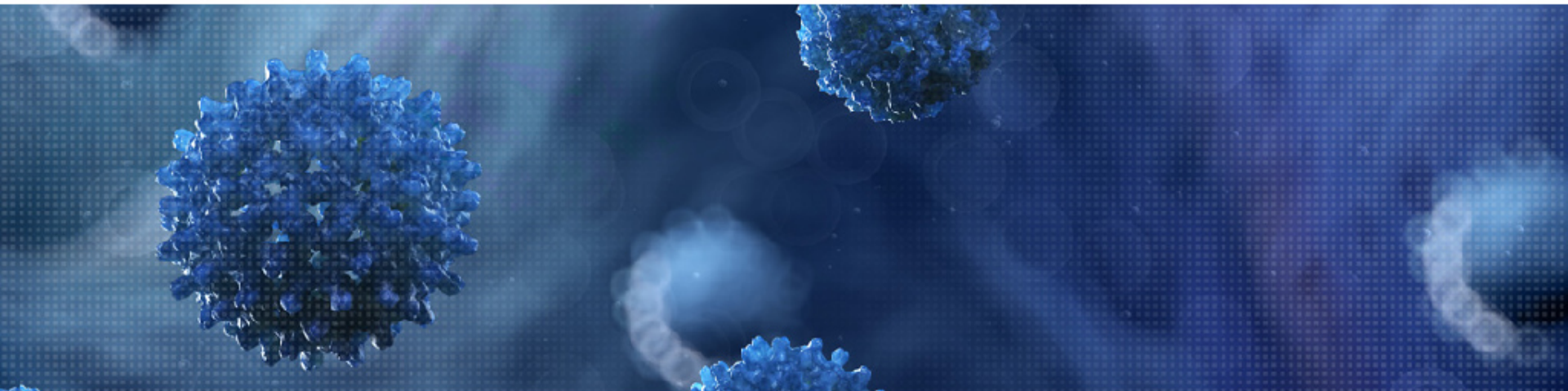


Erasmus MC



**Viroscience lab**

WHERE SKILLS MEET TO STUDY & PROTECT



Bridging the gap between clinical research and public health in infectious disease outbreaks

Prof Dr Marion Koopmans

# Key public health questions at early stage of an outbreak



- How bad is it?
- How far has it got?
- How fast does it spread?
- What can we do about it?

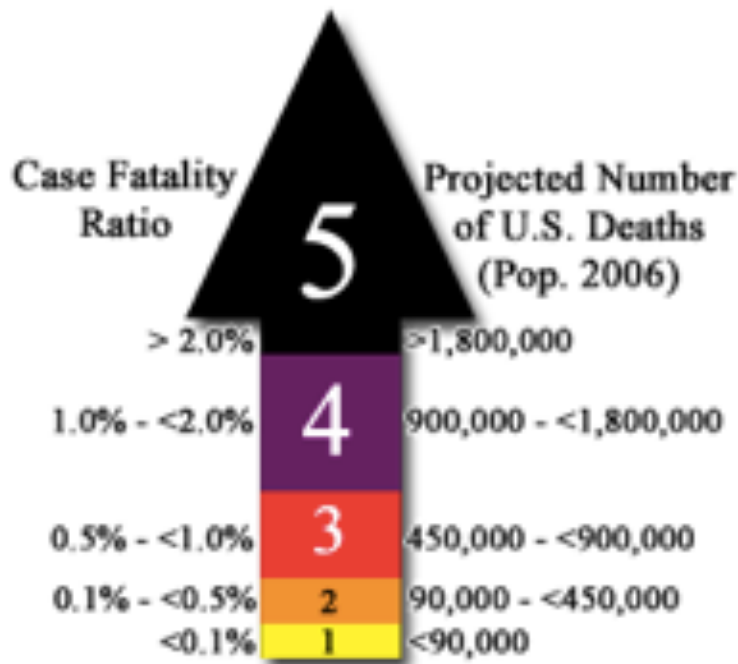


# Key public health questions at early stage of an outbreak

- How bad is it?
  - *What is the age profile? risk profile? Severity? Outcome?*
- How far has it got?
  - *Who is infected? Who can be ruled out?*
- How fast does it spread?
  - *Household studies, studies in healthcare settings*
- What can we do about it?

# How bad is it: a lesson from 2009

## Pandemics are very different



Assumes 30% illness rate  
and unmitigated pandemic  
without interventions

5. *Spanish flu, H5N1? H7N9?*
- 4.
- 3.
2. *Asian flu, Hongkong flu*
1. *Seasonal flu, Mexican flu*

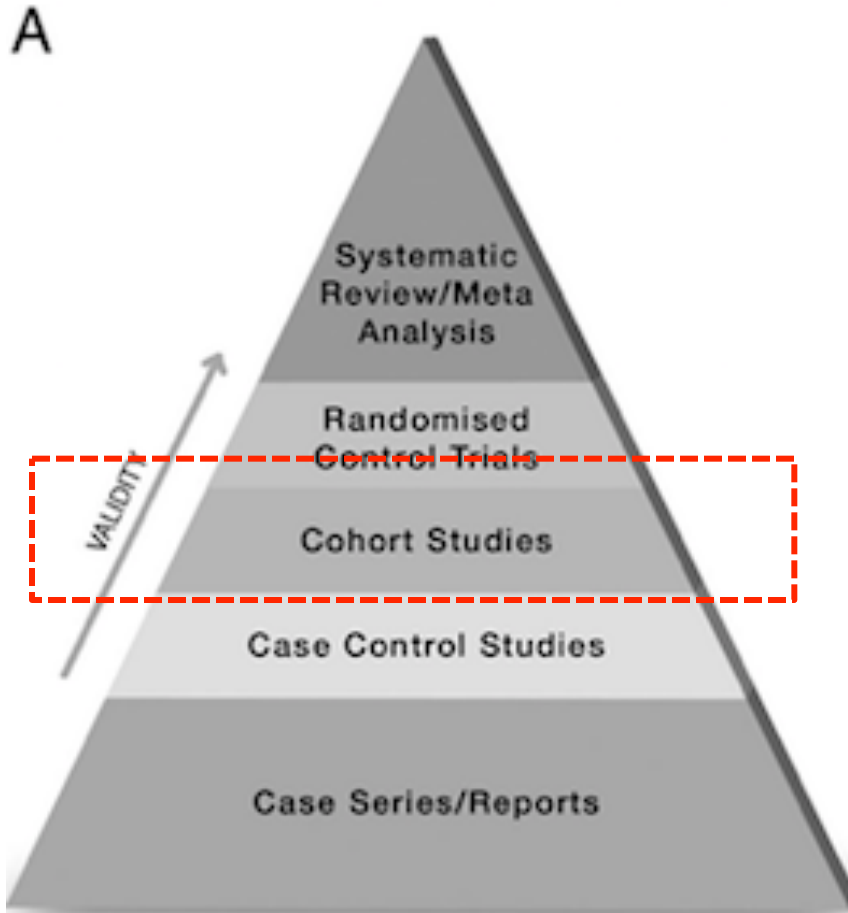
CDC

U.S. Gov.

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# A typical public health response includes the design of “FF100” studies

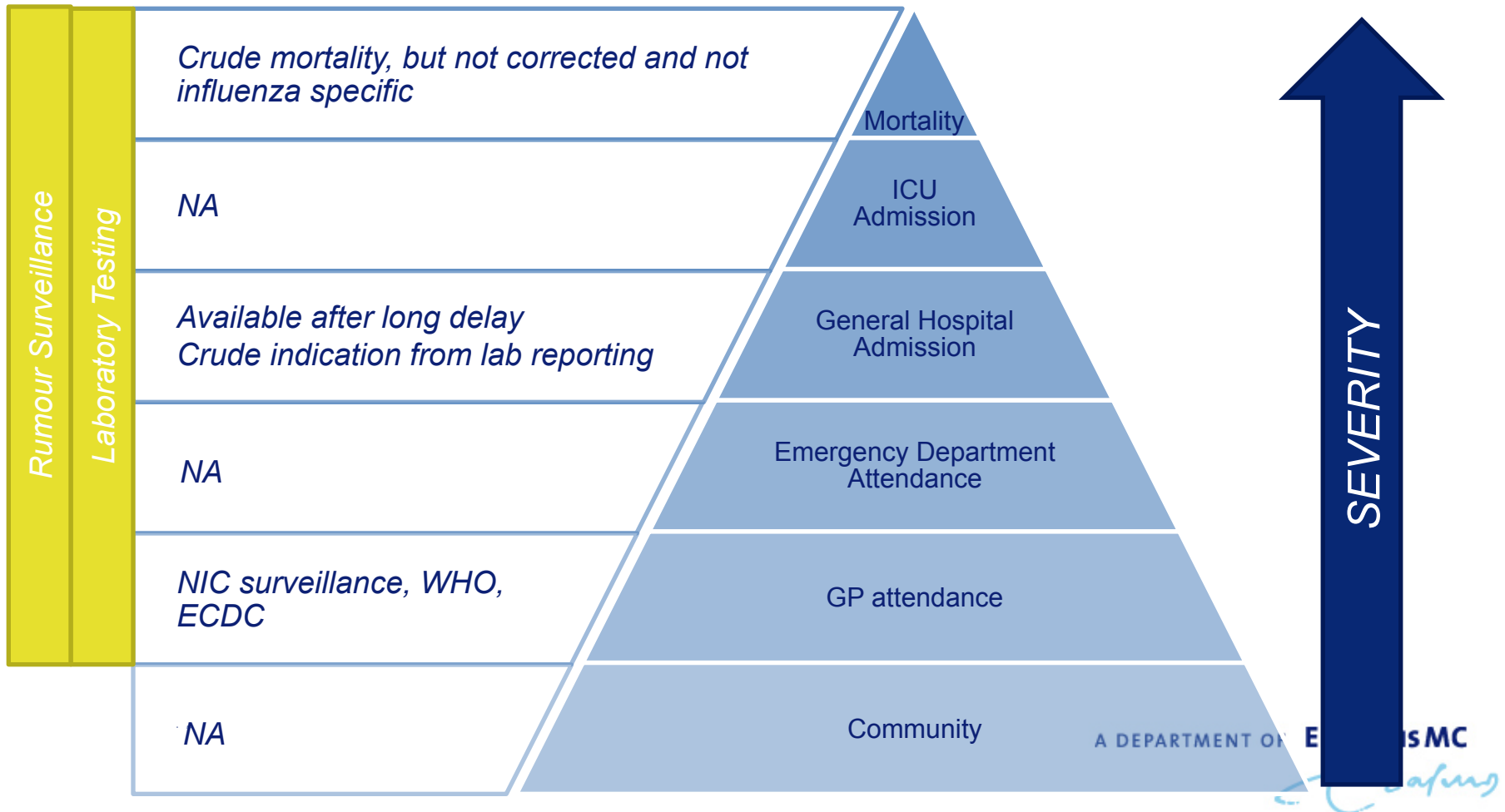


*To understand the spectrum of illness*

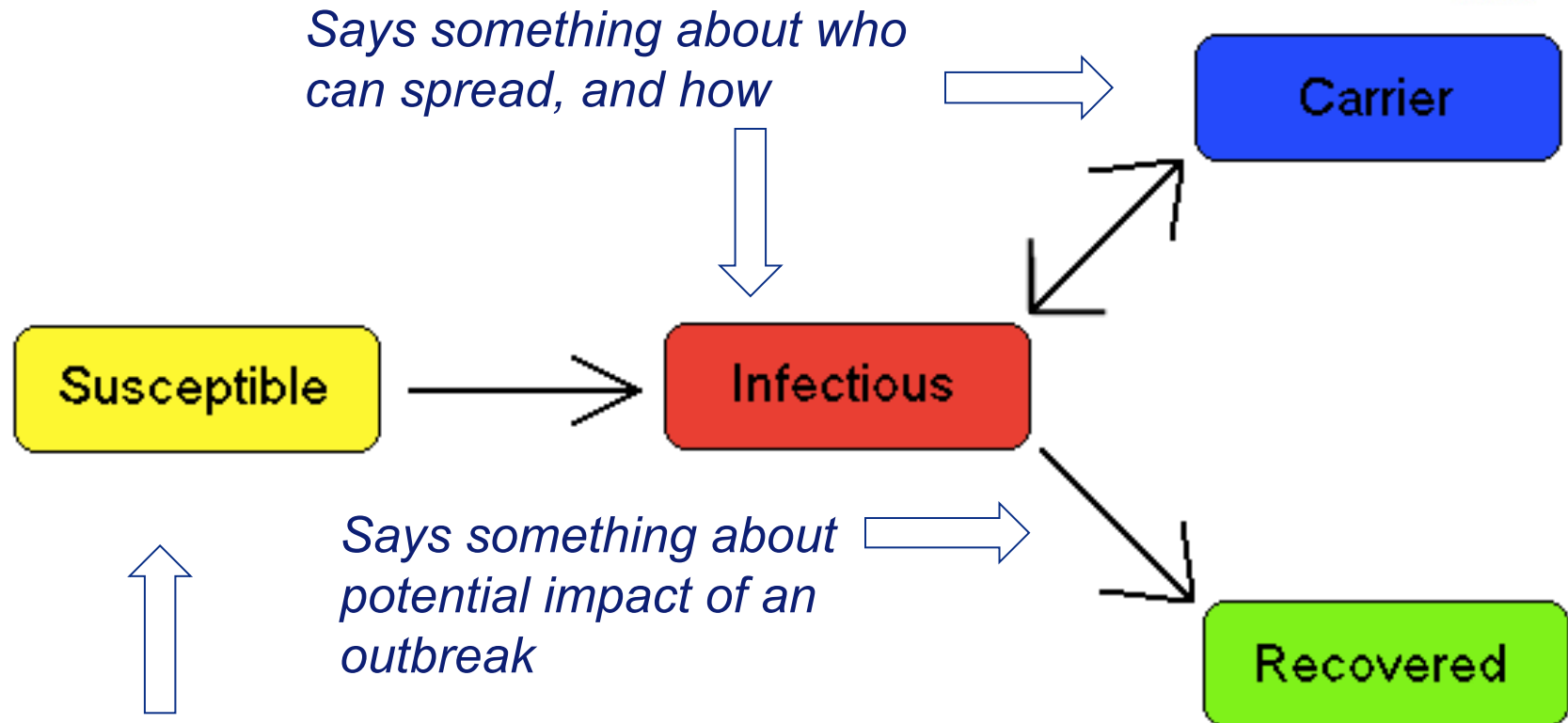
*To obtain basic data on kinetics of shedding, immune response*

*To use that data to inform modelling*

# Challenge: Determining severity in real time

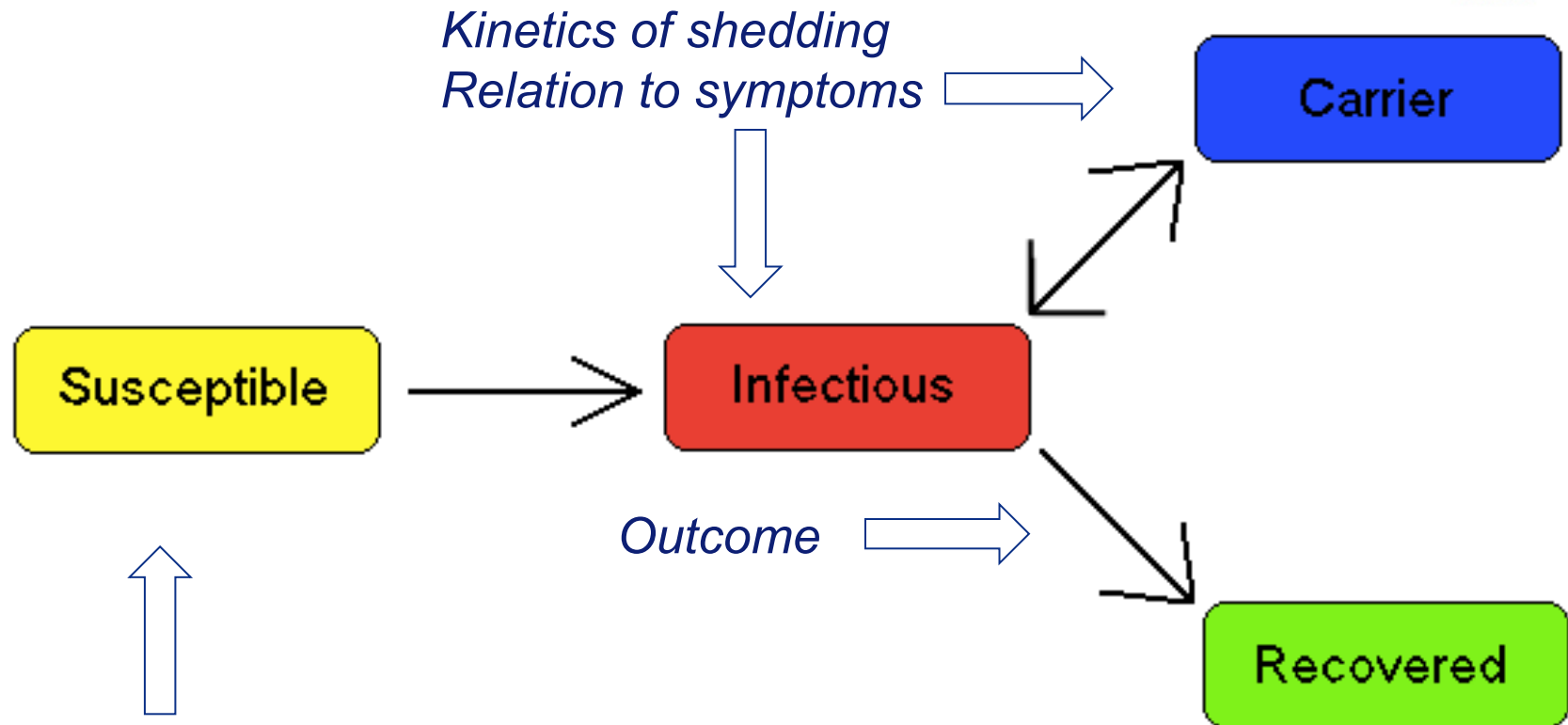


## Essential data to inform modelling



*Says something about how widespread the outbreak can be*

## Essential data to inform modelling



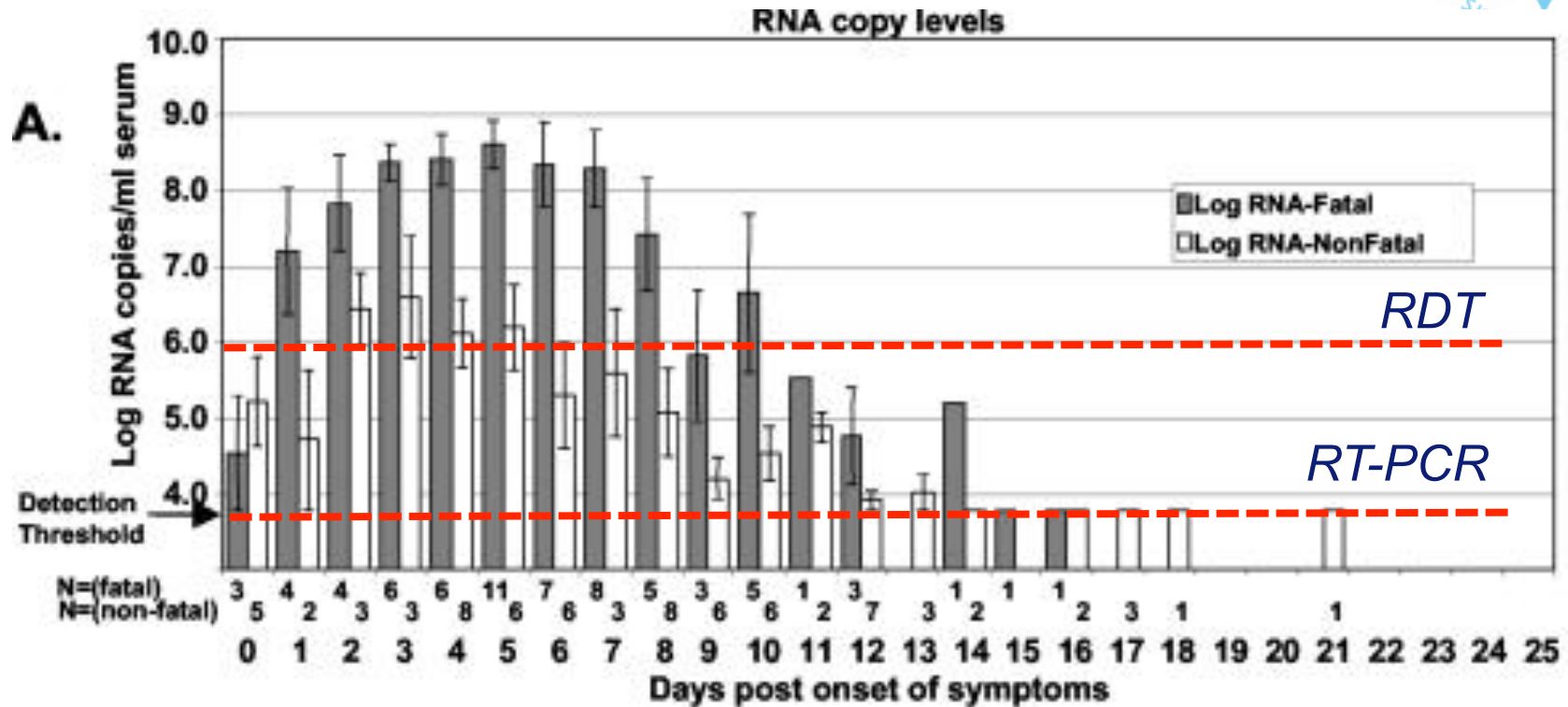
*Immune-response studies*  
*Validation of assays for serosurveys*  
*Kinetics of antibody response*

# The myriad of questions that can be addressed with some proper case series: examples from the 2014 Ebola outbreak



- How long is the virus shed?
- Is shedding equal to being infectious?
- Does intensive care handling create opportunity for aerosol transmission?
- How long does it remain infectious?
- When can quarantine be lifted?
- How reliable is a negative test result? Do we miss cases?
- Can we use a rapid test?
- Could immunotherapy work? How long after onset?
- Is a recovered patient protected? Could we use them as nurses?

# Essential data to inform PH decision making



**Viremia may be undetectable in first 48 hours upon onset of illness**

*(Towner et al., 2004)*

## Ongoing observational studies



Three observational studies: in primary care and hospitalized adult and pediatric patients, comprising:

- Sepsis-like syndrome (SLS) in infants – Start 06/2016
- Acute respiratory infection (ARI) in children (PED-MERMAIDS) – Start 06/2016
- Acute Respiratory Infections in Adults (ARI) – Started
- Arboviral compatible febrile illness Start 05/2016

**> WP3-6-7 plan to try to use these as a pandemic preparedness exercises**



# Influenza the last season season: more severe?

**Extra ziekenhuisbedden voor patiënten met griep**  
*Algemeen Dagblad 08-01-18*



**Vijftien geplande operaties Catharina Eindhoven uitgesteld vanwege griep**  
*Eindhovens Dagblad 01-03-18*

NEWS

## Flu season wreaks havoc on German workforce

Influenza is taking its toll on productivity, affecting schools, offices, public transportation and even professional soccer. Germany's Robert Koch Institute has already registered 136 deaths in 2018.



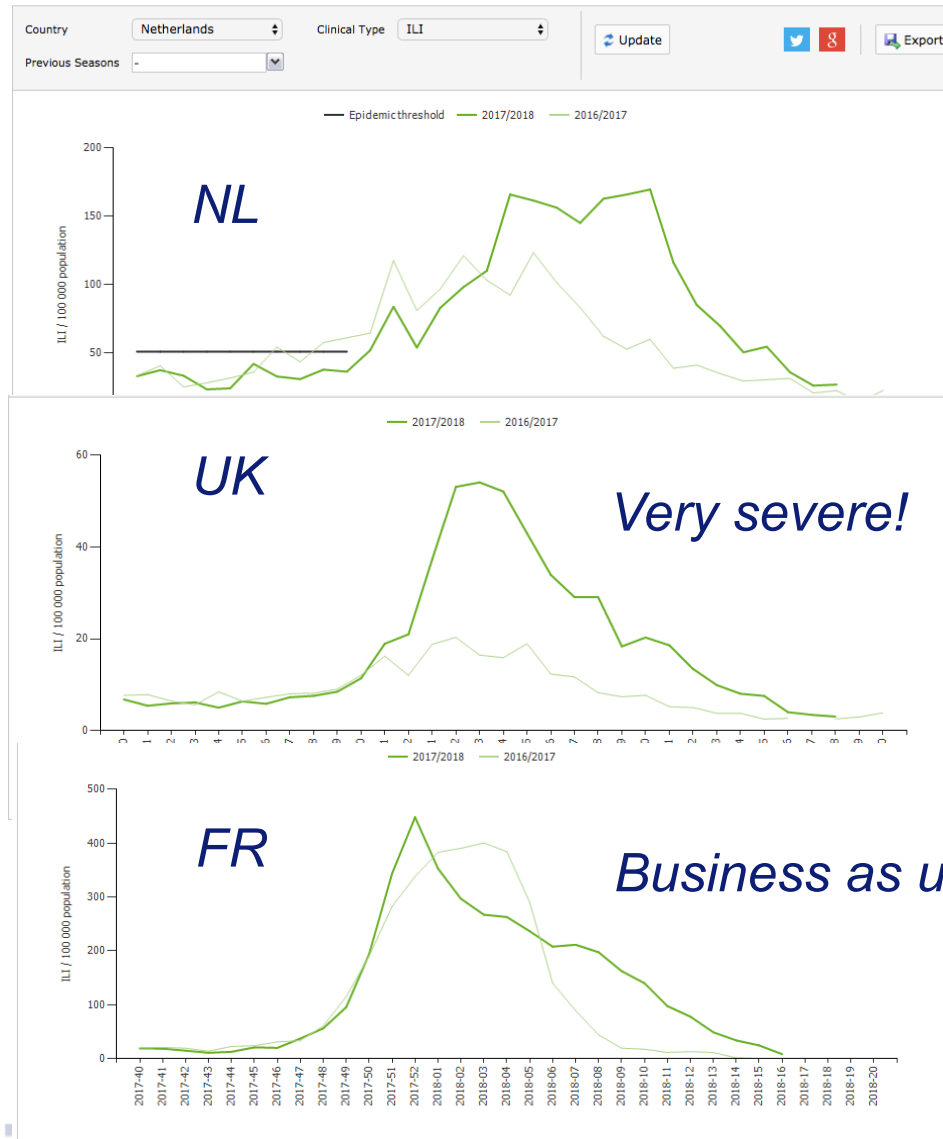
Influenza B dominance in most of Europe

Mismatch with trivalent vaccine but still considerably vaccine effectiveness

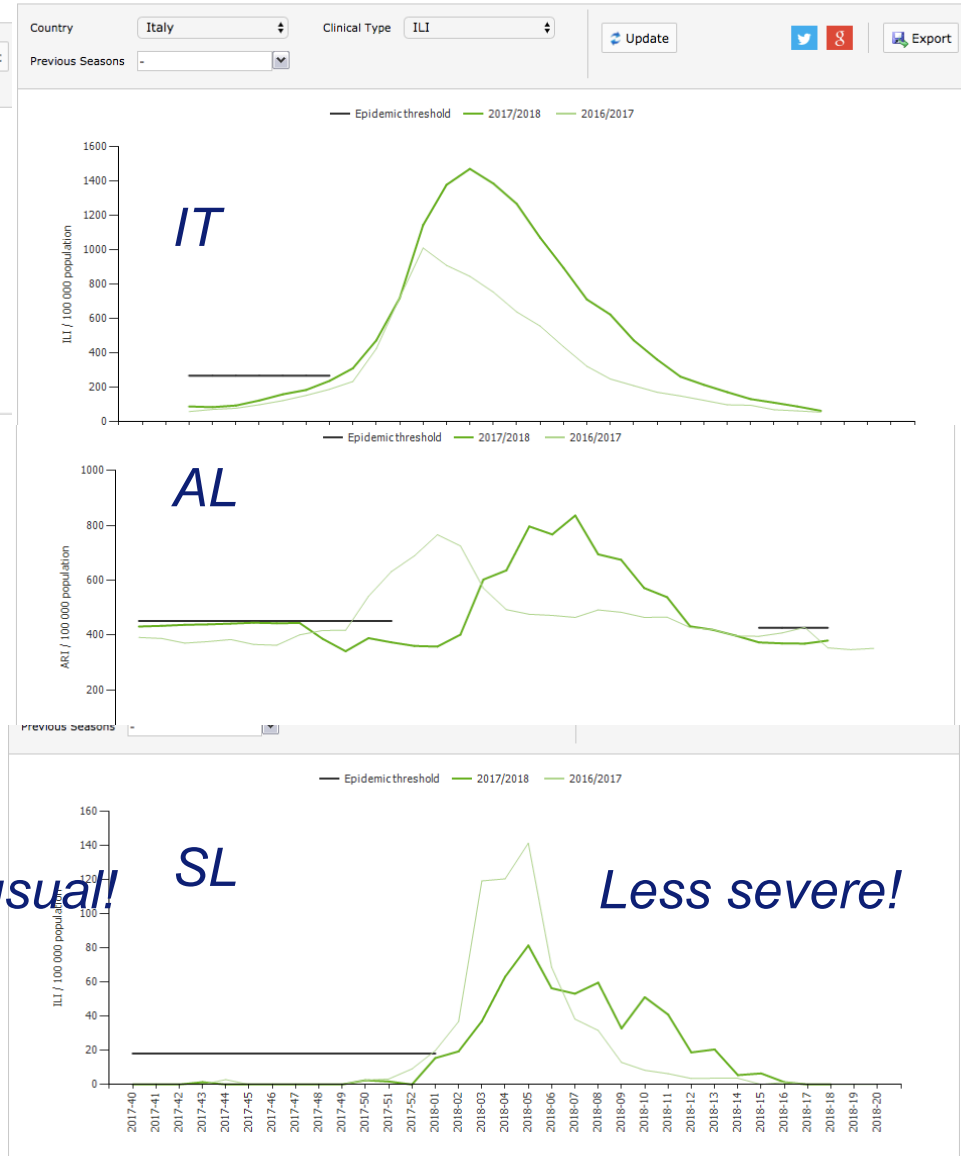
# What if the past season had been a first pandemic wave?



## Consultation rates for influenza-like illness (ILI) by country



## Consultation rates for influenza-like illness (ILI) by country

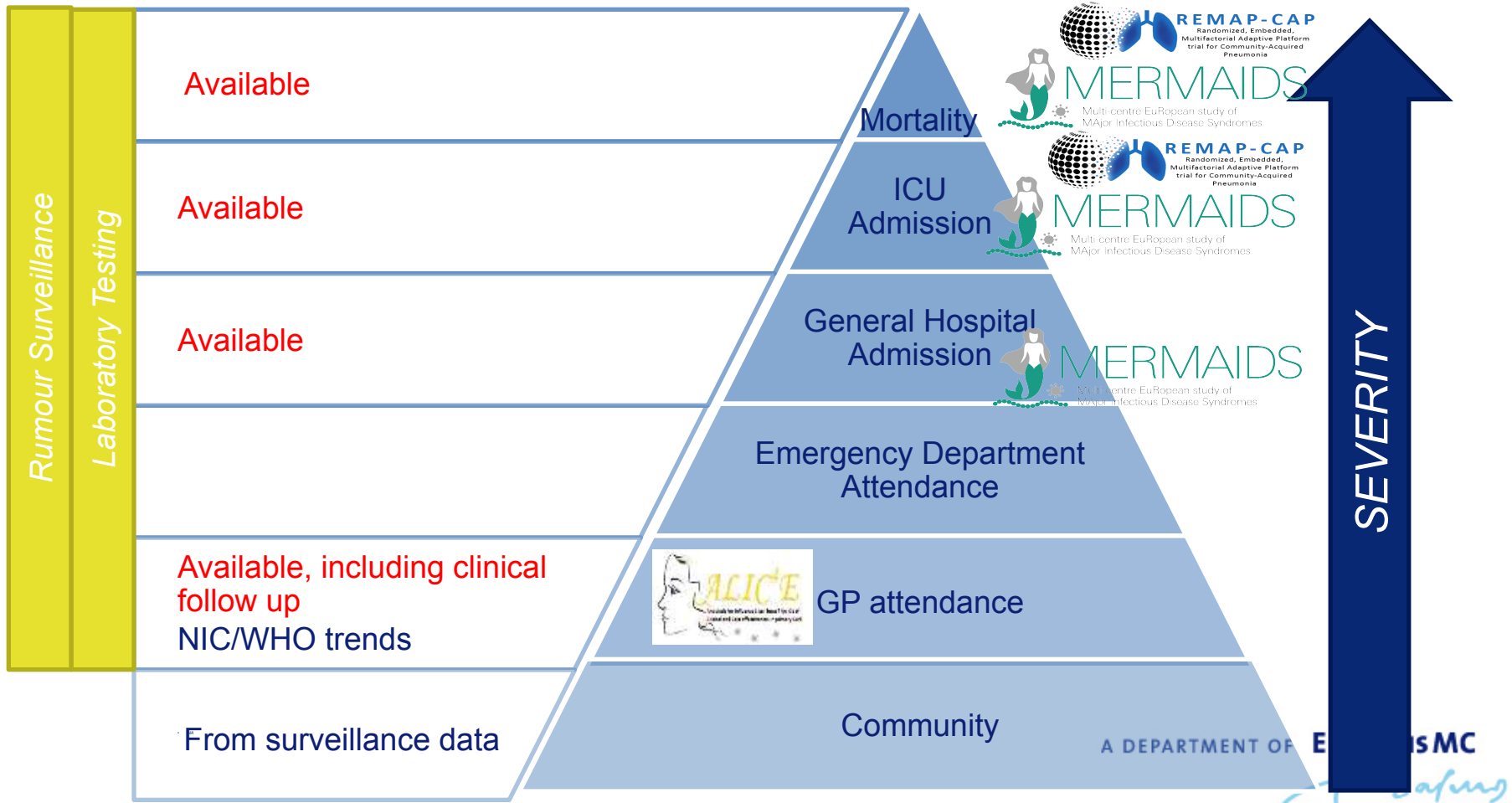




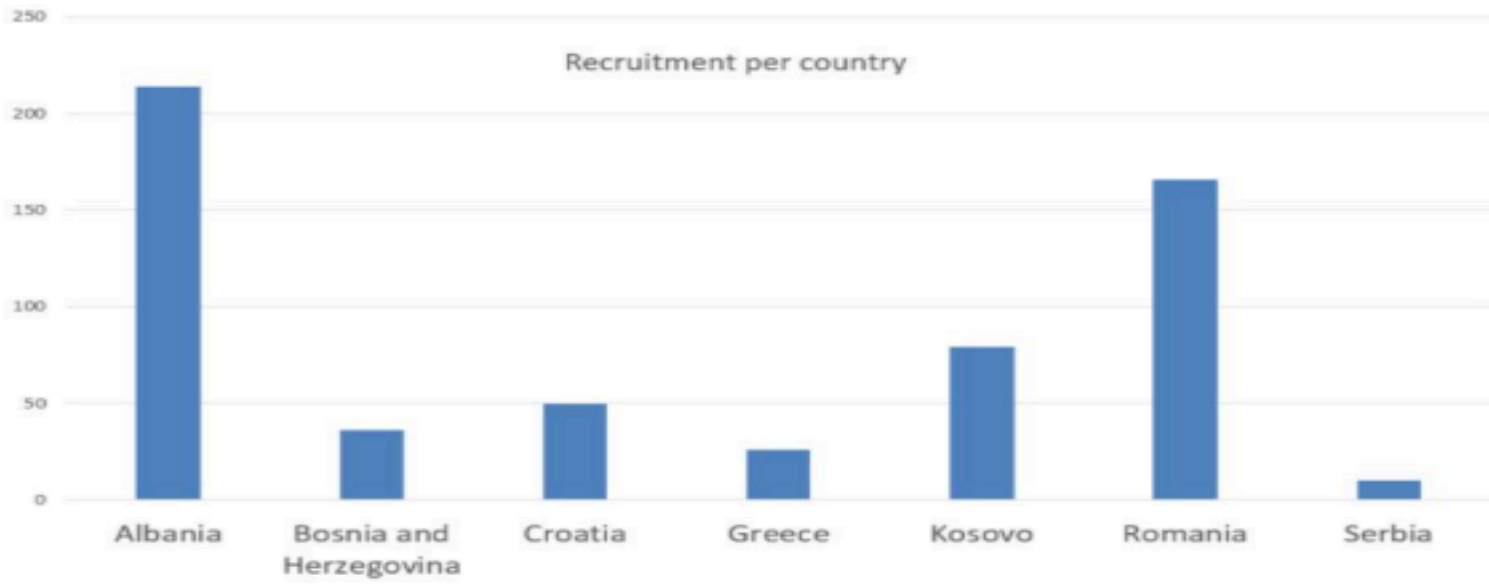
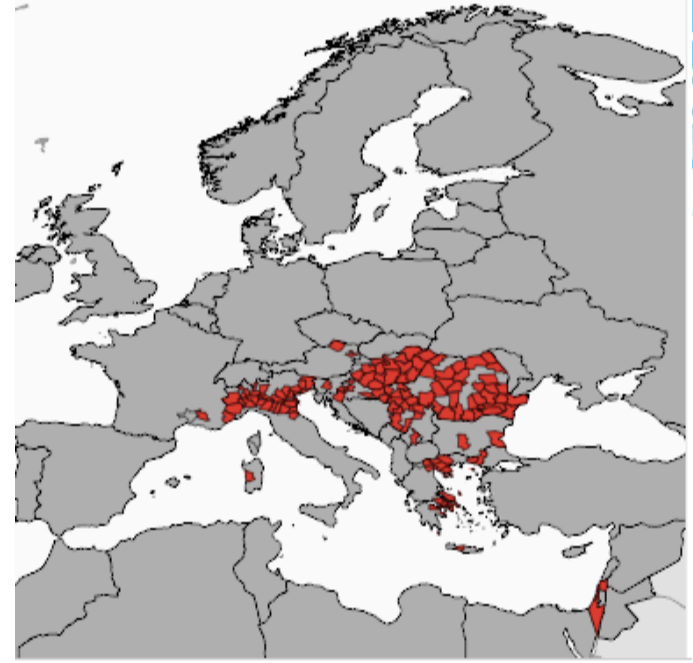
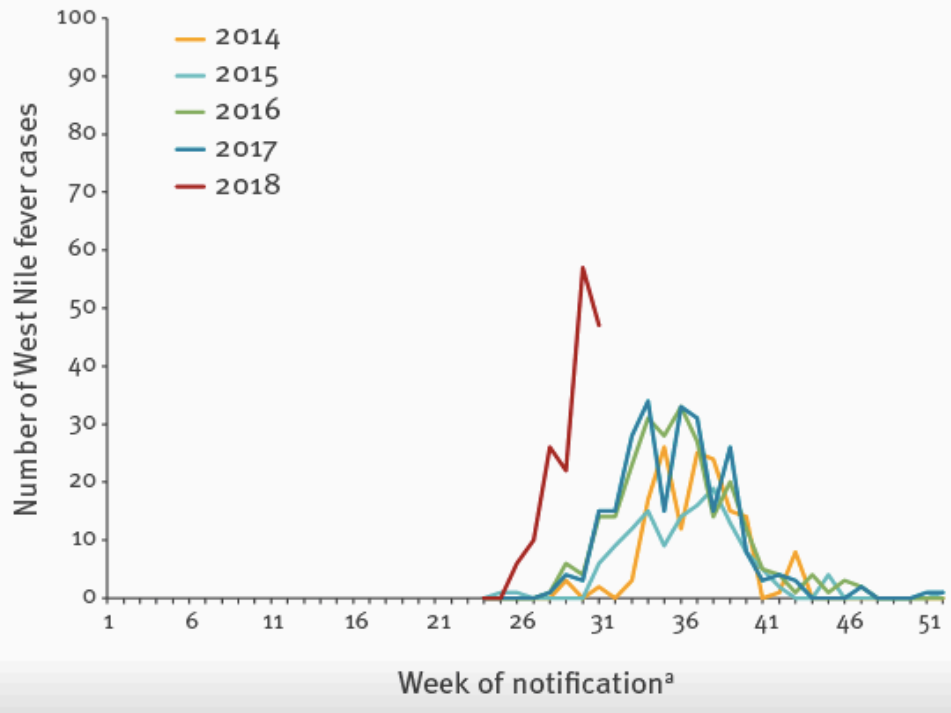
# Outstanding questions

- How severe are flu B infections?
- How severe are THESE flu B infections?
- (Why) was this season more severe in some countries, not in others?
  
- ...

# PREPARE studies that could inform rapid severity assessment if prepared accordingly (rapid, real-time integrated analysis)



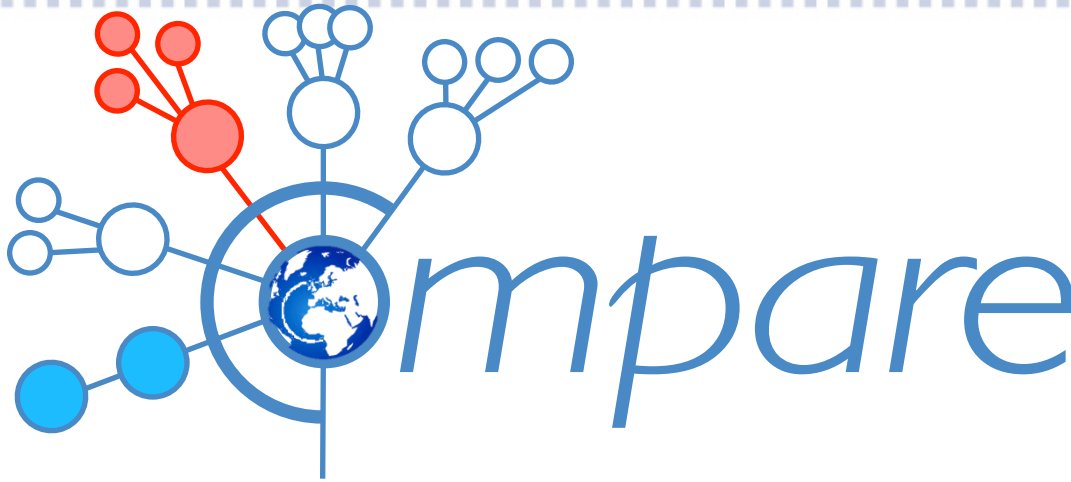
Week September 7-14, 2018





## Some outstanding questions

- If sufficient numbers: longer term outcomes in different countries
- Which viruses are involved? Strain differences?
- Do outcomes differ by lineage?
  
- > Link with COMPARE
- .....



*Collaborative Management Platform for  
detection and Analyses of (Re-) emerging  
and foodborne outbreaks in Europe*

# *New horizons in EID detection: the era of next generation sequencing, multiplex assays, and bioinformatics*

*A global platform for the sequence-based rapid identification of pathogens*

*Prof Frank Aarestrup, coordinator, DTU microbiology/AMR, DK*

*Prof. Marion Koopmans, deputy coordinator, virology, EID, NL*



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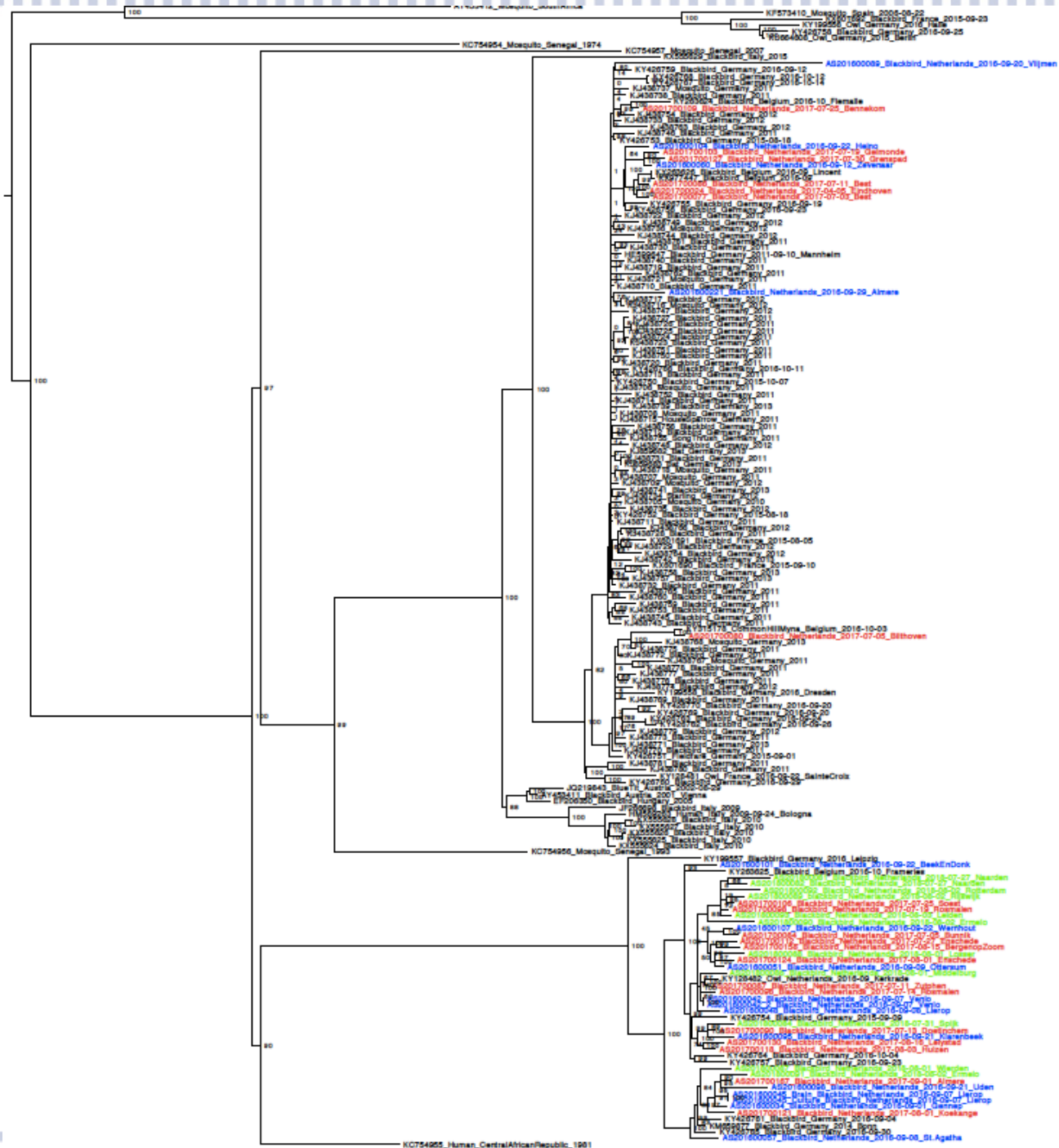
*This project has received funding from the European Union's Horizon 2020  
research and innovation programme under grant agreement No 643476.  
research and innovation programme under grant agreement No 643*





## Key components of COMPARE

- Developing an enabling environment for rapid sharing of critical outbreak data, that includes genomics data
- One health approach
- Focus on clinical, public health and research
- Datahubs under a governance mechanism, building from existing infrastructure (EBI-NCB-DDBJ)
- Research into barriers to data sharing (globally)
- EU-CAN-SHARE (new funding to develop data sharing infrastructure that includes high density data)



Blue: year one  
 Red: year two  
 Green: year 3

Usutu viruses  
 (related to West  
 Nile virus) in  
 birds

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## Conclusions

- Observational studies can inform public health decision making
- Having data from different tiers in the population is extremely valuable but is not considered in current clinical trial networks
- Timeliness of results is currently a bottleneck
- Linking data across tiers is currently not possible > recommendation for future
- Governance of data sharing for public health use versus sponsored trials requires specific attention

