Epidemics, pandemics and how to control them.

Christopher Whitty
Gresham College 2018

In Sir Thomas Gresham's lifetime (c1519-1579) infectious diseases dominated medicine.

- Many were a constant presence, but serious epidemics occurred.

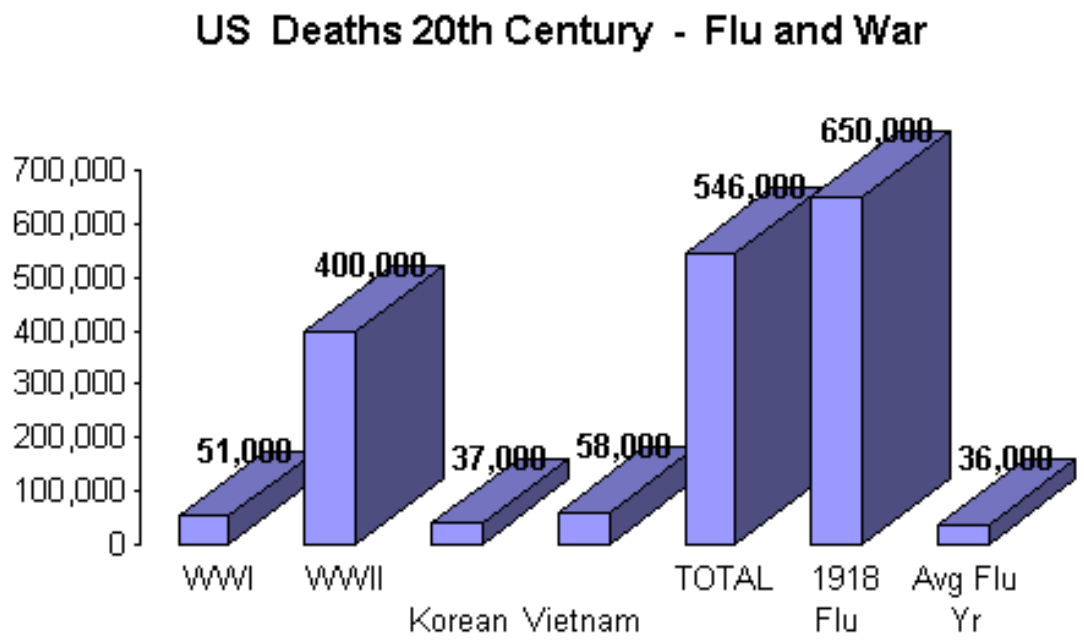
Included:

- Plague (1563, 1578)
- Syphilis
- Smallpox (epidemic 1562)
- Typhus
- The Sweating sickness (1528, 1551)

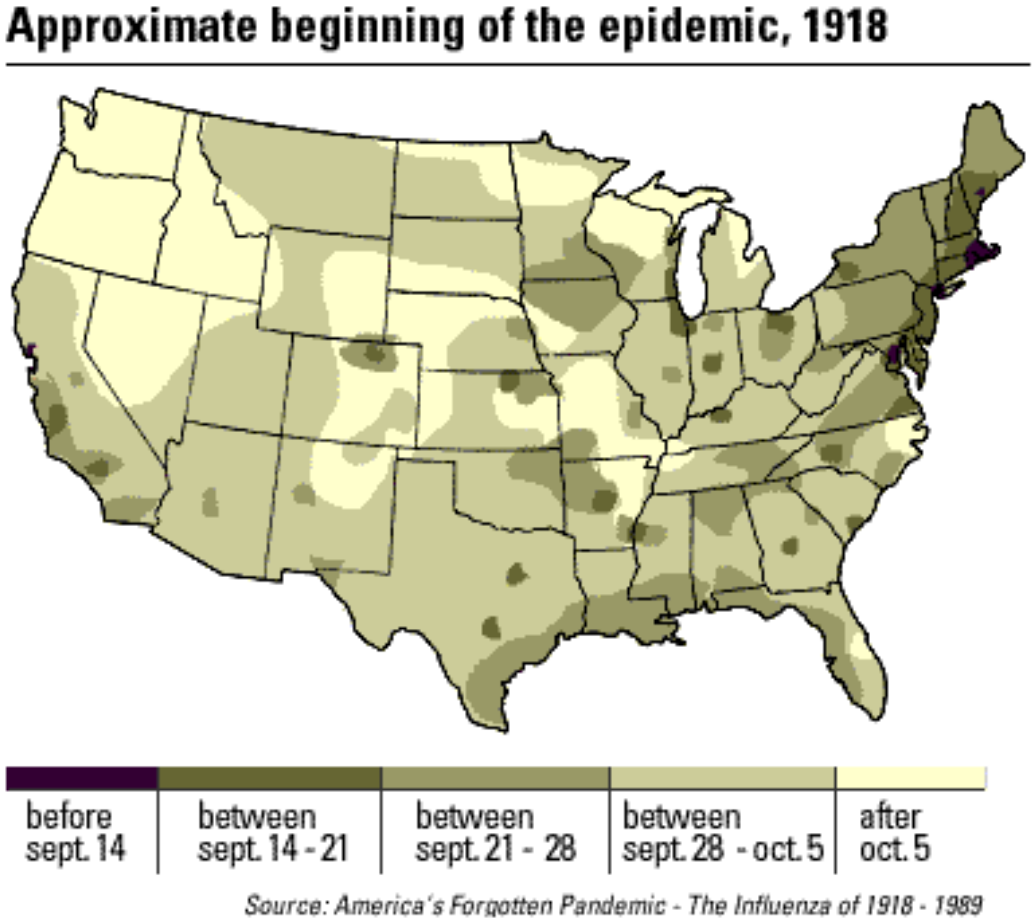
Plague an example of the power of infectious disease to shape human history- and human capacity to respond.

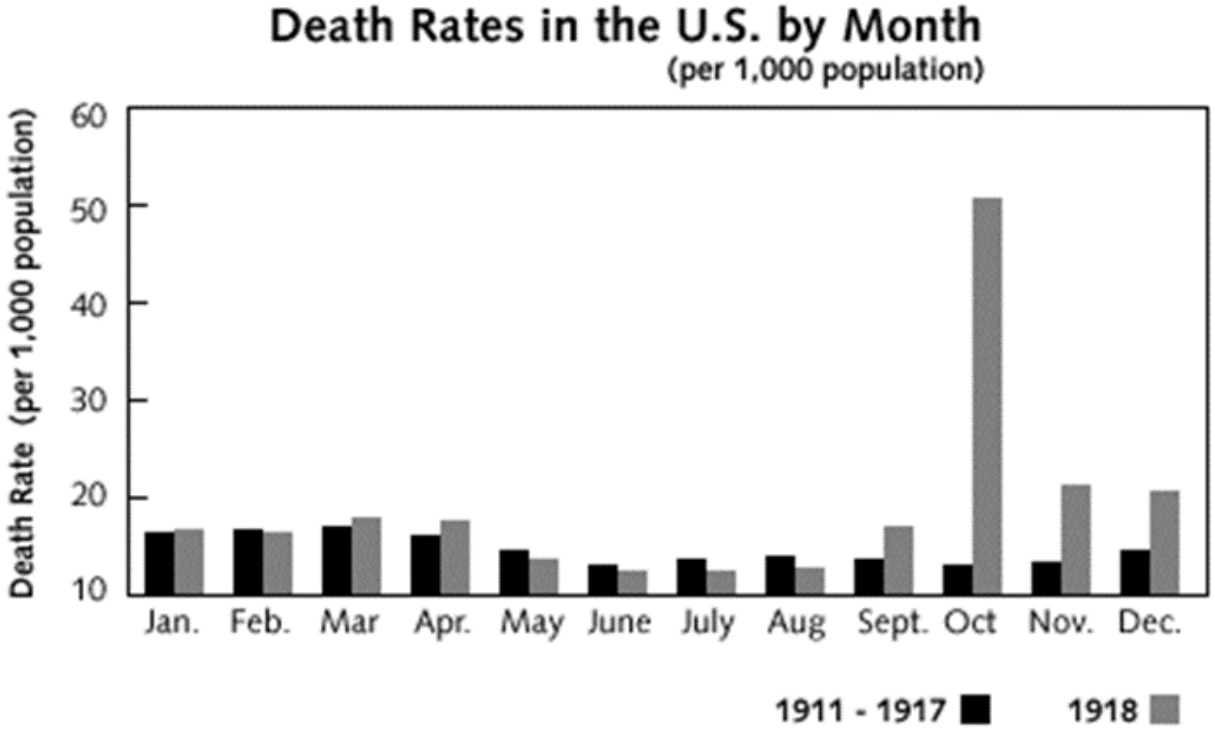
- Plague reduced the world population from an estimated 450 million down to 350–375 million in the 14th century.
- 30-60% of Europe's population died.
- Risk of a plague pandemic now zero (WHO).

Another centenary. 1918-20 H1N1 influenza pandemic ('Spanish flu') probably killed 50-100 million people.

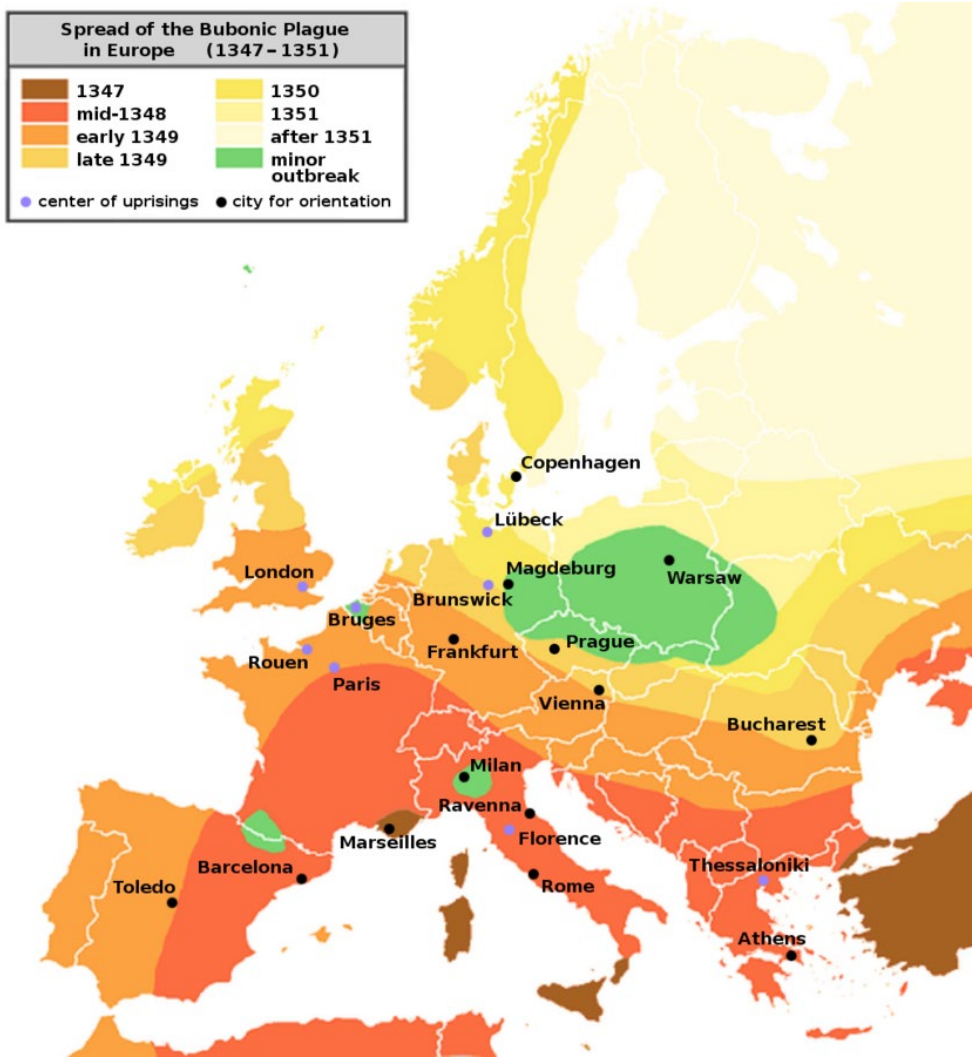


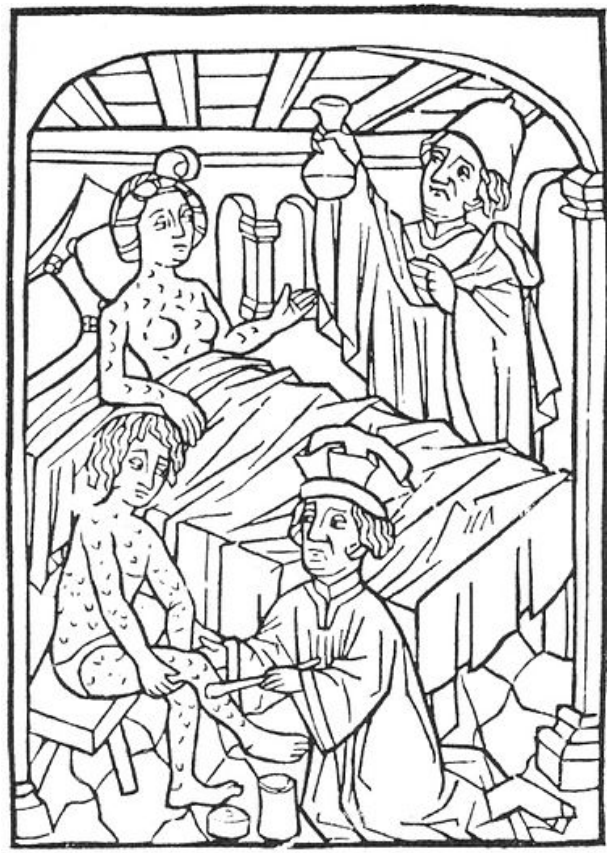
Epidemics can be very sudden and spread rapidly: the 1918 influenza pandemic.





Global spread rapid even in pre-industrial times: plague and syphilis





Naples 1494/5

Scotland by 1497

It is easy to make a case we are increasingly vulnerable to epidemics. This is wrong- but we do remain vulnerable.

Non-specific hardening of richer societies against epidemics.
Include:

Agriculture

- Better nutrition

Engineering

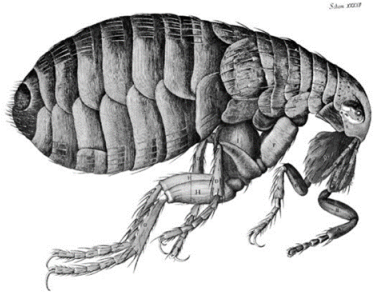
- Better housing
- Sanitation
- Clean plentiful water
- Cleaner heating

Flights data- *Openflights*

Localised outbreaks happen every year; some become epidemics. A few outbreaks/epidemics in 2018.

XDR Typhoid, Pakistan.

Cholera, Zimbabwe, Yemen.



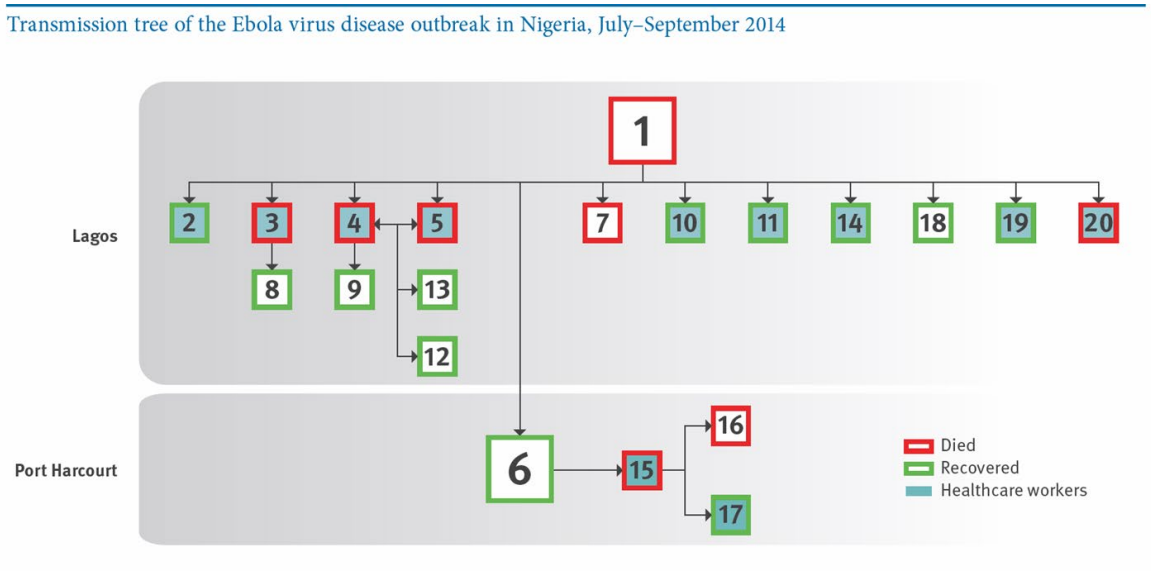
Plague, Madagascar.

Monkeypox, Nigeria (UK cases).

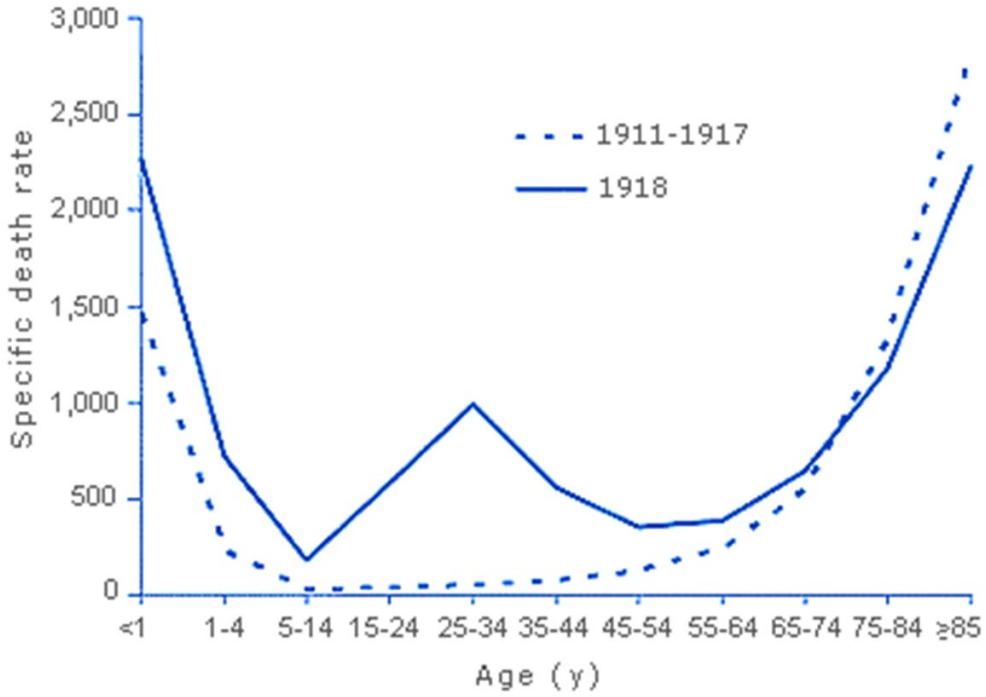
MERS, Saudi Arabia (UK case).

Ebola, DRC x 2.

Societal impact depends on how many and who is affected. It may be certain societal groups, occupations or agegroups.



Healthcare workers and Ebola



Source: CDC Emerging Infectious Diseases · Vol. 12, No. 1, January 2006
Link: http://www.cdc.gov/ncidod/EID/vol12no01/05-0979.htm

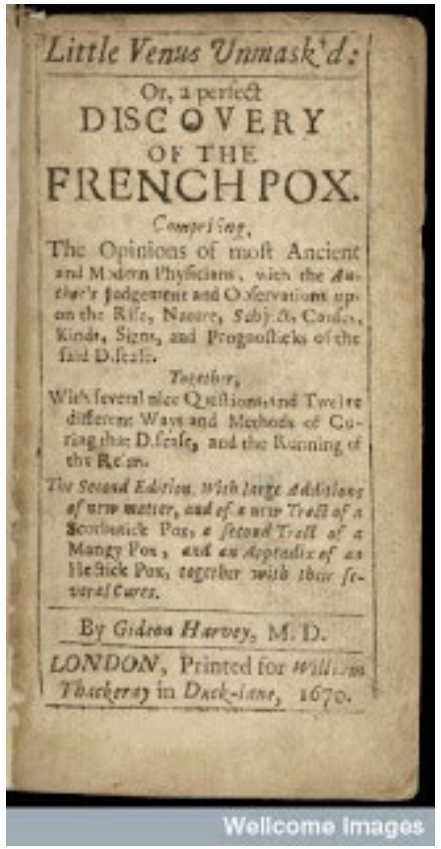
Pandemic H1N1 influenza and age

Epidemics cause panic, and can have substantial social and economic impact even if the epidemic itself is limited.

- Between November 2002 and July 2003 SARS caused 8,273 cases and 775 deaths in 37 countries.
- Around $40bn cost to global economy.

- A major influenza pandemic would have a massive social and economic impact.

Predicting or trying to prevent epidemics is hard. Most new and emerging infections from animals (although we often blame foreigners).


Little Venus Unmask'd:
Or, a perfect
DISCOVERY
OF THE
FRENCH POX.
Comprising,
The Opinions of most Ancient and Modern Physicians, with the Author's Judgement and Observations upon the Rise, Nature, Subject, Cause, Kinds, Signs, and Prognosticks of the said Disease.
Together,
With several nice Questions, and Twelve different Ways and Methods of Curing that Disease, and the Running of the Reins.
The Second Edition, With large Additions of new matter, and of a new Treat of a Scorbutick Pox, a second Treat of a Mangy Pox, and an Appendix of an Hectick Pox, together with their several Cures.
By Gideon Harvey, M. D.
LONDON, Printed for William Thackeray in Duck-lane, 1670.
Wellcome Images

Although the first reaction is usually panic, epidemics should be addressed systematically. Panic kills.

How we respond depends on:

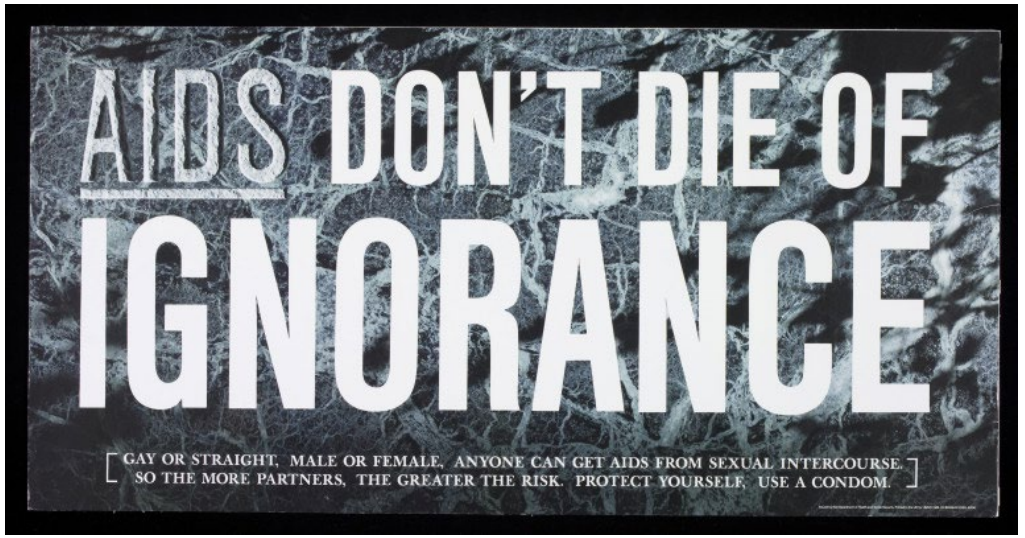
Mortality, severity (virulence).

Treatment available?

Vaccine availability.

Force of transmission.

Route and duration of transmission.



Definitions of epidemic and pandemic.

- Endemic

The background rate of an infectious disease.

May be zero, or very high, but it is the local normal.

May vary by season.

- Outbreak, Epidemic

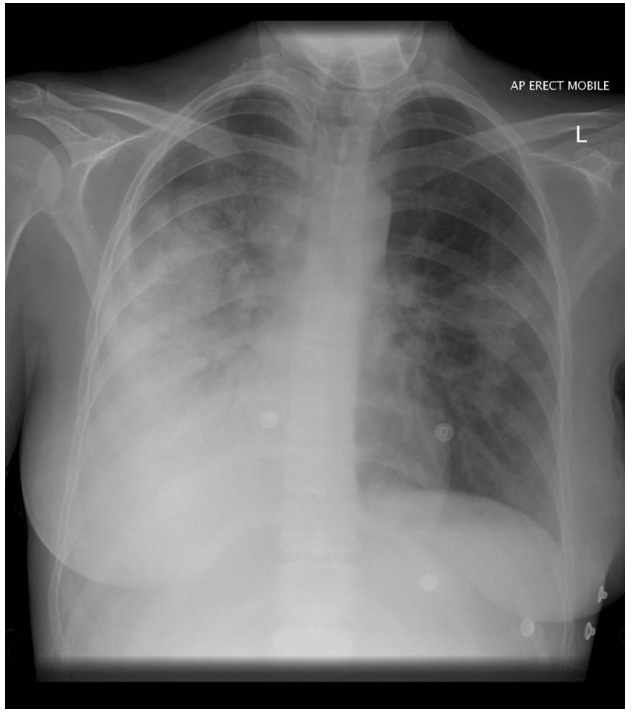
A spike in cases above seasonal background.

Outbreak often used meaning limited in geography.

- Pandemic

An epidemic occurring worldwide, or over a very wide area, crossing international boundaries.

Pneumonia: 29,000 UK deaths/year.



Prof Frank Gaillard, Radiopaedia

Mortality (case fatality ratio) varies widely in epidemics.

- Ebola 60-70%
- Smallpox 30%
- 1918 H1N1 flu 3%
- nvCJD (BSE) 100%

Can vary by nutritional status or age

- Measles- epidemics 5-10% (1:10)
- Measles- endemic UK 1:5000

(figures approximate)

Measles: USA CDC, Nigeria Mike Bligh

Transmissibility and virulence (mortality) of influenza. *Data approximate.*

	Low mortality	**High mortality**
High transmission	**2009 Swine ‘flu (H1N1). 0.3% mortality. 10-200 million cases.**	**1918 ‘Spanish’ ‘flu (H1N1). Around 3% mortality.**
Low Transmission	**Not worth worrying about.**	**2013-18 (H7N9) avian ‘flu. 30% mortality. <2000 confirmed cases.**

Even if controlling the epidemic is not possible, stopping people dying or other serious harm may be. Treatment.

Specific

- Antibiotics. Most new bacterial infections are antibiotic-sensitive.
- Antivirals. These tend to be virus-specific.
- Antiparasitics.
- Disease-specific- eg Vit A in measles.
- Secondary: antibiotics in severe influenza.

Supportive

- Fluids.
- Ventilation.

Wiki

Control of epidemics. Ever since Jenner, get a vaccine….

Known epidemic diseases, effective vaccine.

- Yellow fever, measles, polio, smallpox.

Variants of known diseases with known vaccine.

- Influenza. Lead time 4 months- at least. Vaccine efficacy varies.

New disease: a vaccine will usually take years.

Many diseases vaccines biologically hard- decades.

- HIV, malaria examples.

Vaccine strategies in epidemics.

- The whole population.

Low side effects, easy, (cheap).
Herd immunity.

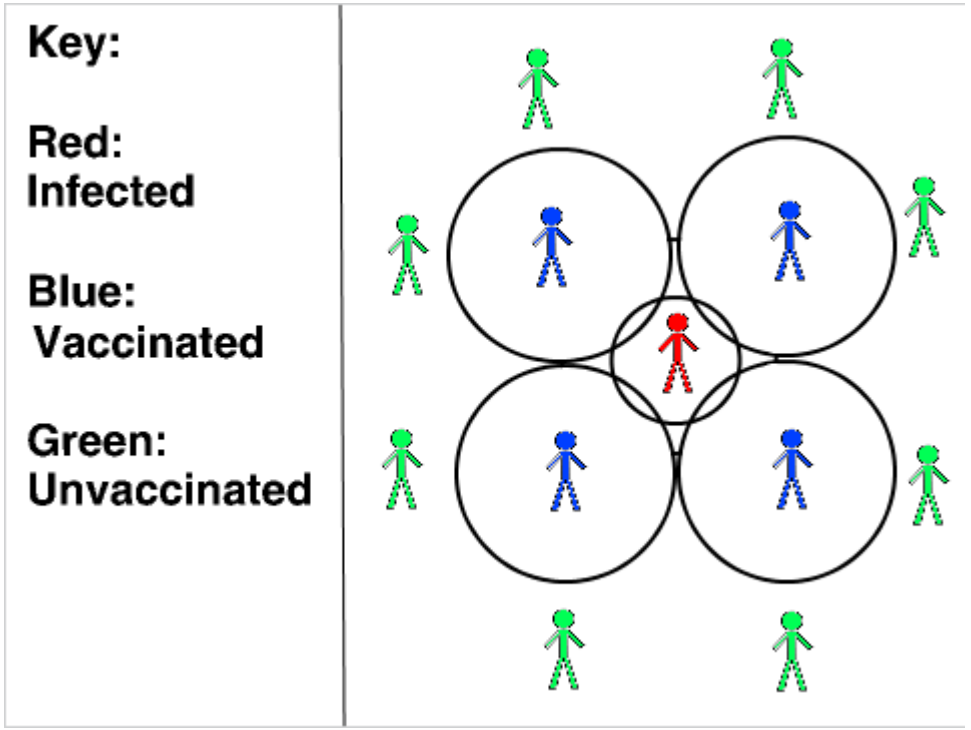
- High risk groups / transmitters.

Effective, (fast acting).

- Ring vaccination.

Fast acting.

Ring vaccination.

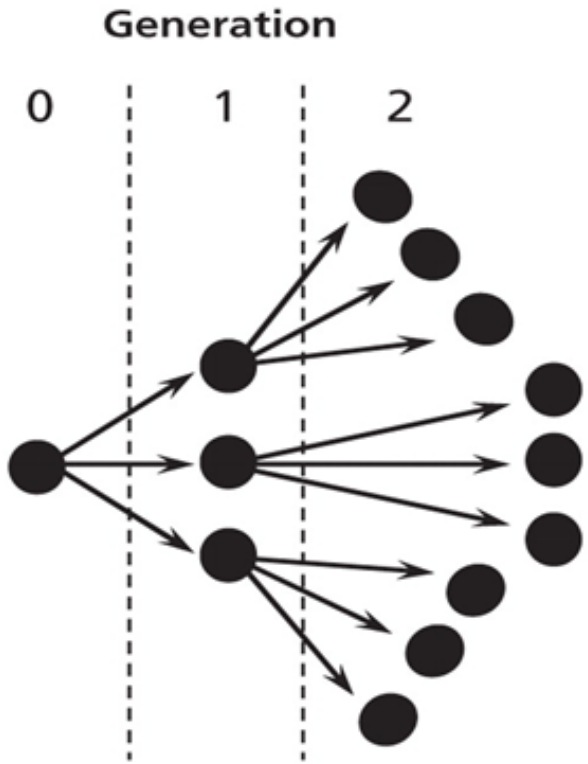


Tom Griffin, CDC, Alex Szymanski

Force of transmission- R_0 and doubling time.

By definition an epidemic must have R_0 over 1.

- ***If*** you can get R below 1 the epidemic dies.



- Ebola epidemic- R 1.2-2.5
- 1918 'flu pandemic R 2-3
- Polio R 5-7
- HIV expansion phase R 2-5
- Measles epidemics R >10
- Malaria in parts of Africa R >100

- Doubling time- how long it takes for twice as many cases.

Route of transmission is key to control.

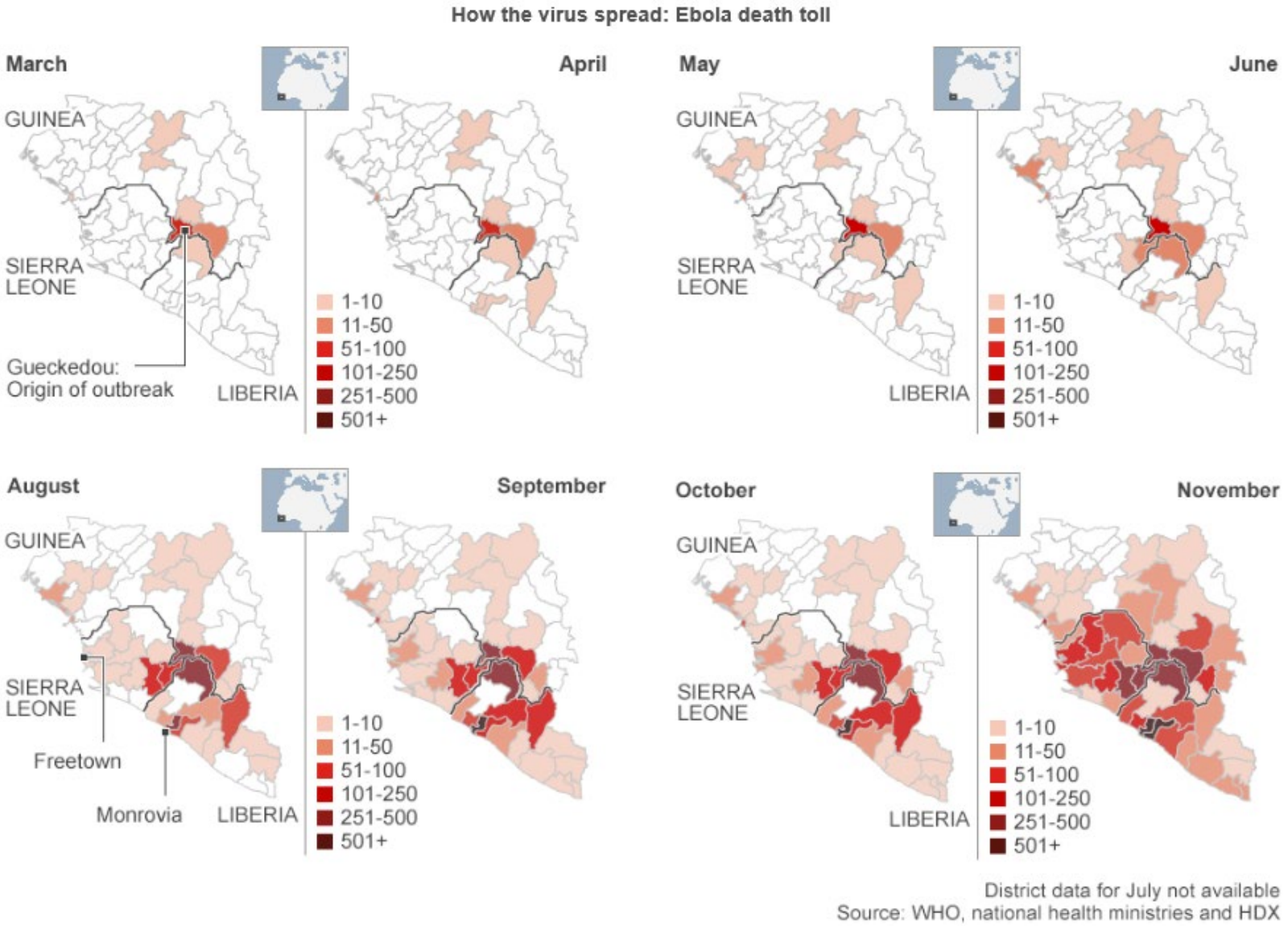
- **Airborne**. Influenza, MERS, SARS.
- **Food, water.** Cholera, typhoid, BSE/CJD.
- **Touch**. Ebola, Lassa.
- **Vector**. Zika, dengue, plague.
- **Sexual (& bloodborne).** HIV, syphilis.

- Usually one route dominant. Sometimes secondary routes.

CDC, Wiki

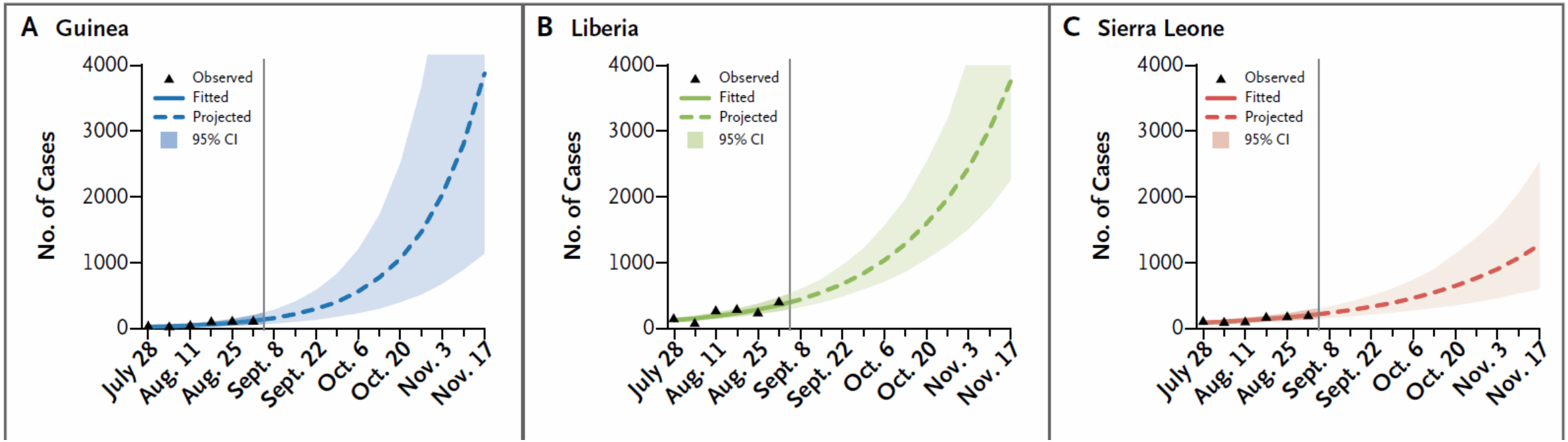
Ebola, April to August 2014. Touch.

(adapted from BBC, data from Ministries and WHO).



Ebola: *The First 9 Months of the Epidemic and Forward Projections.*

WHO- NEJM Aug 2014



Ebola. Situation at the start of the 2014 epidemic.

- High mortality (>60%). Over 11,000 died.
- Medical countermeasures limited.
- No vaccine, although extensive animal data. At least a year.
- R_0 1.5-2.5.
- Doubling time about 2 weeks.
- Main route of transmission touch.
- Only infectious when symptomatic.
- Infectious after death.

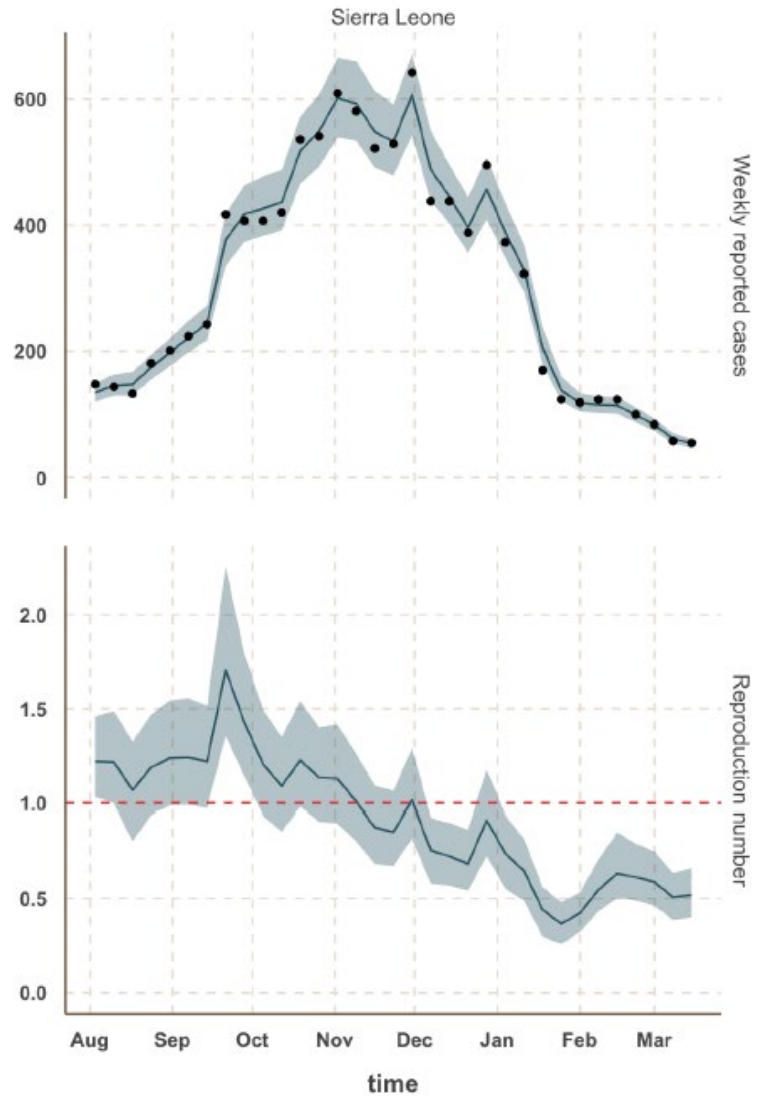
Cosmos for MSF

Interventions to get R_0 below 1.
Isolate and barrier-nurse sick and dying people, reduce touching.

- Reduce transmission in hospital and other healthcare settings.
- Reduce transmission around death and safe burial.
- Reduce transmission in the community by shortening the time between first symptoms and isolation.
- Increase social distancing.

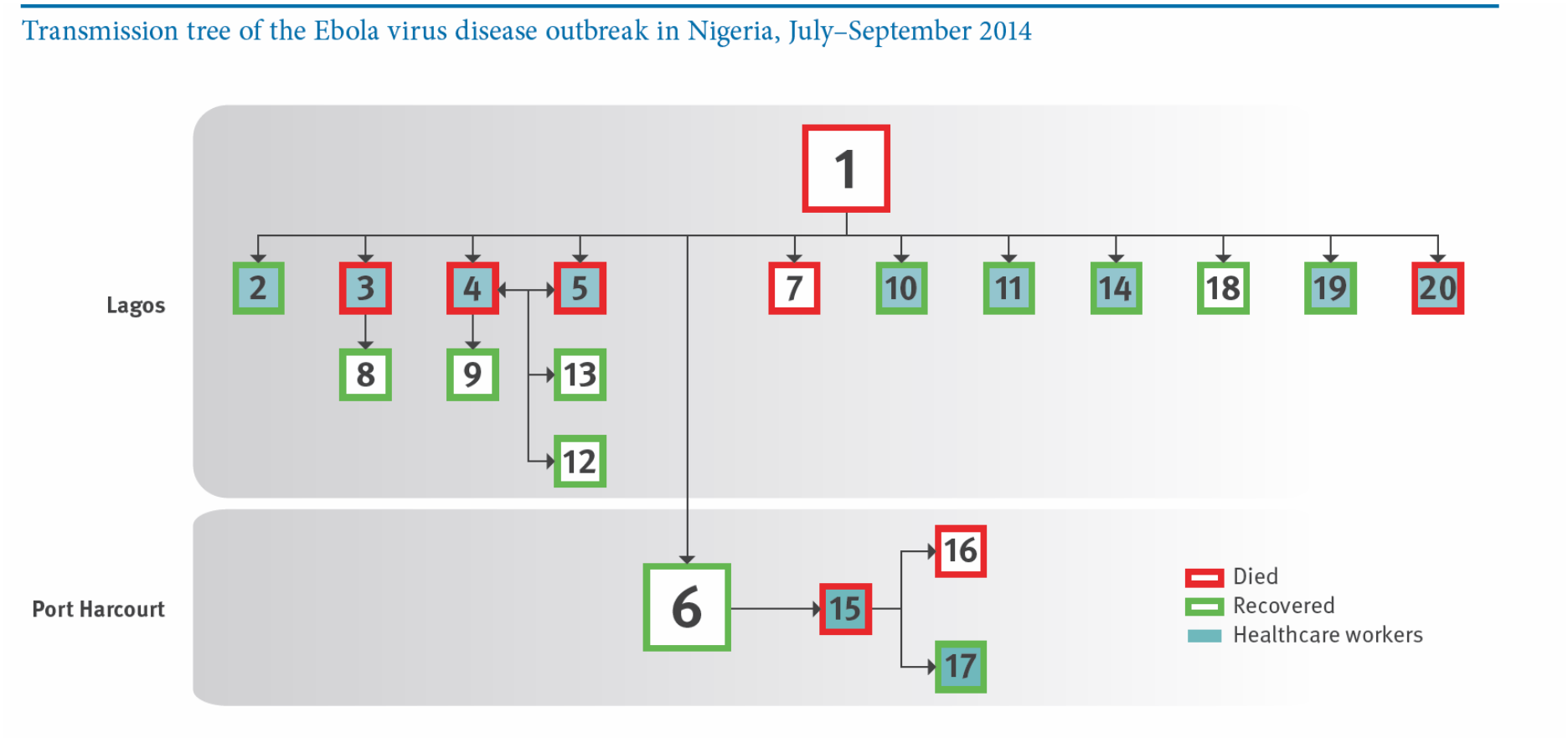
Dr Umar Khan
(*Sierra Leone Telegraph*)

R_0 Sierra Leone- much more useful than raw numbers to guide tactical response. *(Edmunds et al)*



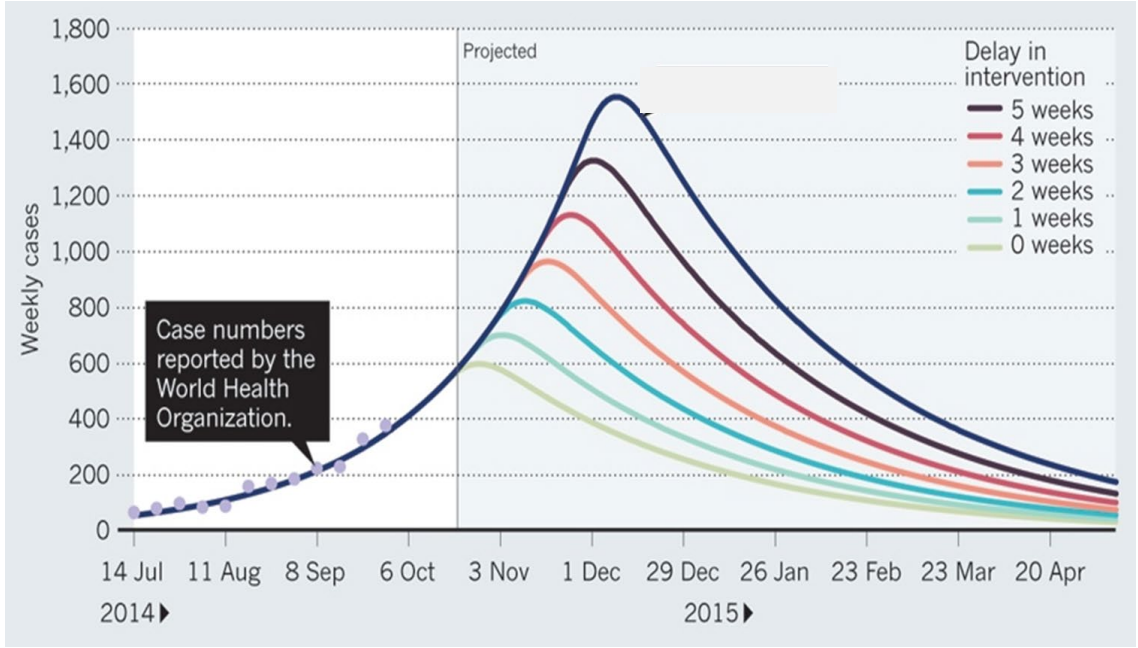
The heavy burden on healthcare workers: Ebola virus disease outbreak in Nigeria, July-Sept 2014

F O Fasina. Eurosurveillance



Between a rock and hard place on response- heathcare workers most essential, most vulnerable.

- Massive epidemiological advantage to rapid reaction.
- This depends on healthcare workers (HCWs).
- The initial incidence of Ebola in HCWs estimated around 8-10% per person per year. Over 70% died.



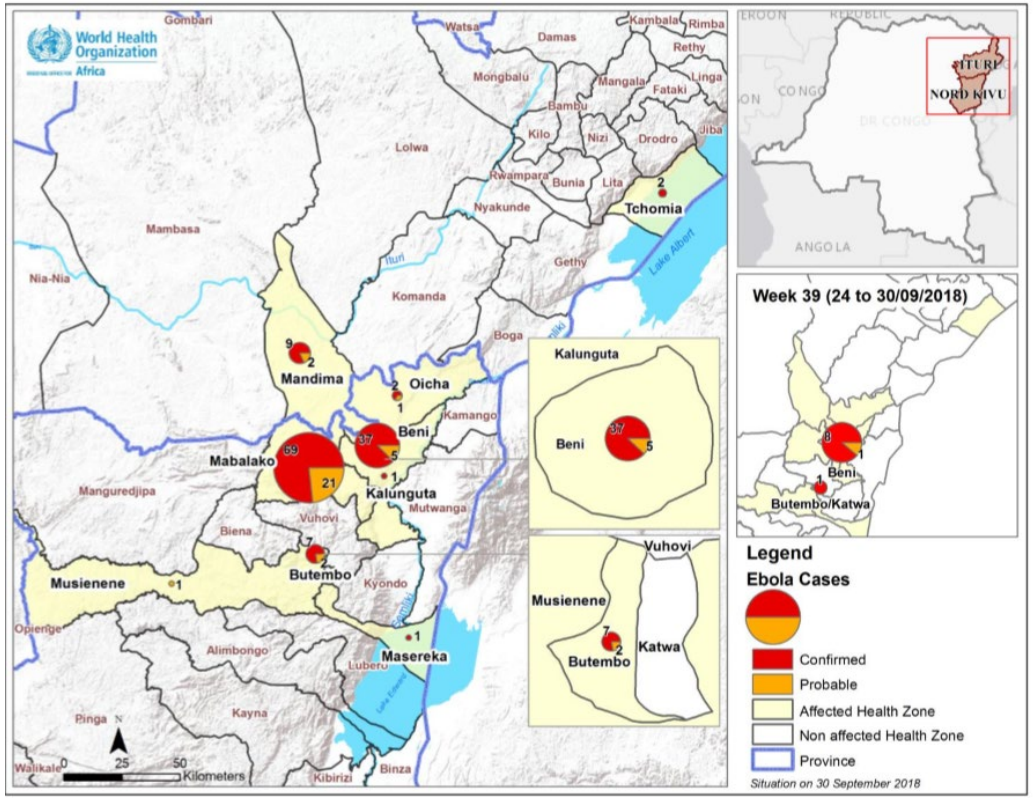
Modelling the impact of delay in intervention by week in Sierra Leone.

(Whitty et al Nature, analysis by Ferguson et al)

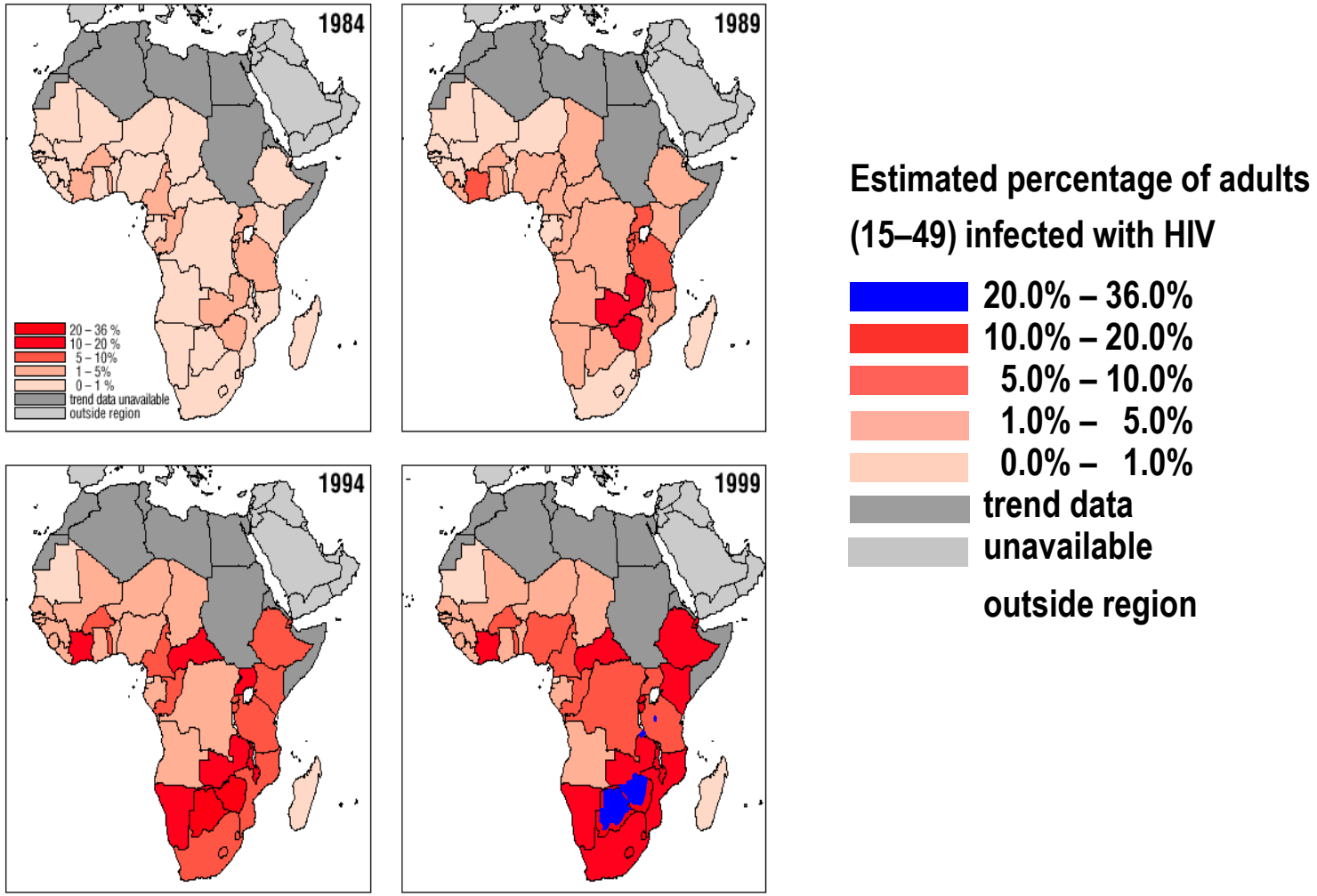
Ebola DRC 2018 (second outbreak of the year).

- The positive difference is we have a vaccine.
- Used for ring vaccination.

- Social interventions more difficult.
- Armed groups, politics, distrust of the government.
- Around 160 cases so far.

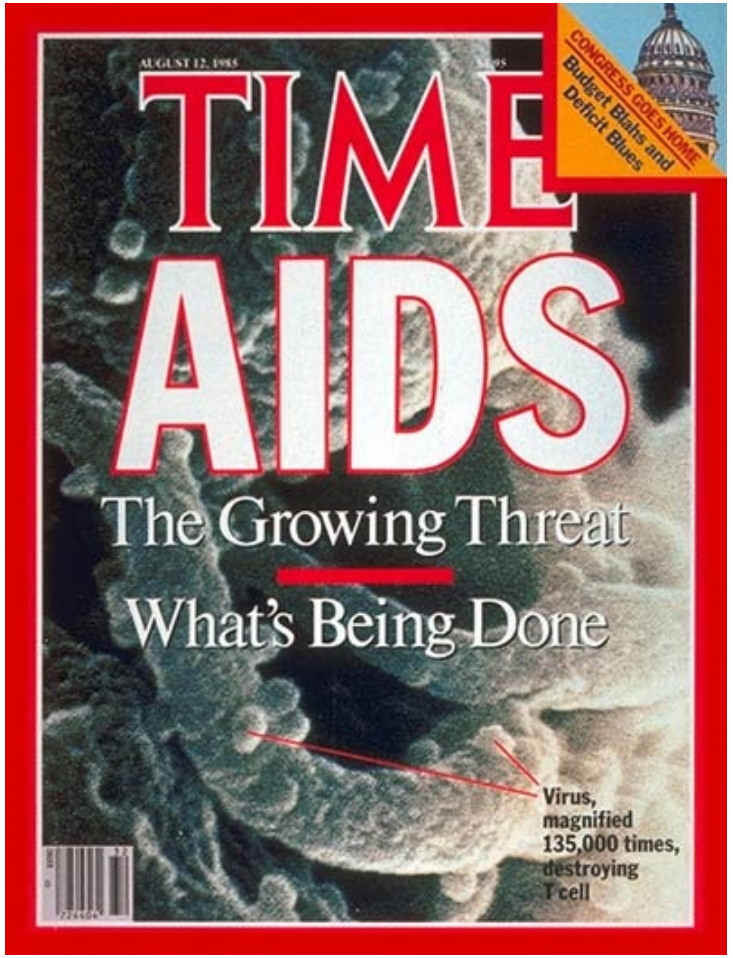


HIV/AIDS pandemic: sexual (intravenous). Around 35 million deaths. Spread of HIV sub-Saharan Africa, 1984-99.



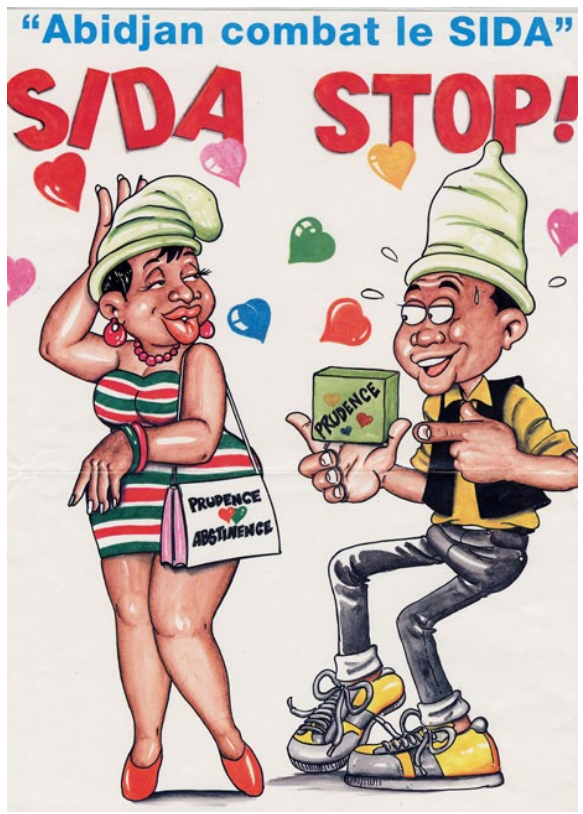
HIV. Situation at the start of the epidemic (1981 recognised).

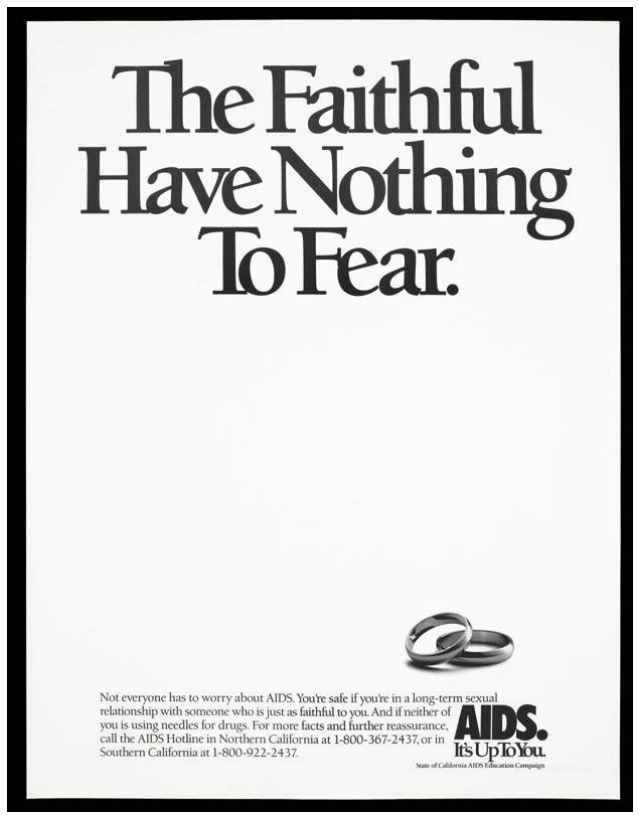
- High mortality (>99%). Around 35 million deaths to date.
- Medical countermeasures limited.
- No vaccine.
- R_0 2-5 (highly variable).
- Main route of transmission sexual.
- Secondary route intravenous.
- Infectious when not symptomatic, for many years.



Time, 1985

Many approaches to changing sexual behaviour. Not all work.
Getting people to know their HIV status important.





Intravenous drug route- behaviour change and needle exchange.

Drugs to treat people living with HIV/AIDS.

- First antiretroviral (AZT) 1986. Failed fast (within weeks).
- Combination treatment (HAART) era started 1996. Very expensive, side effects.
- Gradual increase in effectiveness, reduction in price.
- Now widespread use (but still under 50% of those with HIV globally).
- At least as good outlook as those without HIV.
- Suppress- not cure.

NIAID/Wiki

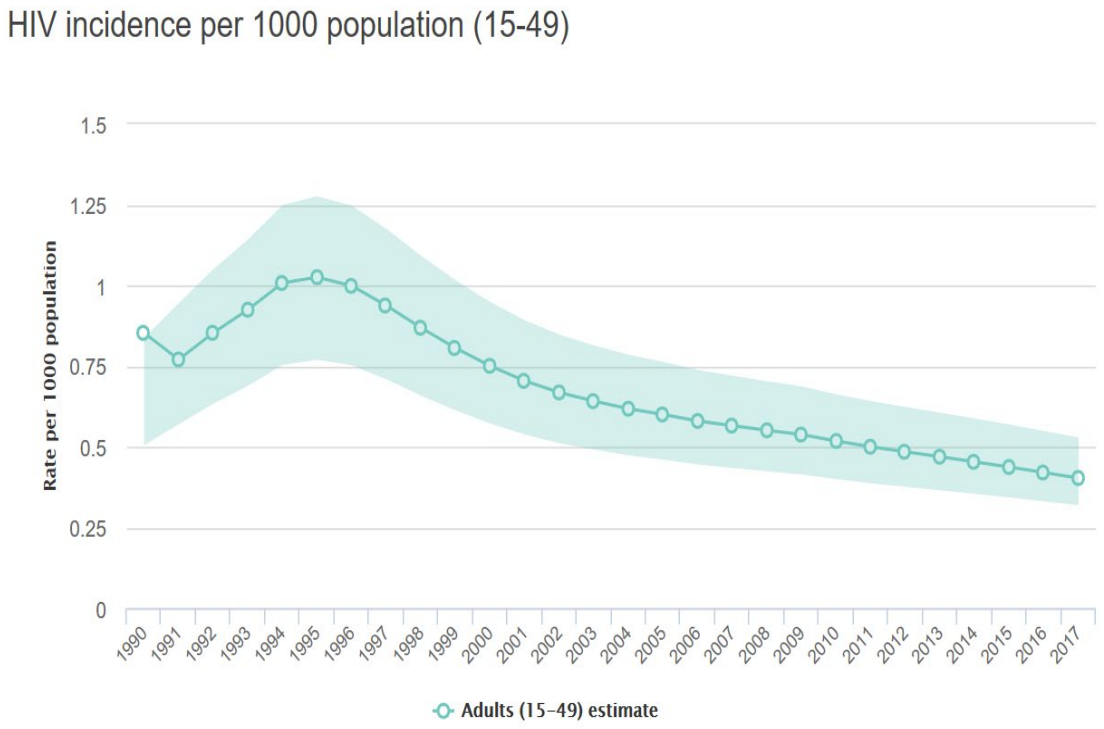
Vaccines, and drugs to *prevent* HIV.

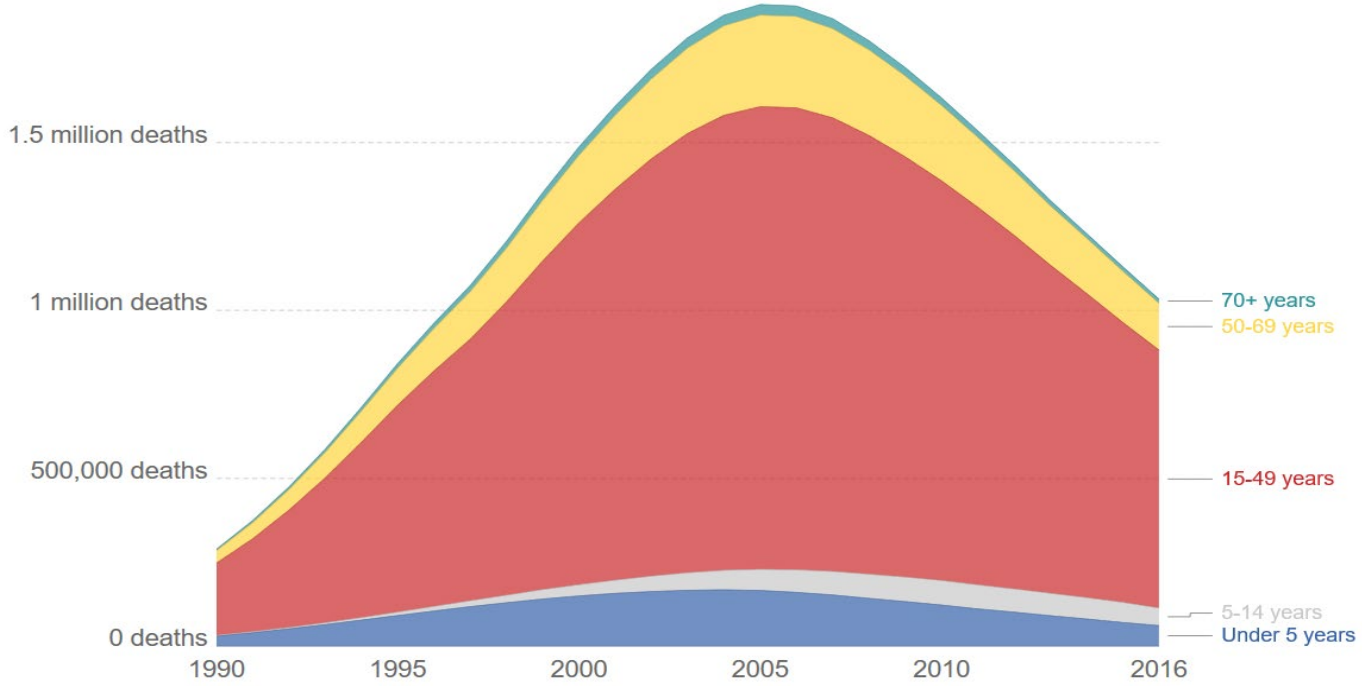
- There has been huge investment and great science to get an HIV vaccine over several decades.
- We still do not have one.

- People on effective drug treatment are much less infectious.
- Drugs can be used as prophylaxis in high-risk encounters.

HIV incidence age 15-49 and deaths by age. 1990-2017.

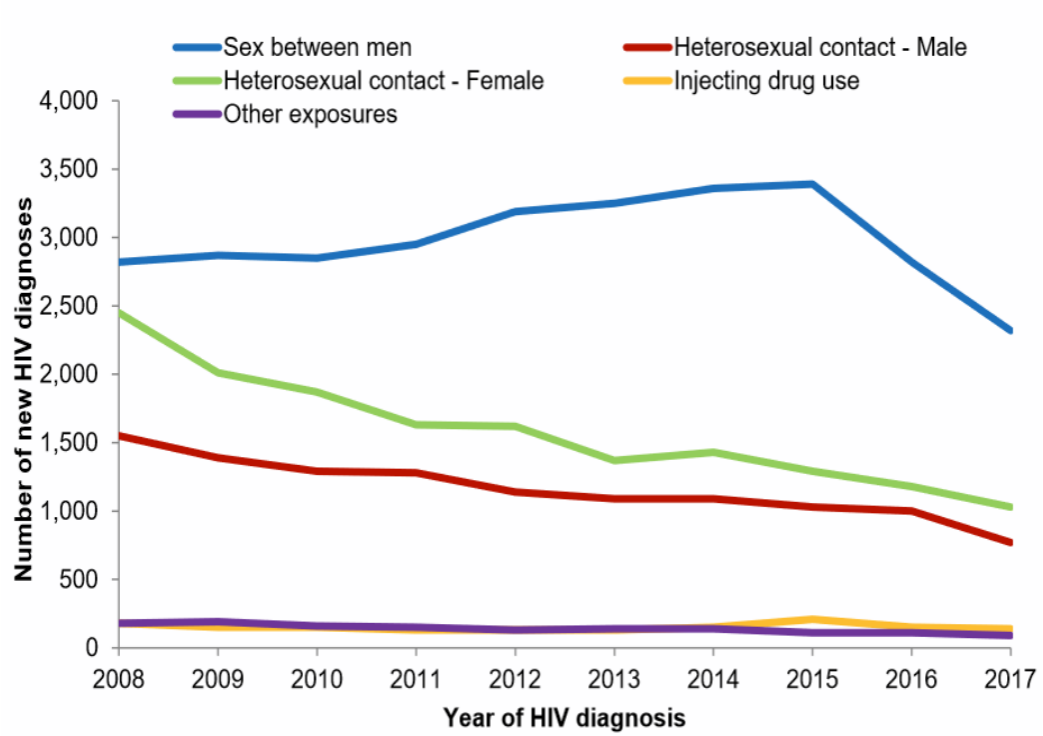
(UNAIDS/IHME/Our World in Data)





In high-income countries HIV new cases generally dropping, deaths rare. UK experience.

- HIV pandemic has dropped out of the news because deaths are much rarer.
- Around 1.8 million people became newly infected with HIV in 2017.
- 940 000 people died from AIDS-related illnesses (UNAIDS).
- Likely we will need either a vaccine, or a curative drug to terminate it.
- But it is in slow retreat.
- Some parallels with syphilis in UK.



*Adjusted for missing route of exposure

PHE data, Sept 2018.

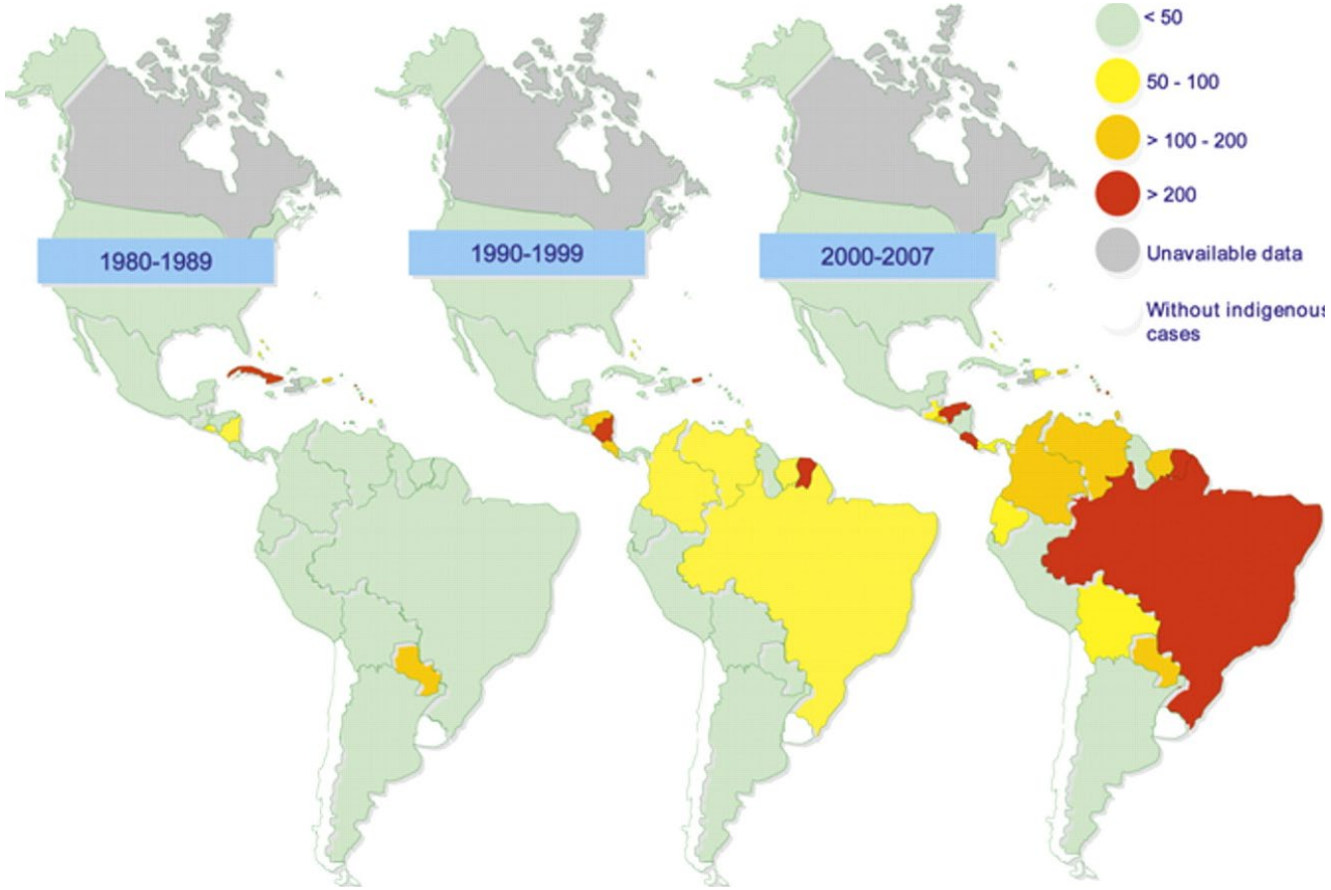
Vector-borne epidemics- now rare in UK but remain a global risk.

- Vector-borne epidemics were common in England when this College was founded.
- Epidemic typhus (flea)
- Plague (flea)
- Malaria (mosquito)

- UK currently has few vectors with epidemic potential- ticks, midges.

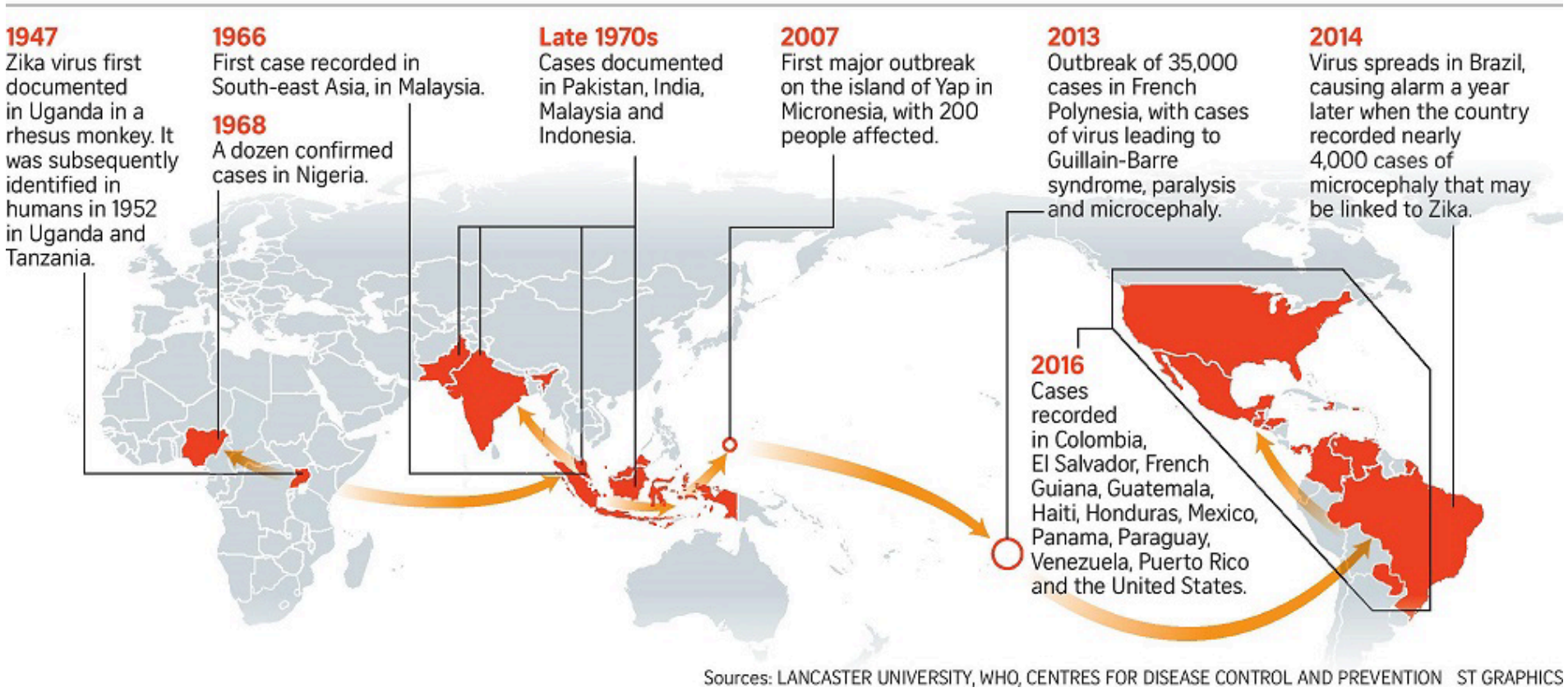
- Globally vector-borne epidemics are common.
- Mosquitoes the main culprit.
- Sandflies, fleas, biting flies, ticks, mites all capable of transmitting disease.

Aedes adapted to peri-urban living. Dengue spread in the Americas. Global dengue reported cases from 0.4M 1996 to 3.2M 2015 (WHO).

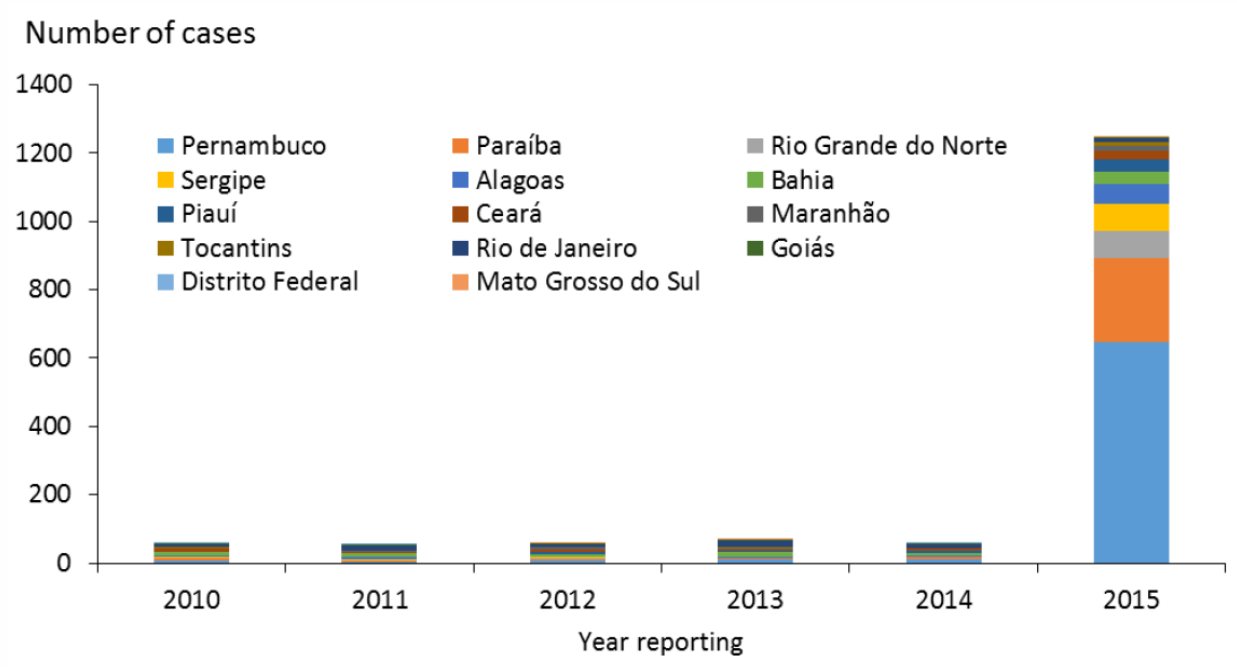


San Martin JL et el 2010 JASTMH. Incidence/100,000

Zika: vector-borne.



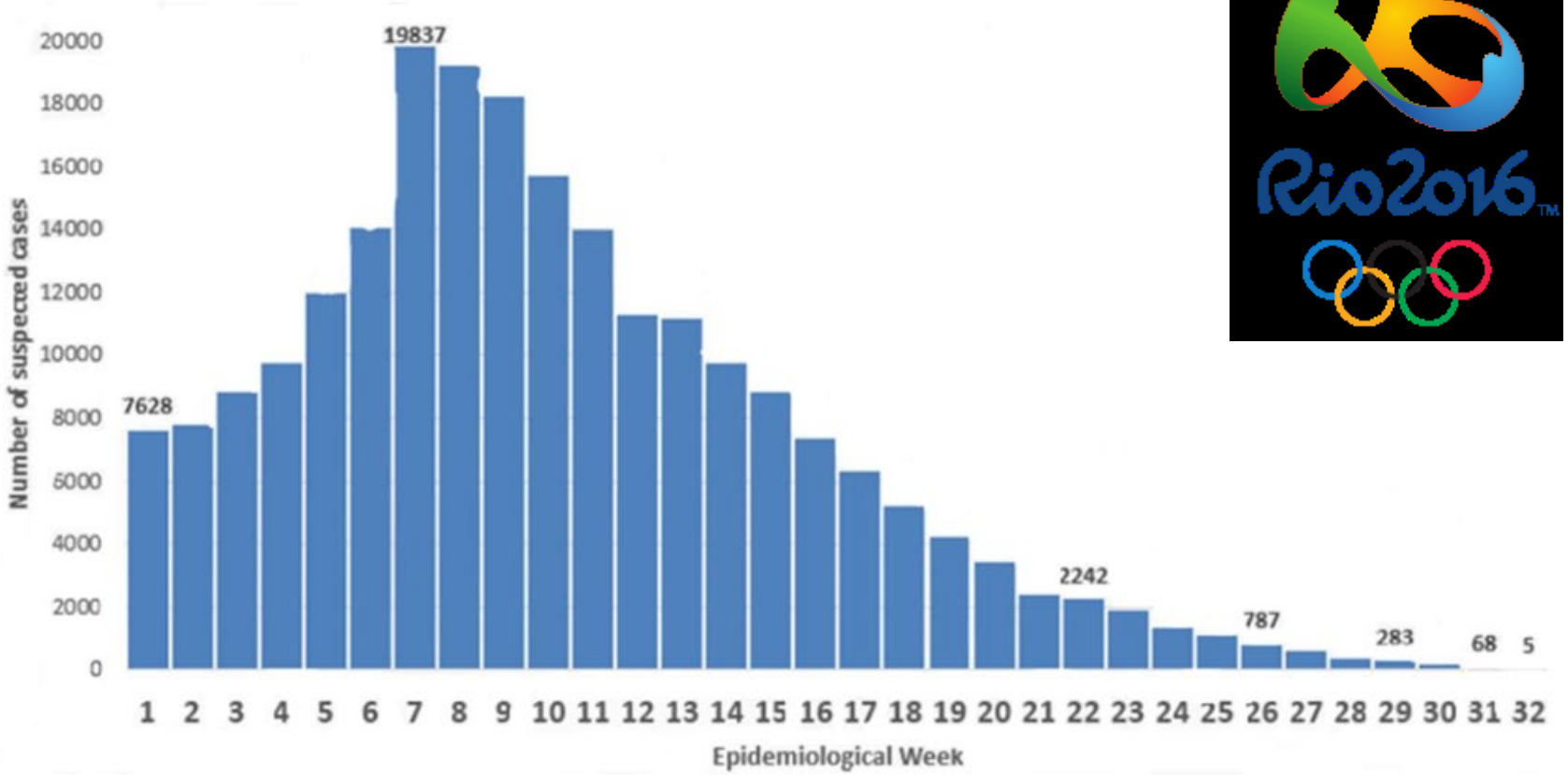
Notified cases of microcephaly in Brazil, November 2015.



Zika. Situation at the start of the 2015 epidemic.

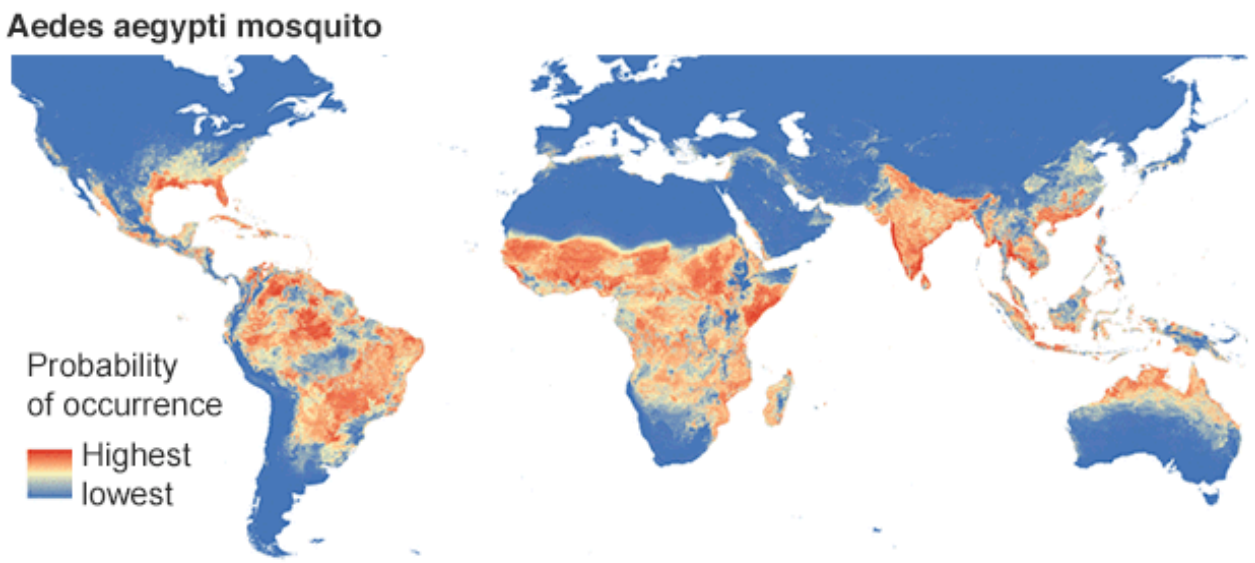
- High transmission in Brazil.
- Around 12% of pregnancies in first trimester, (lower later trimesters) had fetal abnormalities.
- No drugs.
- No vaccine.
- Route of transmission Aedes mosquito- not easy to control.
- Secondary route sexual?

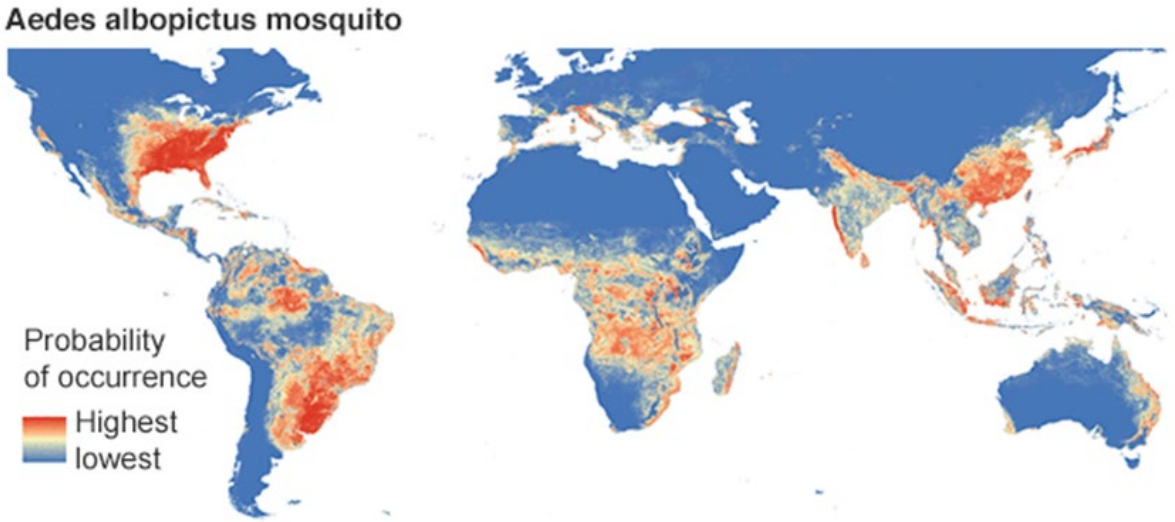
Zika cases by week, Brazil, to September 2016.



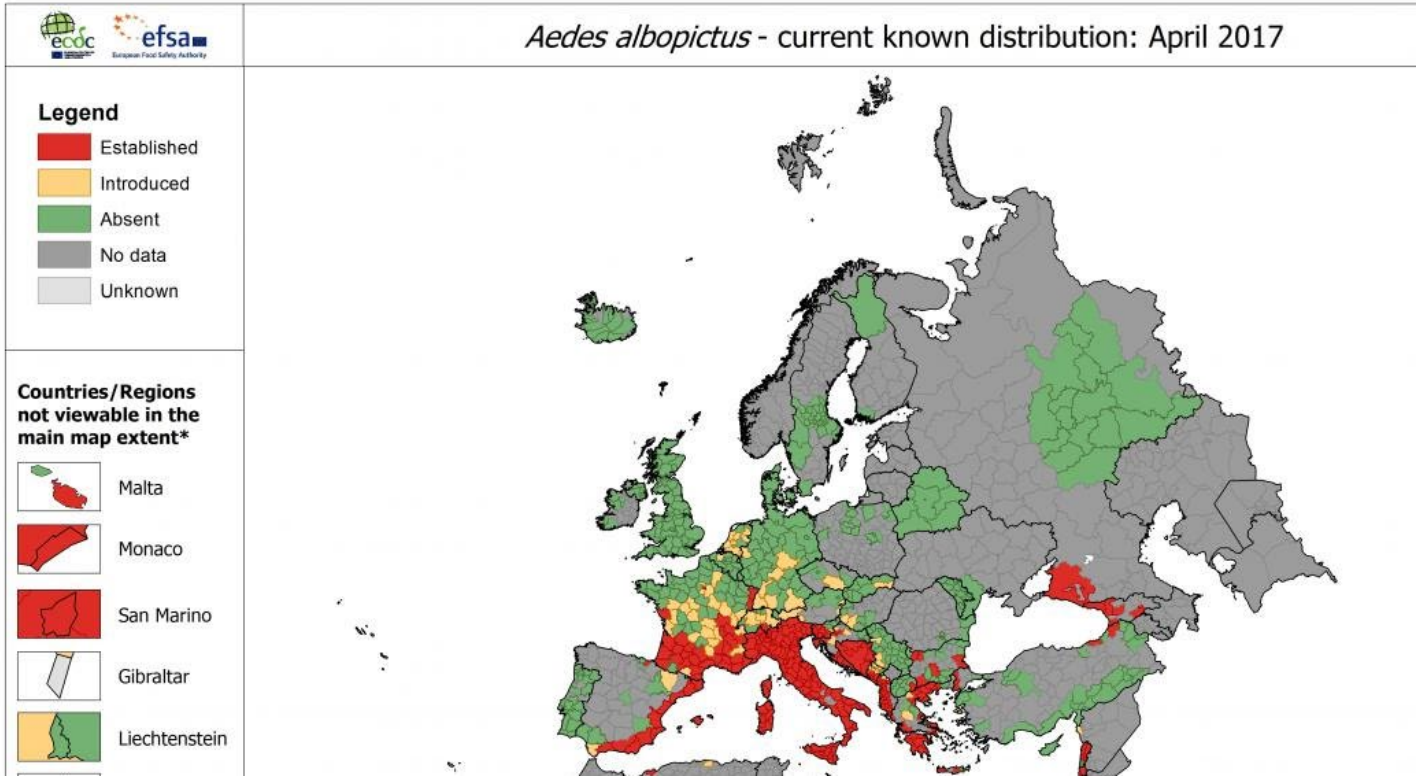
Source- PAHO

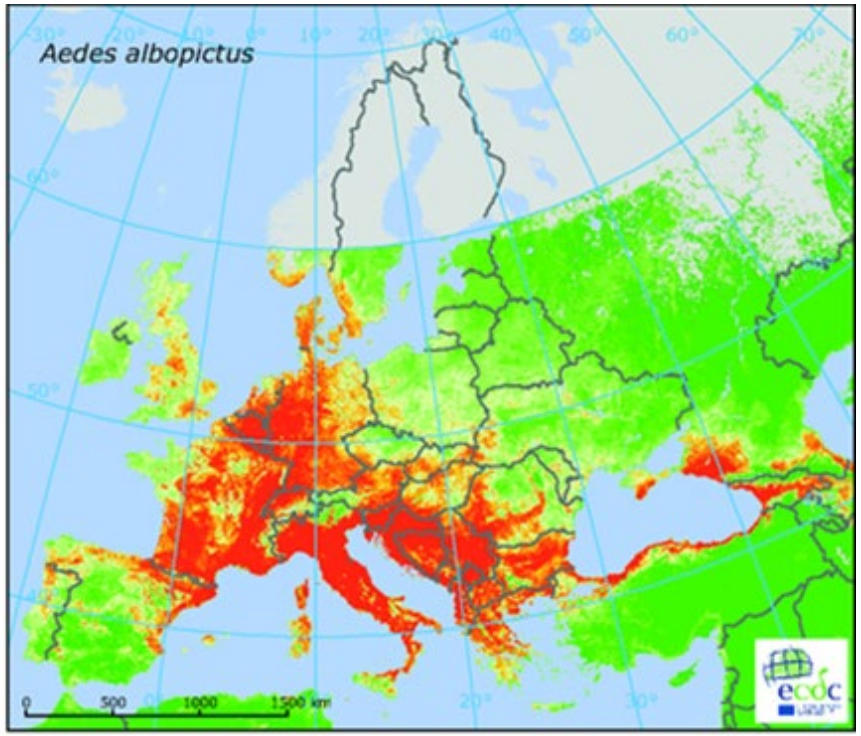
Potential for spread limited to vector distribution *(CDC).*

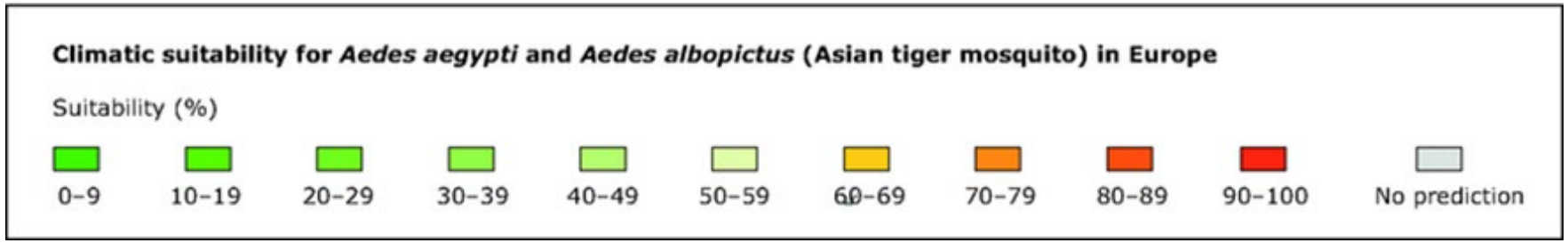




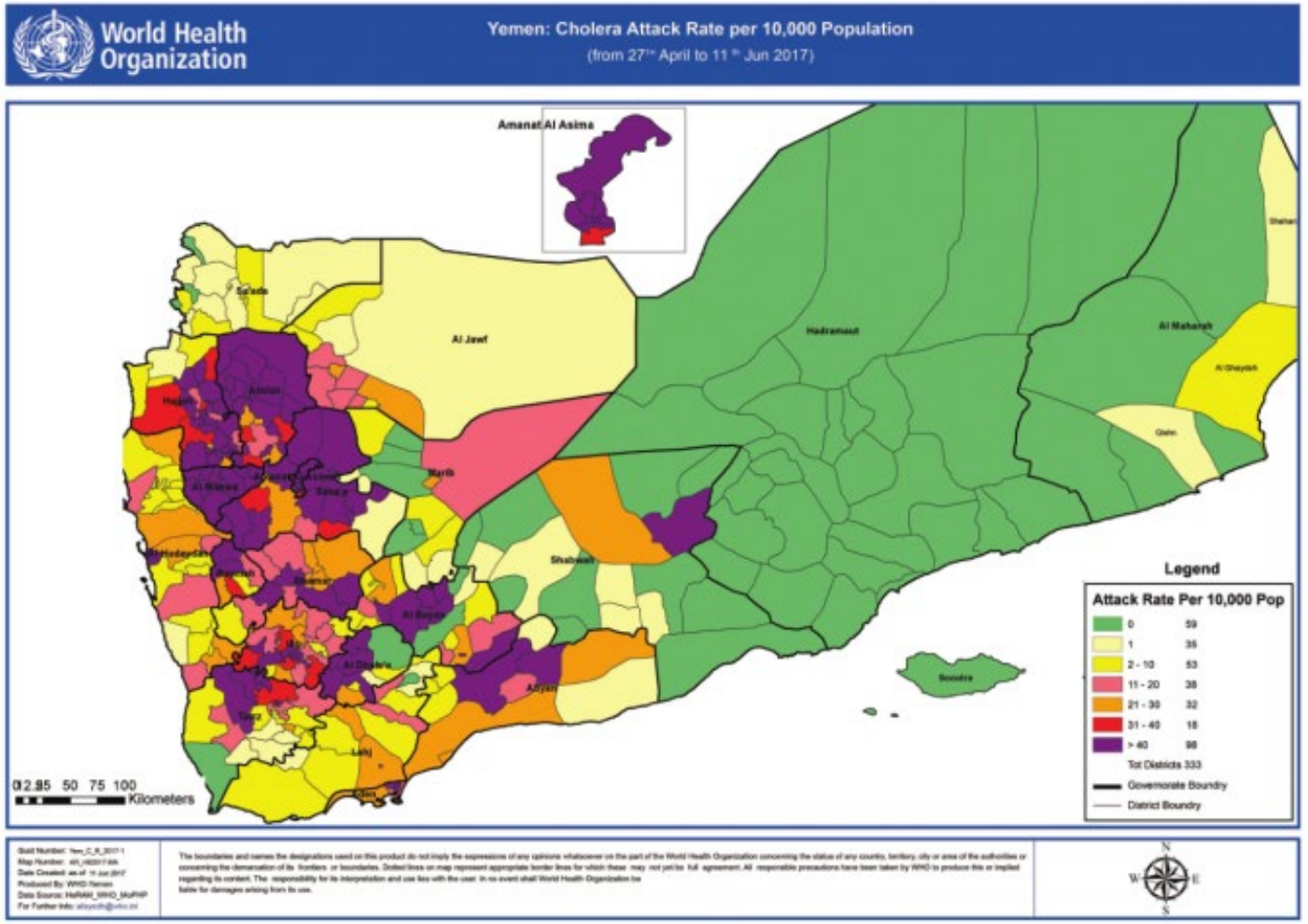
Current and potential *Aedes albopictus* in Europe (*ecdc*).



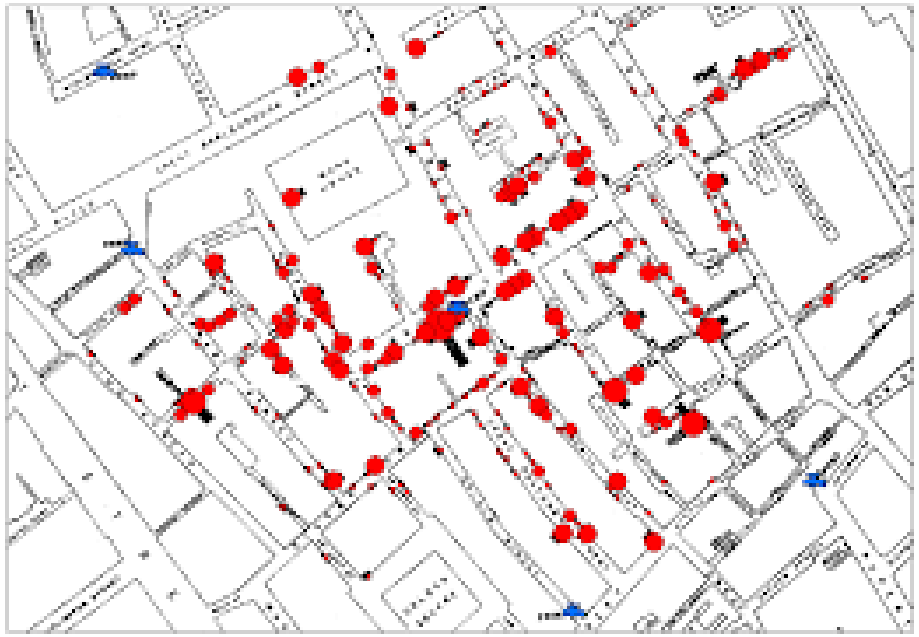




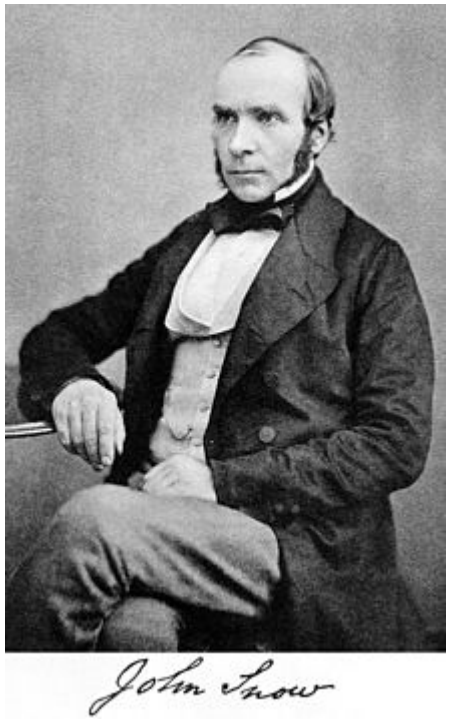
Cholera- water. Yemen 2017-18. 1.2 million suspected cholera cases and 2,515 associated deaths. 29% cases children <5. Currently about 10,000 cases a week. *UN/WHO*



Cholera one of the first properly epidemiologically investigated diseases. We know what to do in the absence of conflict. Sanitation, clean water.



R. Wilson augmented John Snow's original map of 1854

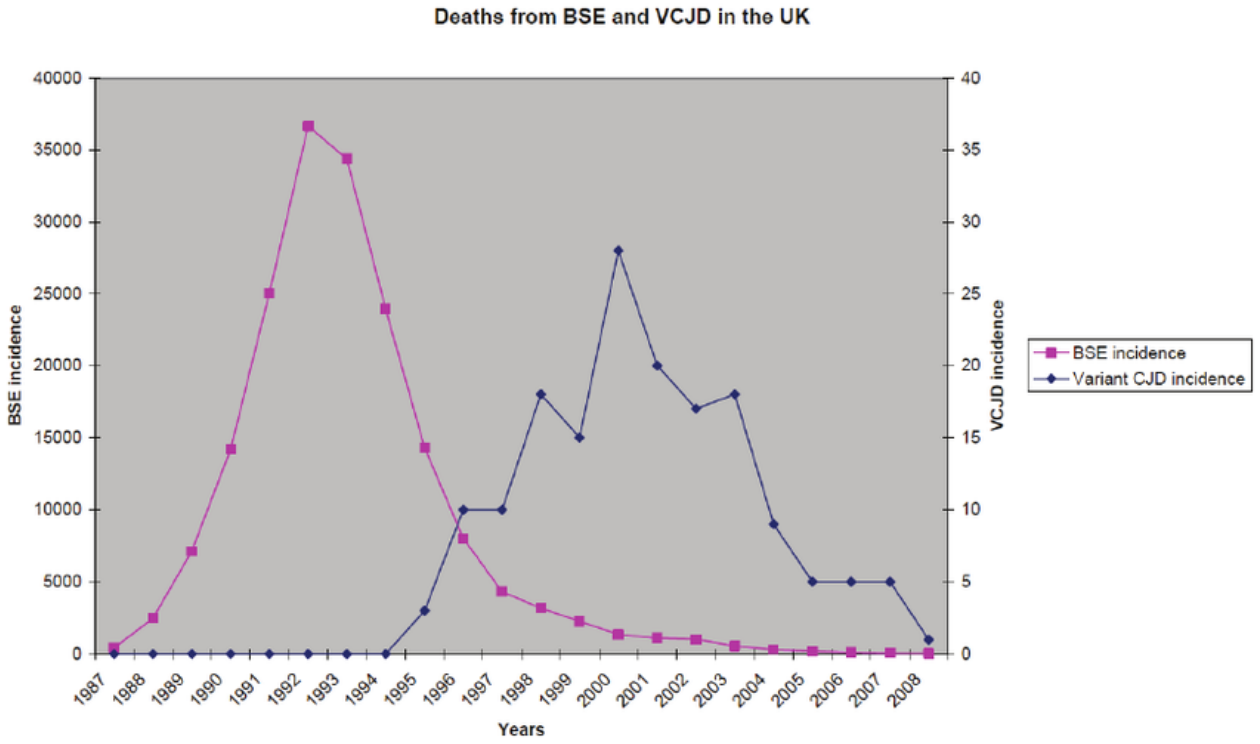


War, civil unrest and disaster: epidemics have always followed, always will. ‘Development in reverse’.

- Water, sanitation, housing, vaccine programmes, nutrition destroyed.
- Old foes like typhoid, typhus, cholera remerge.
- Rapid movement of populations exposing non-immunes to endemic diseases.
- Move into marginal land, flooding- vector-borne diseases.
- Breakdowns of social norms- STI.

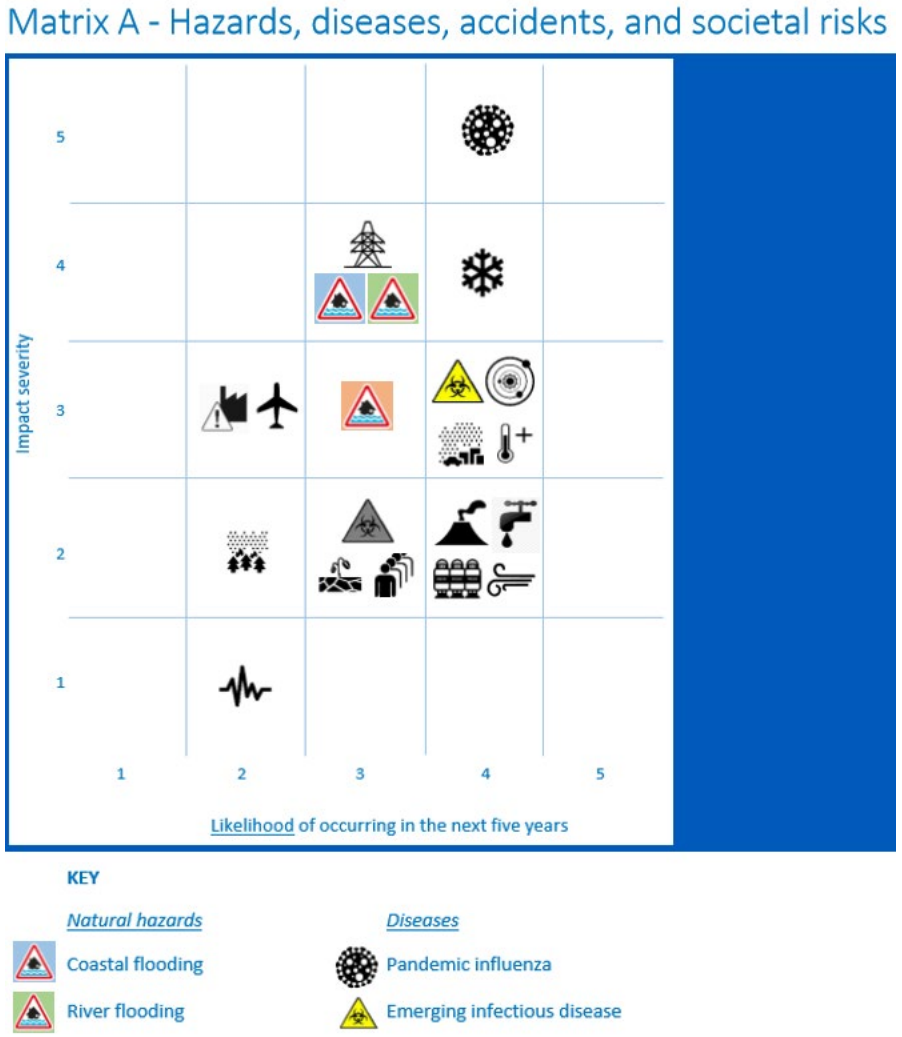
War, famine, pestilence, death.
(Durer: Four horsemen of the Apocalypse)

BSE/nvCJD. Food. Not destroyed by cooking, so removing from the foodchain was essential. Over 180,000 BSE cases, 178 cases nvCJD UK. Massive culling, removal of offal and neurological tissue, change in feed.



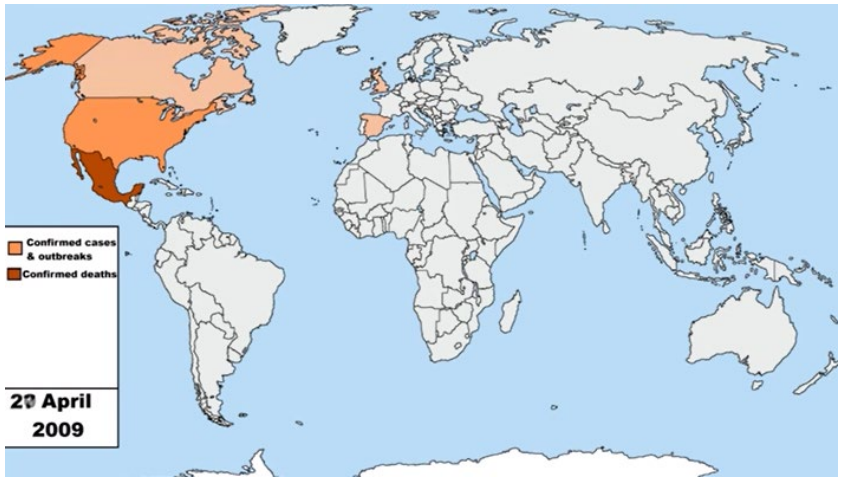
Mackay et al 2011

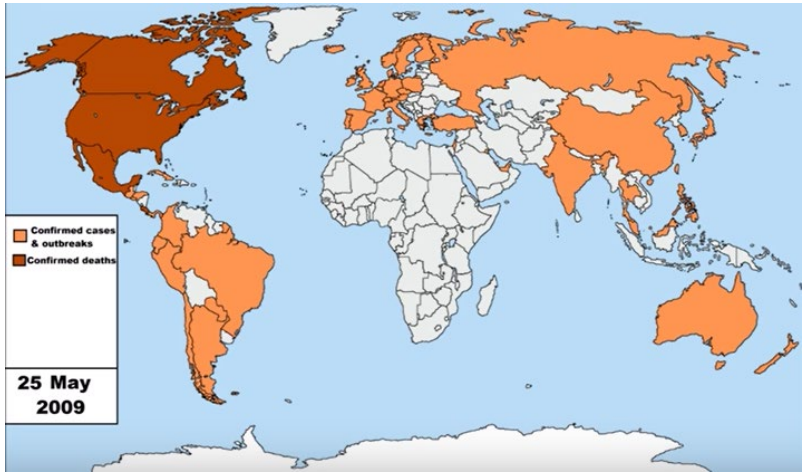
There is a reason pandemic influenza remains the highest risk on the UK National Risk Register.

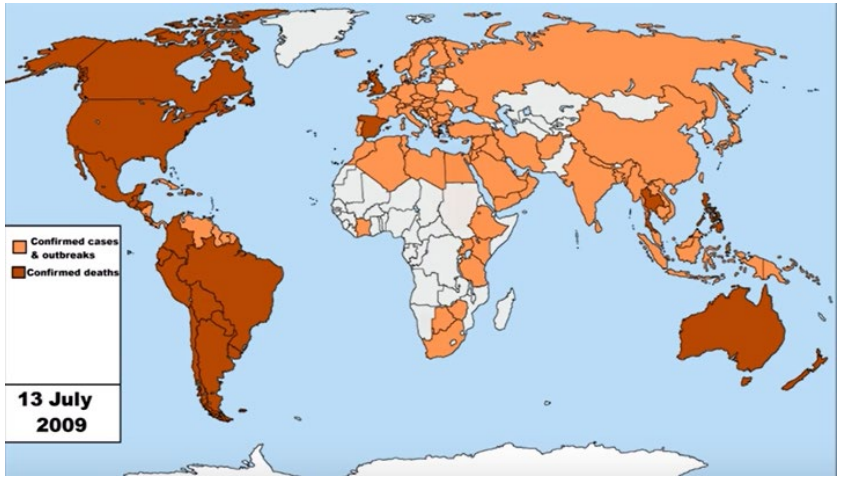


- Airborne disease is indiscriminate.
- Much more difficult to interrupt than other transmission routes.
- The speed of an influenza pandemic is rapid, and high proportions of the population would be affected.
- The last pandemic we had (2009) relatively low virulence, but substantial numbers.

H1N1 2009.







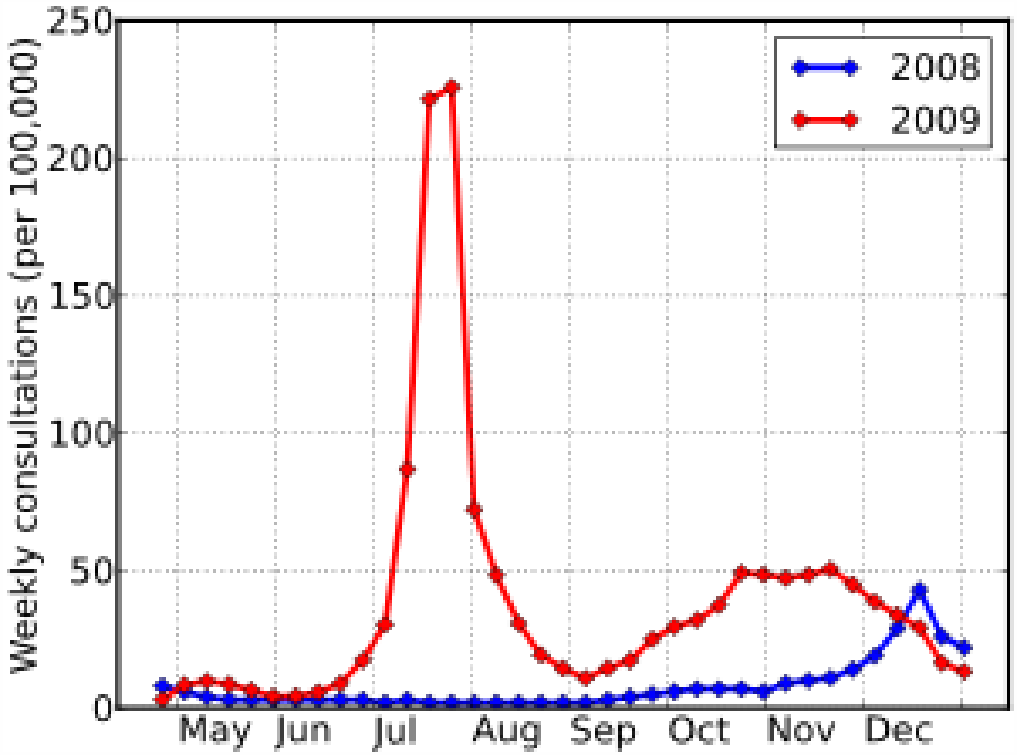
43-89 million cases 2009-10 (CDC)

8-18 thousand deaths (CDC)

Wide estimates on numbers.

Mark Honigsbaum

The peak of transmission of H1N1 2009 in the UK came on fast.



GP consultations for influenza-like illness.

- Officially 457 deaths. Two waves.
- Vaccine was available, but well after the peak.
- Drugs were controversial. Most useful if taken early. Single mutation renders largely ineffective.
- Various interventions called for- screening at airports, banning travel, closing schools.

We can put the building blocks in place for a pandemic influenza response. No plan survives contact with the enemy…

- Mathematical models to predict global and national course from early data.
- Global virus identification network.
- Pre-decide which bits of the UK health system, education etc we turn off.
- Optimise vaccine production- but 4 months shortest current lead time.
- Antiviral stockpile.

CDC, wiki

Although the first reaction is usually panic, epidemics should be addressed systematically. Panic kills.

How we respond depends on:

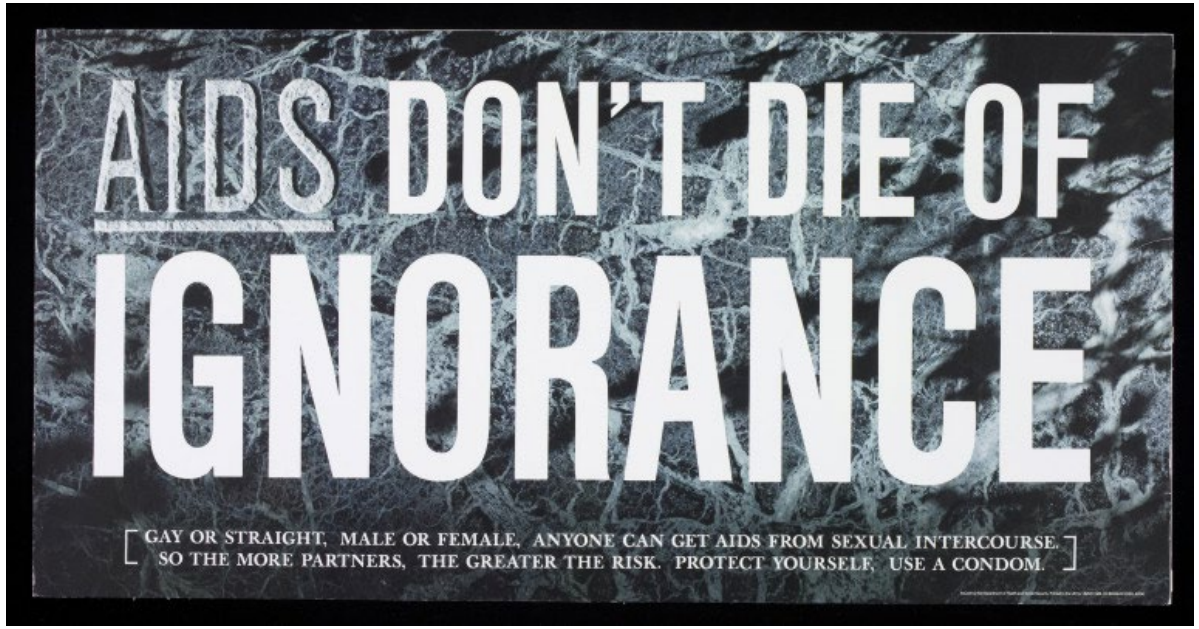
Mortality, severity (virulence)

Treatment

Vaccine availability

Force of transmission

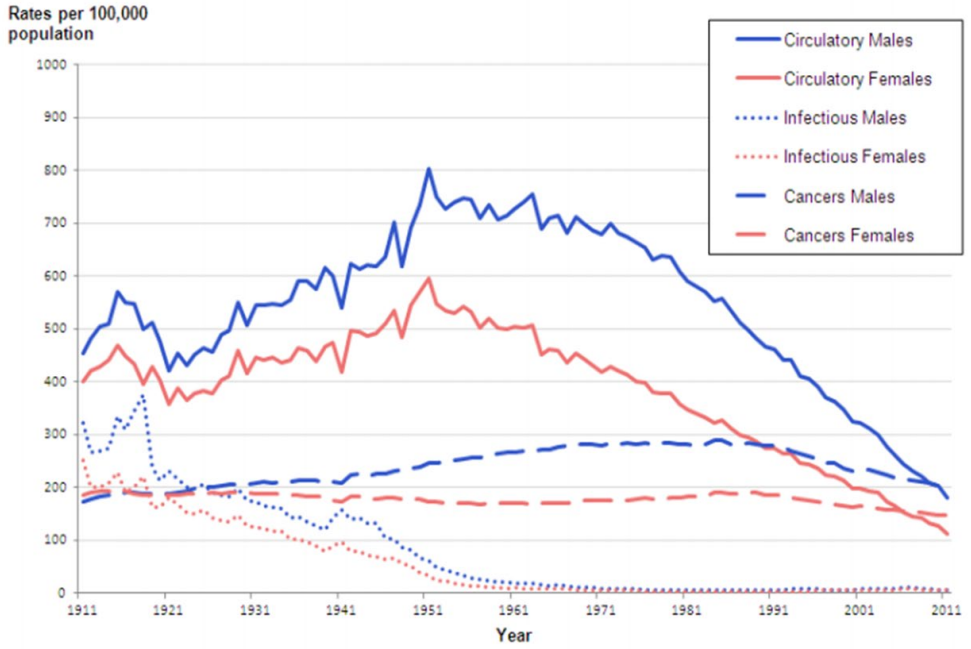
Route of transmission.



Once we determine route and force of transmission of epidemics:

- Ebola. Behavioural change, isolation, now vaccine.
- HIV. Behaviour change, drugs.
- Zika. Vector control, vaccine.
- Cholera, vCJD. Safe water, safe food, absence of war.
- Influenza. Vaccine, drugs, societal organisation.

- Society changing (normal) behaviours is usually central to controlling epidemics by whatever route.



UK mortality. ONS

In Sir Thomas Gresham's lifetime (c1519-1579) infectious diseases dominated medicine.

- Epidemics will always occur, but the risk is substantially smaller.
- Wealthier countries are hardened against epidemics through better housing, nutrition, safe water and food.
- Those who bring peace and prosperity do at least as much to prevent future major epidemics as doctors and scientists.