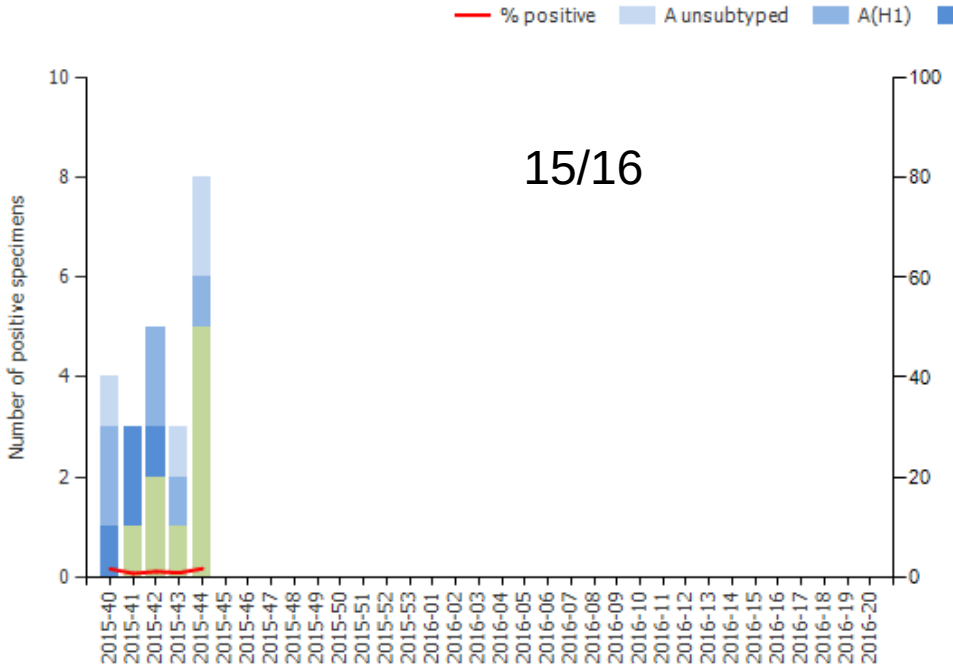
- **Clinical outcome of infection determined by host-related factors….**

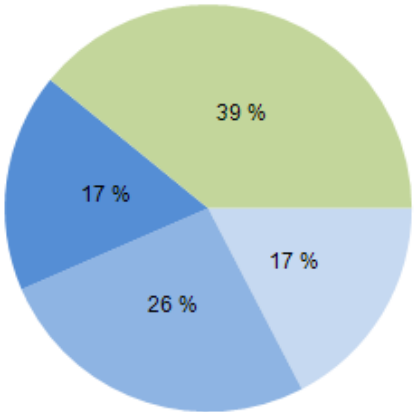
Influenza clinical and public health challenges



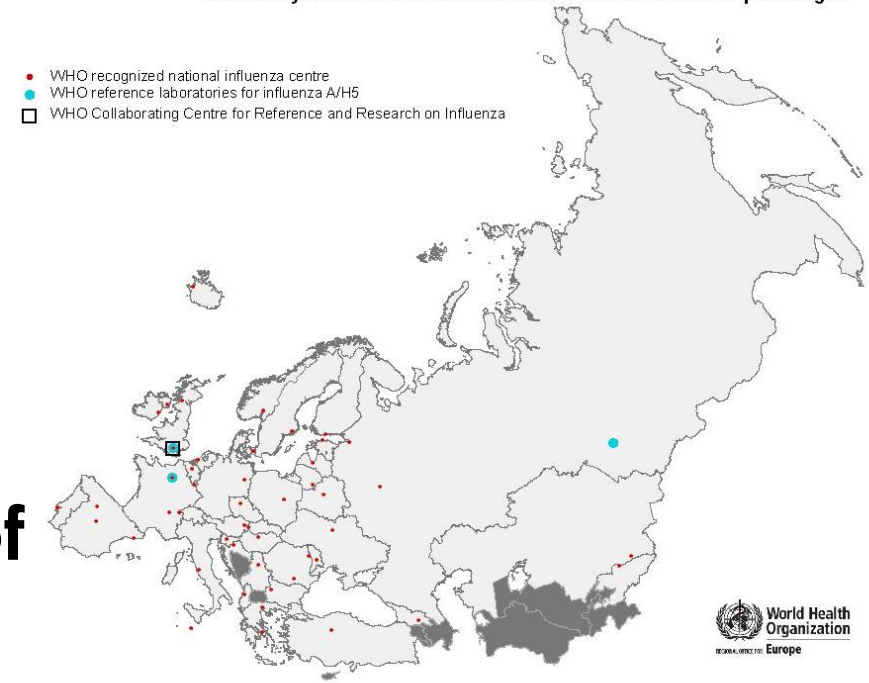
Influenza virus detections in the region

Source: Sentinel



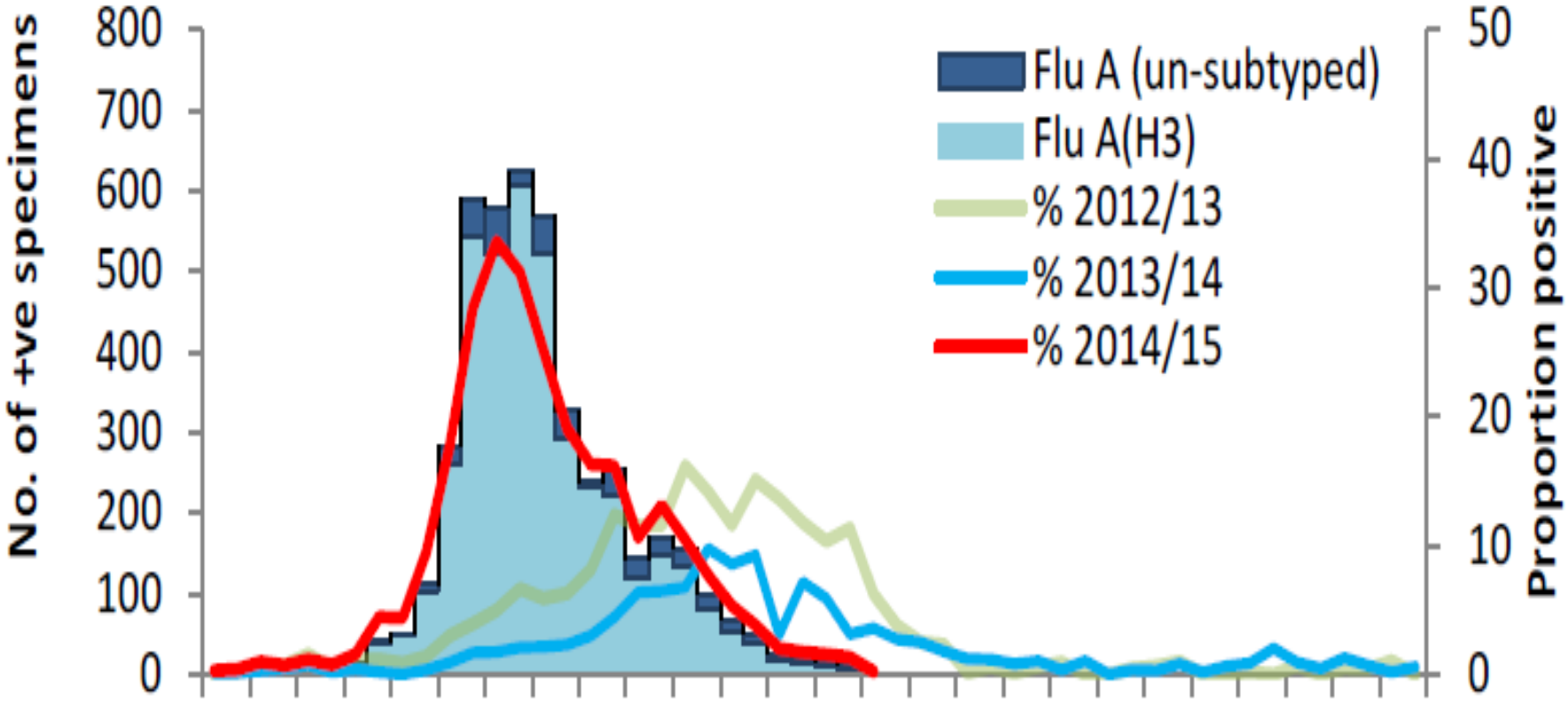


Laboratory network for influenza surveillance in the WHO European Region

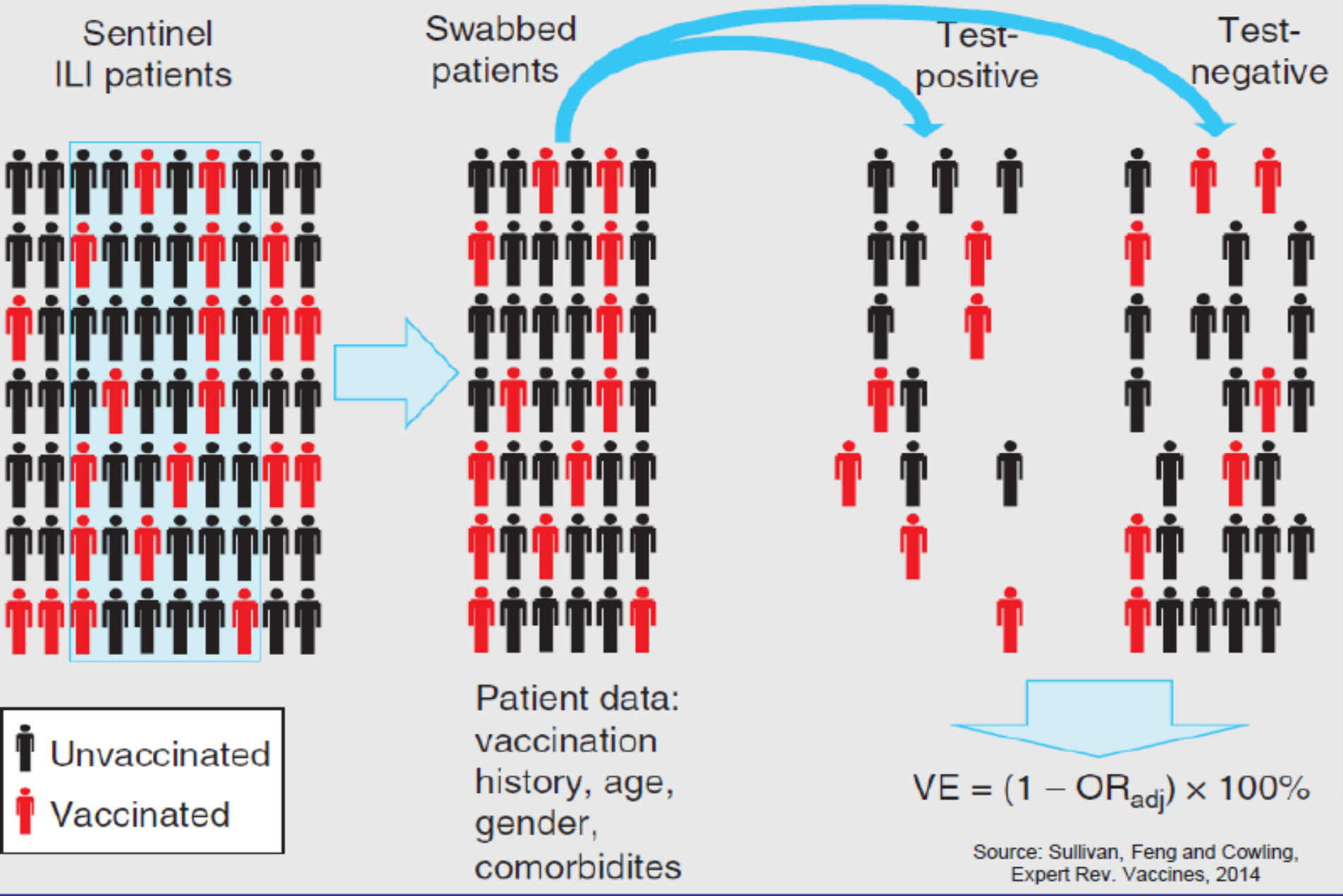


European early warning based on convergence of technologies

Overall activity Influenza A 2014/15
Developing the information



Test-negative design for estimating influenza VE



Low effectiveness of seasonal influenza vaccine in preventing laboratory-confirmed influenza in primary care in the United Kingdom: 2014/15 mid-season results

R G Pebody (RIchard.Pebody@phe.gov.uk)[1], F Warburton[1], J Ellis[2], N Andrews[1], C Thompson[2], B von Wissmann[3], H K Green[1], S Cottrell[4], J Johnston[5], S de Lusignan[6], C Moore[7], R Gunson[8], C Robertson[9,10], J McMenamin[3], M Zambon[2]

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Citation style for this article:
Pebody RG, Warburton F, Ellis J, Andrews N, Thompson C, von Wissmann B, Green HK, Cottrell S, Johnston J, de Lusignan S, Moore C, Gunson R, Robertson C, McMenamin J, Zambon M. Low effectiveness of seasonal influenza vaccine in preventing laboratory-confirmed influenza in primary care in the United Kingdom: 2014/15 mid-season results. Euro Surveill. 2015;20(5):pii=21025. Available online: http://www.eurosurveillance.org/ViewArticle.aspx?ArticleId=21025

Article submitted on 30 January 2015 / published on 05 February 2015

Friday, February 6, 2015

Lisa Armstrong
The Indoor Coat – fashion silliness that's also brilliant
Style page 27

Wolf Hall
Is it becoming the great Tudor turn-off?
Features page 23

A British exodus
'Jews aren't safe here any more'
Comment page 19

NATIONAL NEWSPAPER OF THE YEAR

The Daily Telegraph

telegraph.co.uk

Flu jab given to millions is useless

Number of deaths this winter will be the worst for 15 years as vaccination has no effect on most common strain of the virus

By Laura Donnelly, Health Editor

THE flu vaccine given to millions of people in Britain has proved almost useless, health officials have admitted, amid warnings that the number of deaths this winter could be the highest for 15 years.

The dominant strain of influenza in circulation, which is particularly lethal among the elderly, is a different mutation from the type used in the jab, Public Health England warned.

As a result, the vaccine is working in only three per cent of those given it, when it is normally effective in around half.

GPs are being urged to prescribe antiviral drugs to prevent flu among the most vulnerable and in care homes where viruses are spreading.

The alert follows research on more than 1,300 patients admitted to hospitals with the virus. Questions were being asked last night about why health officials had not raised the alarm earlier.

There was concern that rising numbers of cases among those who have been vaccinated had not been tracked properly. Official data about that are not recently as December. PHE also were monitoring samples of just 51 cases a week involving patients with this year's dominant strain.

Last month, after The Daily Telegraph highlighted doctors' concerns that strains in the virus were adding to a rise in emergency hospital admissions, health officials said there was no evidence that the new variant, influenza A (H3N2), would become the dominant strain.

Last night officials said the surge in cases had resulted in staffing in care homes, admissions to hospital and a rise in deaths among the over-65s. The number of "excess deaths" this winter, after other strains of flu, whose circulation could kill more.

The decision about which forms of flu would be most likely this winter was taken 11 months ago by the World Health Organisation, which recommended different vaccines for the northern and southern hemispheres.

The new research found that those suffering from the mutated strain, known as a "drift" strain, would have been better protected had they received the jab given south of the equator.

Until recently, flu levels have been at their highest for three years, but officials said cases were beginning to fall off.

Patient groups last night asked why the strain had been missed in tests about Britain's low levels of protection.

Katherine Murphy, chief executive of the Patients Association, said the declarations were "extremely worrying" for those who had thought they were protected. "It beggars belief that health officials weren't aware just how badly the vaccine was working a long time ago," she said.

"If they didn't realise the scale of the problem until now they aren't doing their job properly."

Officials said that until the study was published, the size of the surprise they had encountered depended on the number of cases sent to them by NHS doctors.

Until January, PHE labs were receiving samples of fewer than 25 cases of influenza A (H3N2) every week.

Dr Richard Pebody, the body's head of flu surveillance, said: "The World Health Organisation monitors influenza globally and each year recommends the strains of flu virus that should be included in the flu vaccine for the forthcoming flu season. It takes from February through to August-September to produce sufficient quantities of the flu vaccine.

"If a change in the virus is detected once production has started it is not possible to change it."

He said that there had "generally been a good match" between the vaccine produced and the strains which subsequently circulated, and urged vaccination of groups considered to be at risk not to be discouraged from having the flu vaccination this year, or in the future.

"The vaccine we have is still expected to protect against the A (H1N1) pdm09 and the B, both of which may yet circulate this season, so anyone in an at-risk group should still get vaccinated if they have not already," he said.

"It's not possible to fully predict the strains that will circulate in any given season, and there is always a risk of a drift occurring."

Will Friday night be rugby night at Twickenham?

Wales's Sam Warburton and England's Chris Robshaw with the Six Nations trophy ahead of

By Gavin Mairs
Rugby News Correspondent

THE prospect of Twickenham staging Six Nations matches on Friday nights will be discussed by the Rugby Football Union after this year's World Cup, The Daily Telegraph can disclose.

Cardiff's Millennium Stadium will host the Six Nations opener between England and Wales tonight – a time slot popular with the tournament's organisers because it helps maximise television audiences. Supporters are less keen on Friday night matches and the RFU recently launched a review of the Six Nations board for Twickenham to host them for the next two seasons because of traffic issues in north-west London.

However, the stadium will host the opening fixture of the World Cup between England and Fiji on a Friday night in September, which could pave the way for Six Nations matches

Mortgage wars to save borrowers £1,700 each

By Nicola Blackmore and Dan Hyde

"

The biggest savings from the mortgage rate war were for people

Labour backer fears Miliband victory

By Christopher Hope and Steven Swinford

ONE of the Labour Party's biggest business backers said yesterday that Ed Miliband has ruled out any chance of the party winning the general election.

Sir Charles Dunstone, the co-founder of Carphone Warehouse, said business people "feel very detached" from the party, and "isolated" by its lurch to the Left under Ed Miliband.

In 2005, Sir Charles was one of 60 business people who signed a letter supporting Labour.

But he told the Financial Times: "As a business person I'm frightened of an environment where there aren't enough emphasis put on growing the economy to get

Greek crisis: Business B1&4

HOME NEWS ELECTION SPORT COMMENT FINANCE TRAVEL VIDS

HEALTH LIFE DIETS GARDEN FOOD STYLE PROPERTY TECH SATURDAY

Home Life & Style Health

Useless flu jab blamed for surge in death toll

THIS year's flu jab is offering almost no protection to vulnerable people at risk of suffering severe effects from the virus, research revealed yesterday.

By ELEANORE ROBINSON

PUBLISHED: 08:52, Fri, Feb 6, 2015 | UPDATED: 21:25, Tue, Feb 10, 2015

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Health

Flu vaccine 'barely effective' against main viral strain

By James Gallagher
Health editor, BBC News website

5 February 2015 Health

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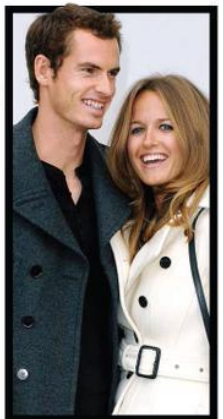
Scottish Daily Mail

SATURDAY, FEBRUARY 7, 2015 90p

Thousands of Scots given jab which only protects 3pc of patients as health chiefs admit they knew about flaw months ago

WARNING OVER FLU VACCINES



FLU JAB IS A WASTE OF TIME FOR 97% OF PATIENTS

THE FLU jab will protect just three per cent

By Sophie Borland
Health Correspondent

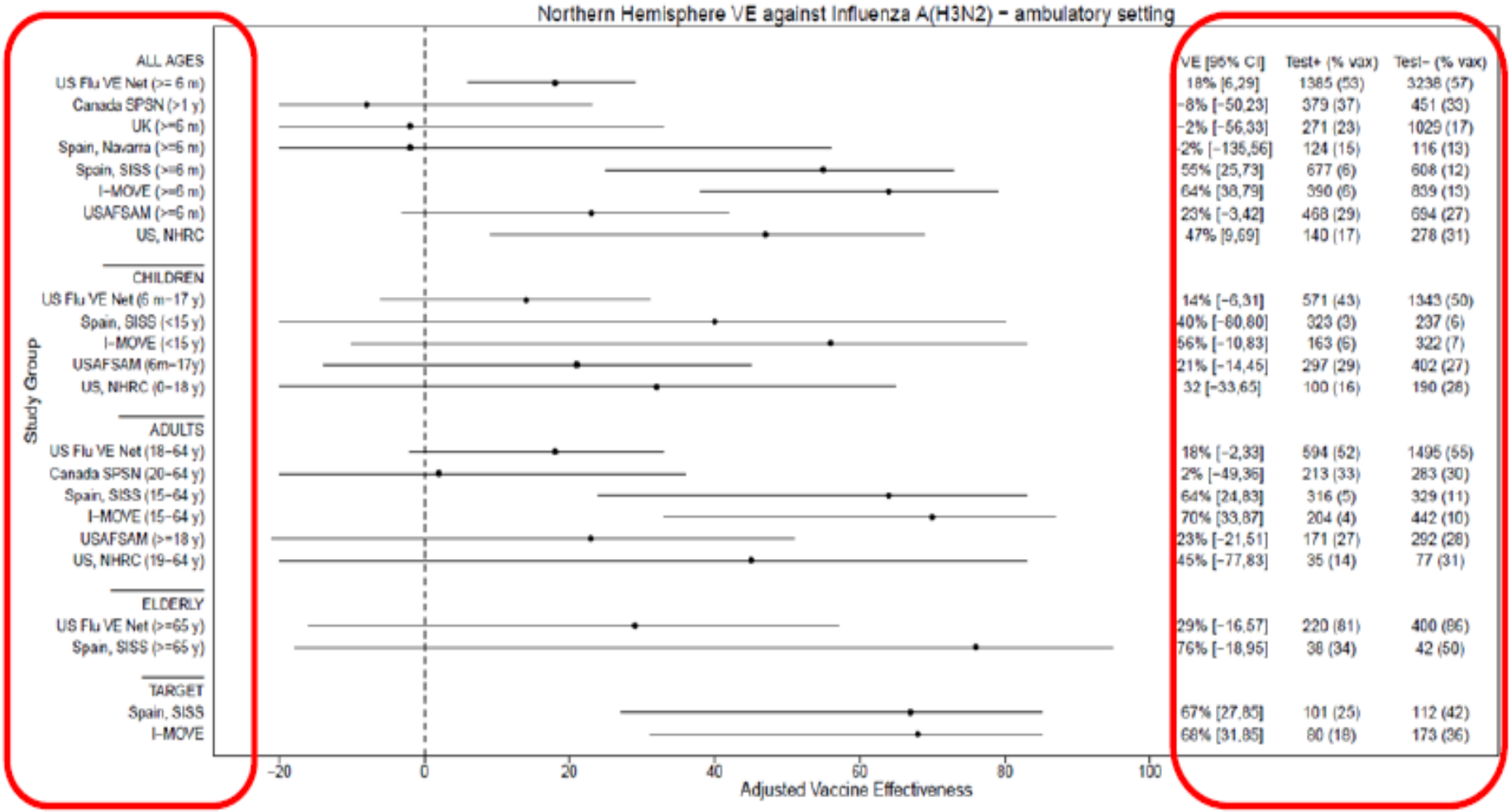
around 60 per cent of patients. Last night questions were being asked about why health officials did not

Email spat: Broadcaster Myleene Klass

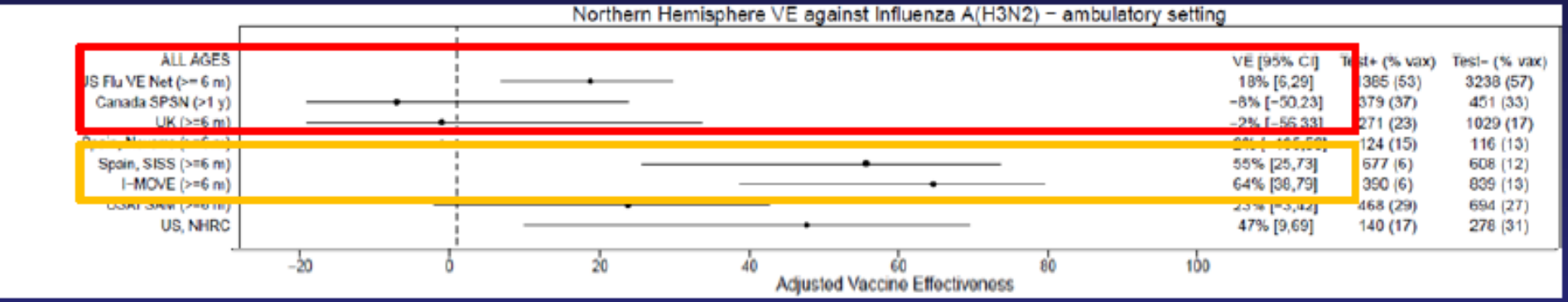
Myleene's war on grasping

Influenza A(H3N2) Northern Hemisphere – Interim Data

Ambulatory setting



Influenza A(H3N2) Northern Hemisphere



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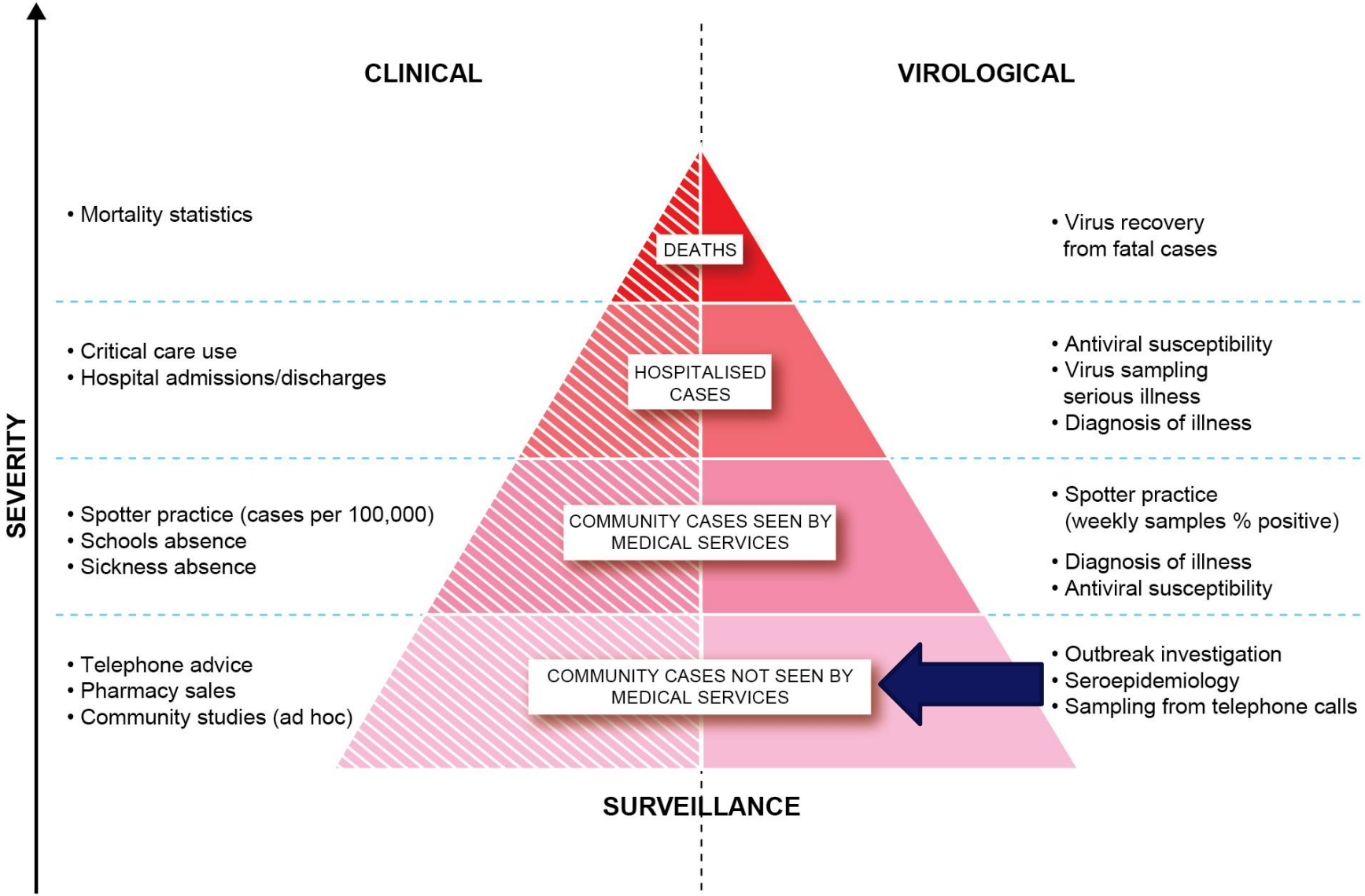
Study Site	H3N2-positive cases	Genetically-characterized H3N2 viruses	Group 3C.2a n (%)	Group 3C.3a n (%)	Group 3C.3 n (%)	Group 3C.3b n (%)
US Flu VE Net	1385	764	624 (82%)	25 (4%)	26 (3%)	89 (11%)
Canada, SPSN	379	226	205 (91%)	0	2 (1%)	
UK	271	44	35 (80%)	0	9 (20%)	
Spain, SISS	677	97	53 (55%)	9 (9%)	35 (36%)	
Europe, I-MOVE	390	27	14 (52%)	3 (11%)	10 (37%)	

Page 10

Influenza clinical and public health challenges



Crowd sourcing ?

Free home flu test kits for Flusurvey participants

Scientists from Flusurvey and i-sense call for public to help monitor spread of UK flu more accurately than ever before

People taking part in this year's Flusurvey, the UK's biggest crowd-sourced study of influenza will for the first time be offered a swab to confirm if their symptoms are caused by a flu virus or not as part of a new collaboration with i-sense. Data from social media and internet searches will also be combined with Flusurvey, allowing flu trends to be monitored across the UK more accurately and earlier than ever before.

Self-sampling for community respiratory illness: a new tool for national virological surveillance

A J Elliot (Alex.Elliot@phe.gov.uk)[1], A Bermingham[2], A Charlett[2], A Lackenby[2], J Ellis[2], C Sadler[2], P Sebastianpillai[2], C Powers[2], D Foord[3], E Povey[3], B Evans[2], H Durnall[4], D M Fleming[4], D Brown[2], G E Smith[1], M Zambon[2]

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2. Public Health England, London, United Kingdom
3. National Health Service Direct, Milton Keynes, United Kingdom
4. Royal College of General Practitioners Research and Surveillance Centre, Birmingham, United Kingdom

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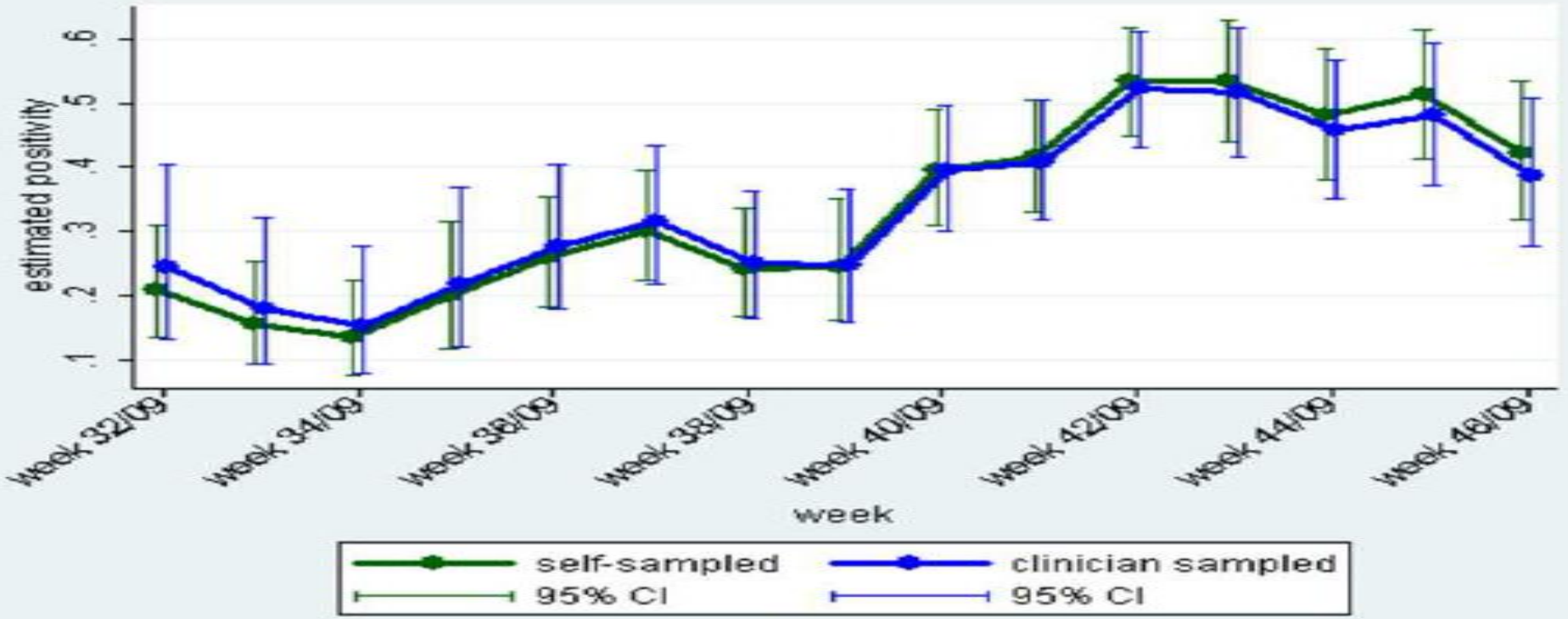
Elliot AJ, Bermingham A, Charlett A, Lackenby A, Ellis J, Sadler C, Sebastianpillai P, Powers C, Foord D, Povey E, Evans B, Durnall H, Fleming DM, Brown D, Smith GE, Zambon M. Self-sampling for community respiratory illness: a new tool for national virological surveillance. Euro Surveill. 2015;20(10):pii=21058. Available online: http://www.eurosurveillance.org/ViewArticle.aspx?ArticleId=21058

Article submitted on 03 September 2013 / published on 12 March 2015



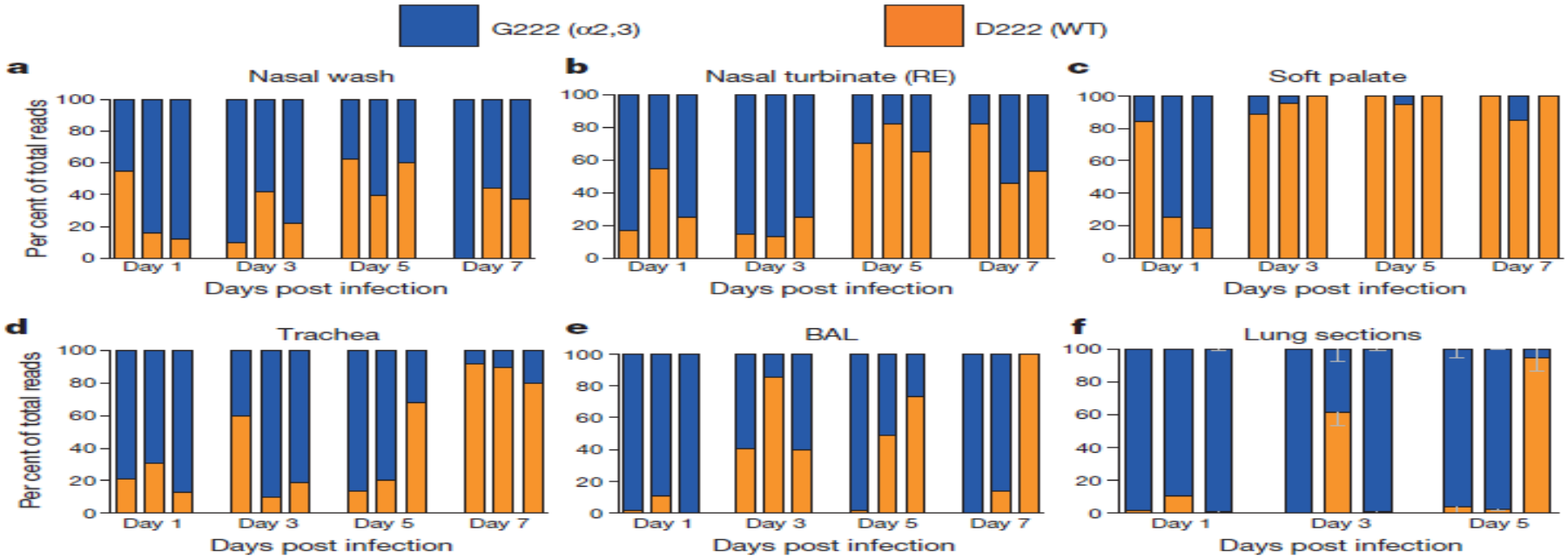
nature International weekly journal of science

LETTER

doi:10.1038/nature15379

The soft palate is an important site of adaptation for transmissible influenza viruses

Seema S. Lakdawala[1]†, Akila Jayaraman[2], Rebecca A. Halpin[3], Elaine W. Lamirande[1], Angela R. Shih[1], Timothy B. Stockwell[3], Xudong Lin[3], Ari Simenauer[3], Christopher T. Hanson[1], Leatrice Vogel[1], Myeisha Paskel[1], Mahnaz Minai[4], Ian Moore[4], Marlene Orandle[4]†, Suman R. Das[3], David E. Wentworth[3]†, Ram Sasisekharan[2] & Kanta Subbarao[1]



Public Health England

The Big Picture

- Switching technologies, improve prediction, increase information strain diversity. WGS/NGS…unbiased information
- **Technology is ahead of Knowledge (Virus & patient)**
- STRATIFIED MEDICINE…Consider the host…link to clinical outcome
- **Population Susceptibility….better methods for prediction of susceptibility**
- Study of vaccine failures will help improve vaccine design

Automated analysis of known drug resistance mutations

Pay attention to the sample. Rubbish in = rubbish out.

Public Health England

Implications & Issues

Moving to an unbiased approach to analysis

Data analysis is bottleneck :

We have more data than we know what to do with

Powerful epidemiological analysis: new insights and hypothesis generation

Data storage and release issues