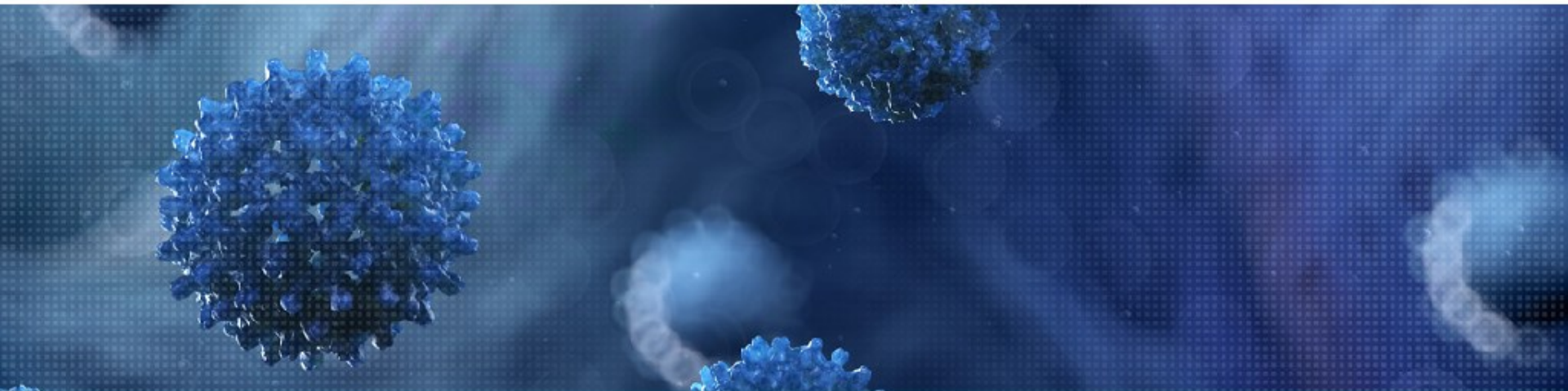


Erasmus MC



**Viroscience lab**

WHERE SKILLS MEET TO STUDY & PROTECT



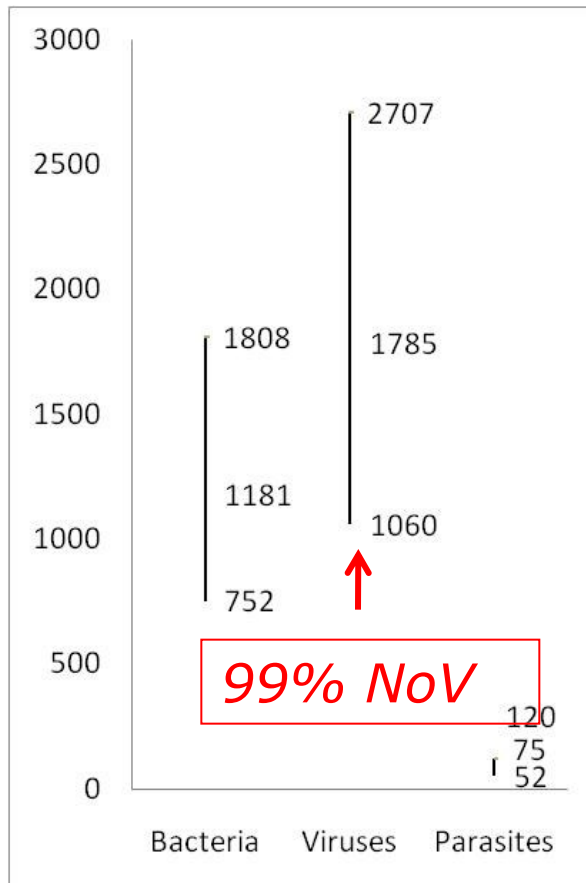
# Challenges and opportunities in risk assessment for viruses

Marion Koopmans @MArionKoopmans

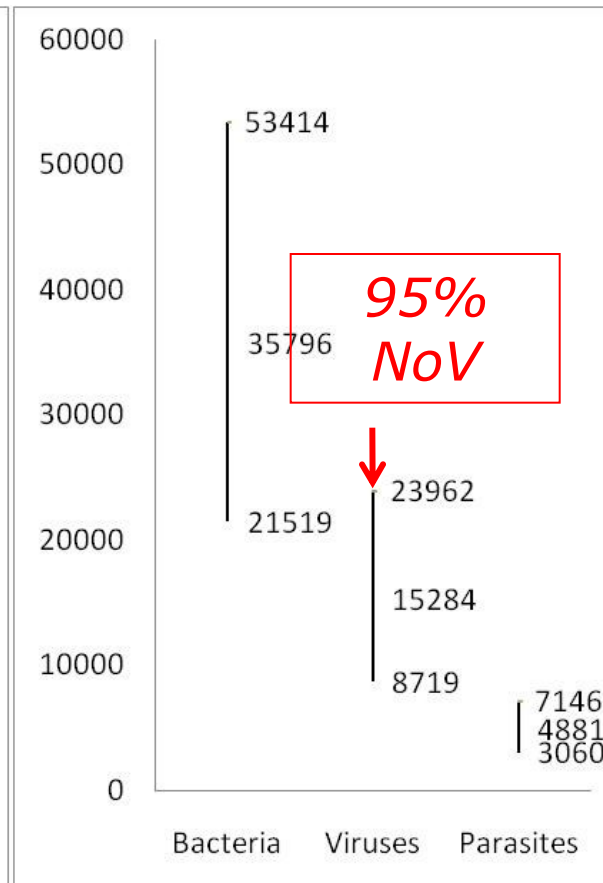


# Estimates of foodborne viral disease, US

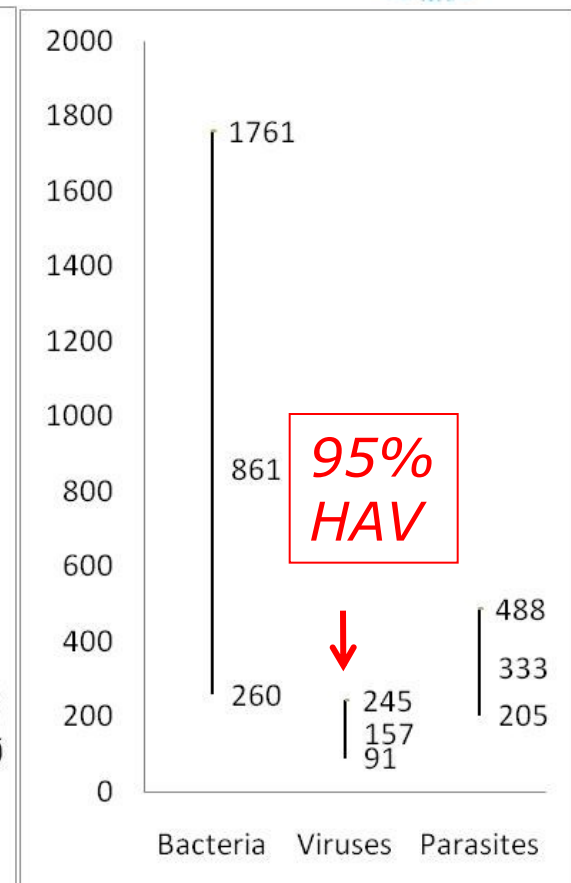
Estimated nr FB cases  
Per 100000



Estimated nr hospitalisations



Estimated nr deaths



Scallan et al., 2011

# Viruses and food, sources



Category	Source	Mode of Tx	Example	Clinical syndrome
Fecal viruses human	Fecal contamination at source irrigation Food handler	Fecal oral	<b>Norovirus</b> Sapovirus Astrovirus Rotavirus Enterovirus <b>Hepatitis A virus</b> Hepatitis E virus? .....	Diarrheal disease Hepatitis Neurological disease
Fecal viruses animal	Fecal contamination at source Irrigation (shellfish, berries)	Fecal oral, zoonotic	Hepatitis E virus Rotavirus .....	Hepatitis Diarrheal disease
Systemic infection animal	Meat, animal products	Zoonotic, including fecal oral	Hepatitis E virus TBE Nipah Avian influenza Rift valley fever MERS .....	Hepatitis Neurological disease Respiratory disease Hemorrhagic fever .....



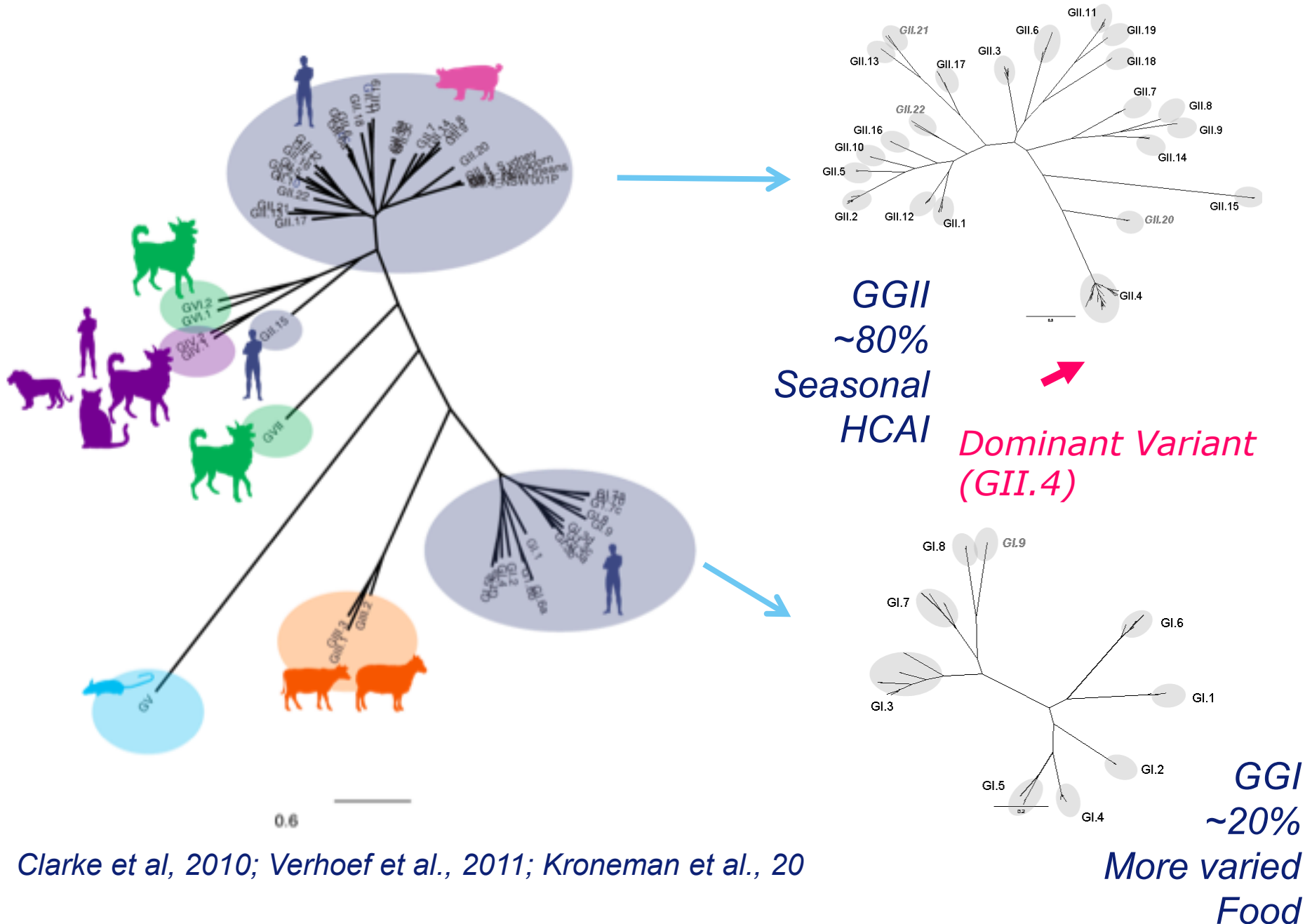
## Issues to address in microbial risk assessment

- Microbial growth and death
- *Genetic diversity and evolution*
- Potential for secondary transmission
- *Immunity*
- *Diversity of health endpoints*
- Heterogenous distribution in environment
- *Detection method sensitivity*
- Population, community, and ecosystem level dynamics
- Routes of exposure
- ....
- Infectome, microbiome and exposome

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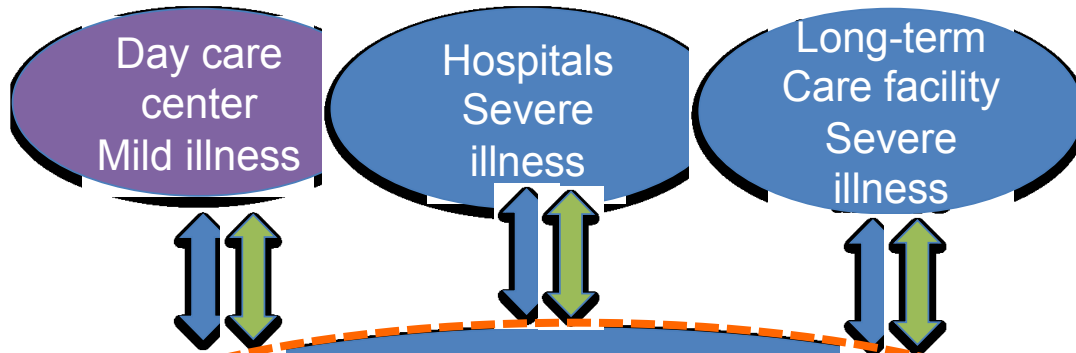
# Family, genus, genogroups, genotypes, variants



Higher association with non-GII.4 NoV

Higher association With GI.4 NoV

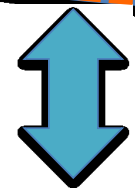
- Prolonged shedding,
- more time for genetic evolution
- less immune pressure



Transmission  
 via food (non-GII.4)  
 via person-to-person contact (GII.4)

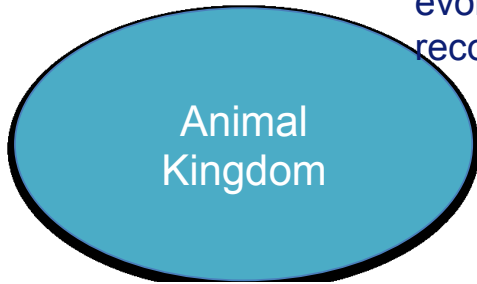


- Genetic and antigenic evolution due to immune pressure



**Zoonotic events ?**

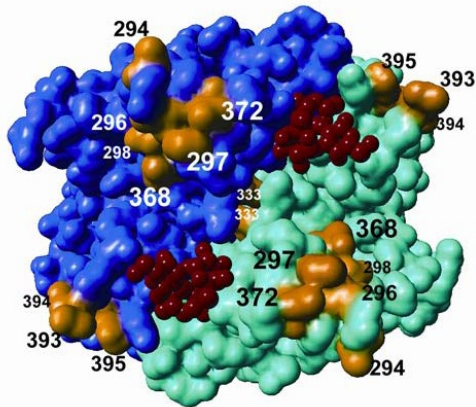
- Genetic and antigenic evolution through recombination



*Evidence for QMRA*

*copying*

# Noroviruses persist in the population through evolution

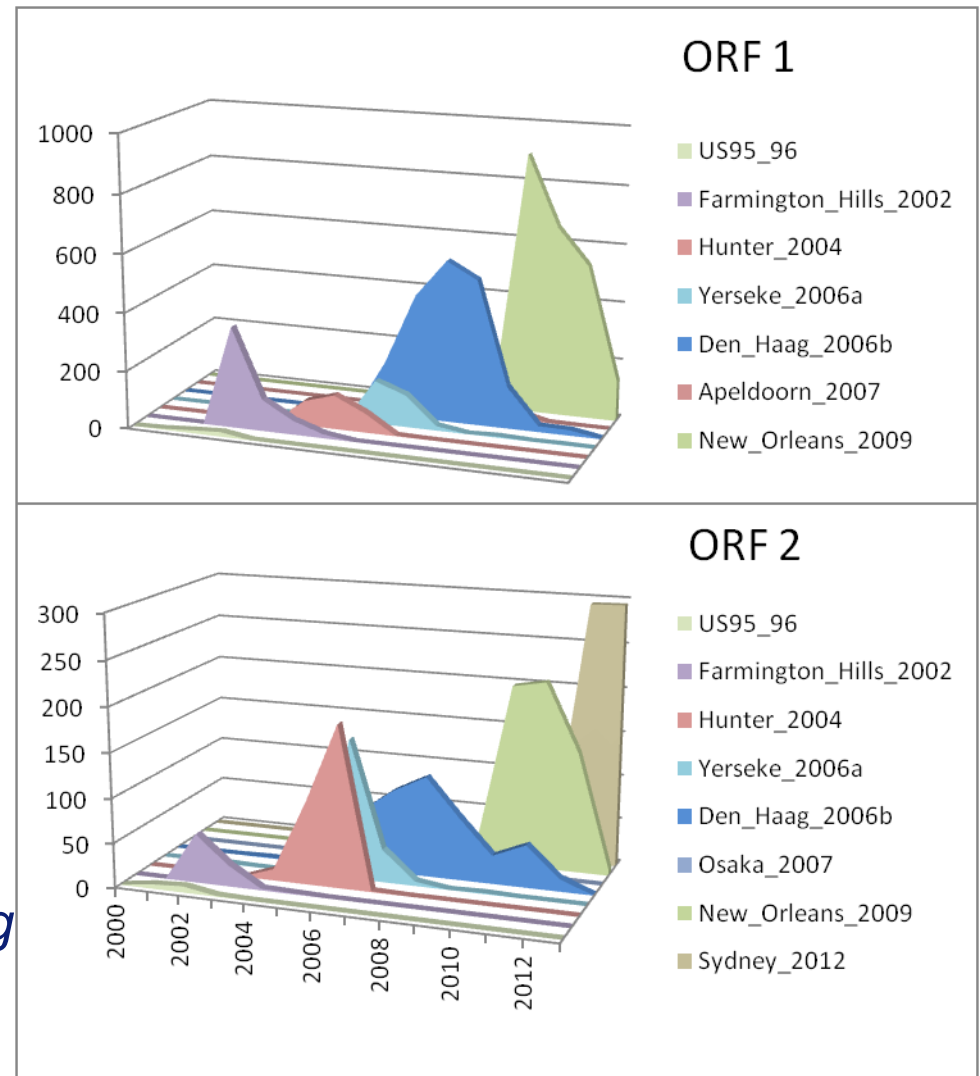


## Effects of mutations:

Escape mutants (drift)

➤ No protective immunity

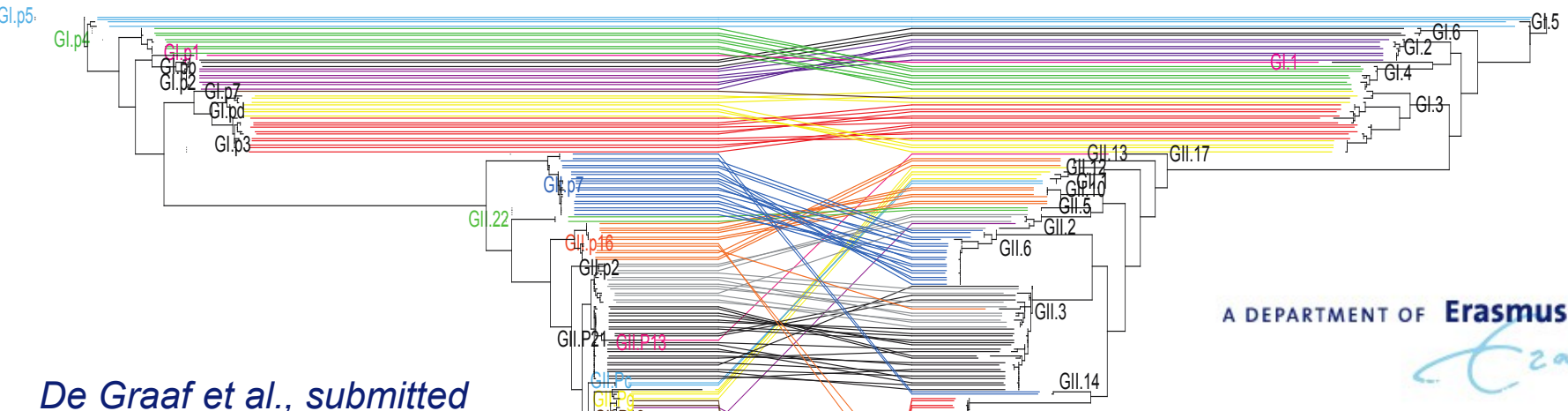
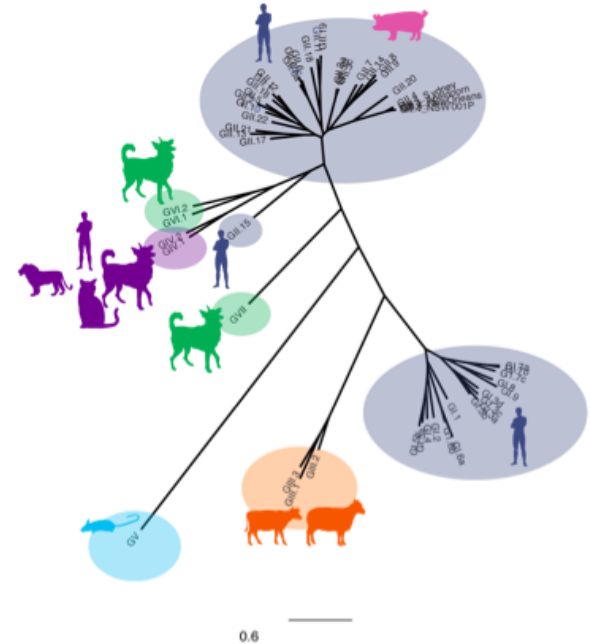
Differences in host cell binding  
> New host range



Siebenga et al., 2008; Allen et al., 2008; Parra et al., 2012; Tan et al., 2003  
Lindesmith et al., 2008; Bok et al., 2009; Siebenga et al. 2010

# Reassortment

- Infection of a single cell with more than one strain > progeny virus with mixed genome
- More likely when humans are exposed to multiple viruses
  - Eg foodborne outbreaks
  - Daycare centres
  - Immunocompromised persons
- Potential for introduction of novel viruses into the population (mixed genomes)



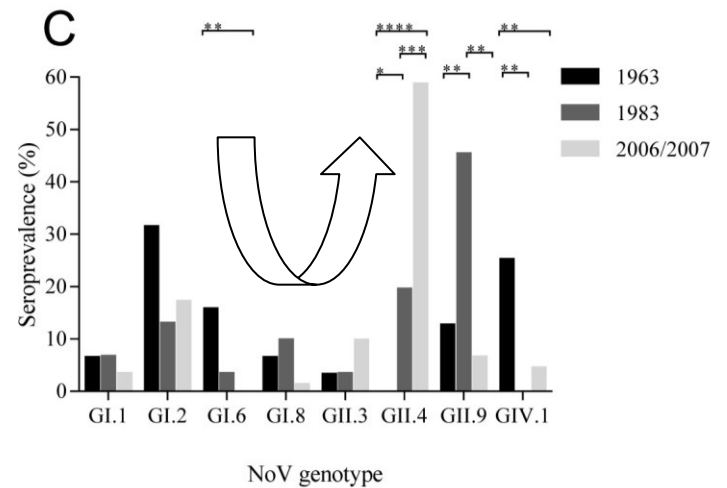
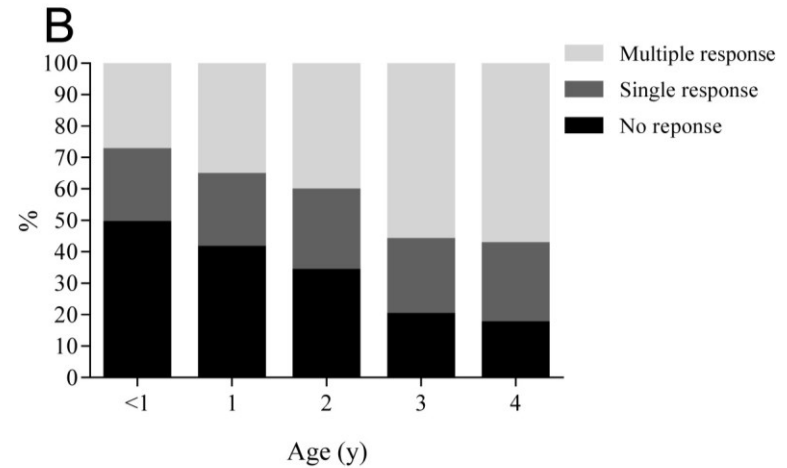
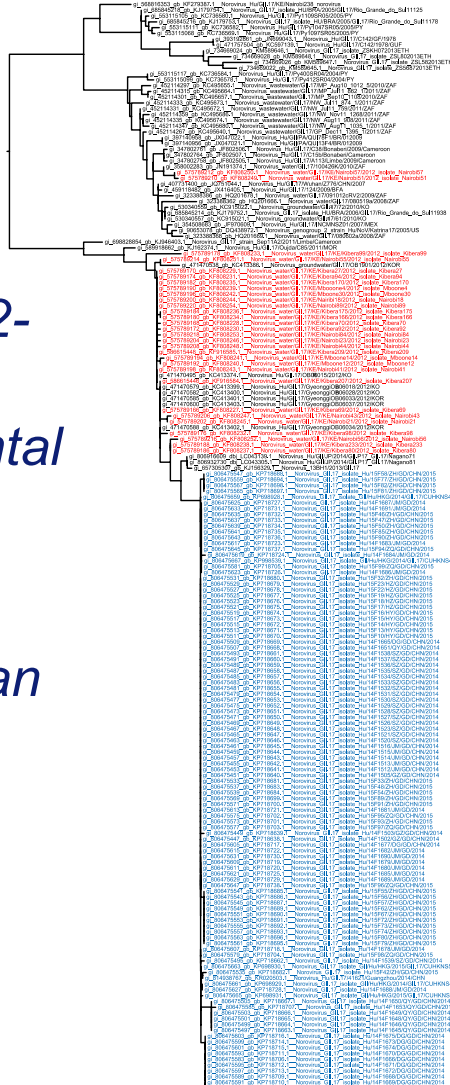


# Emergence of recombinant strains may change impact



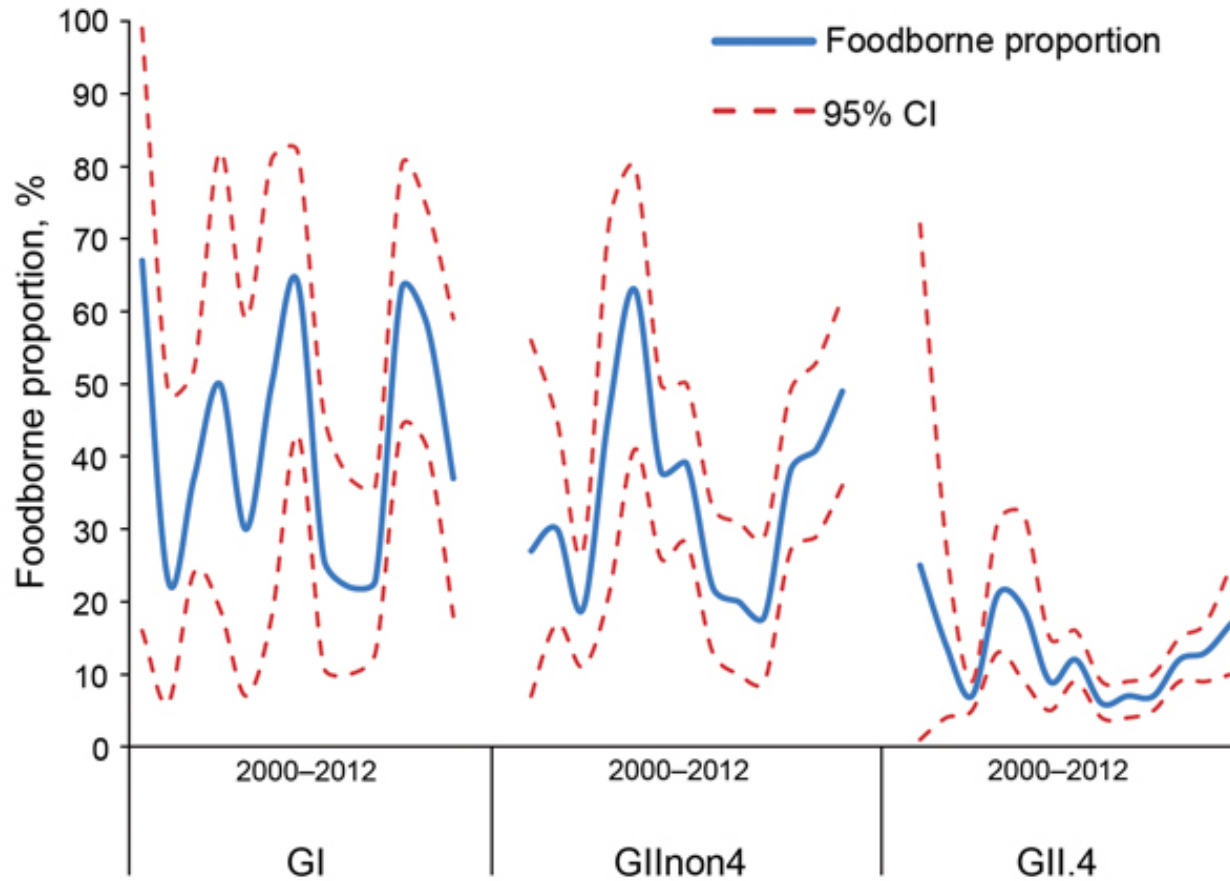
*Kenya 2012-2013, environmental*

*China, Japan 2014-2015, outbreaks*

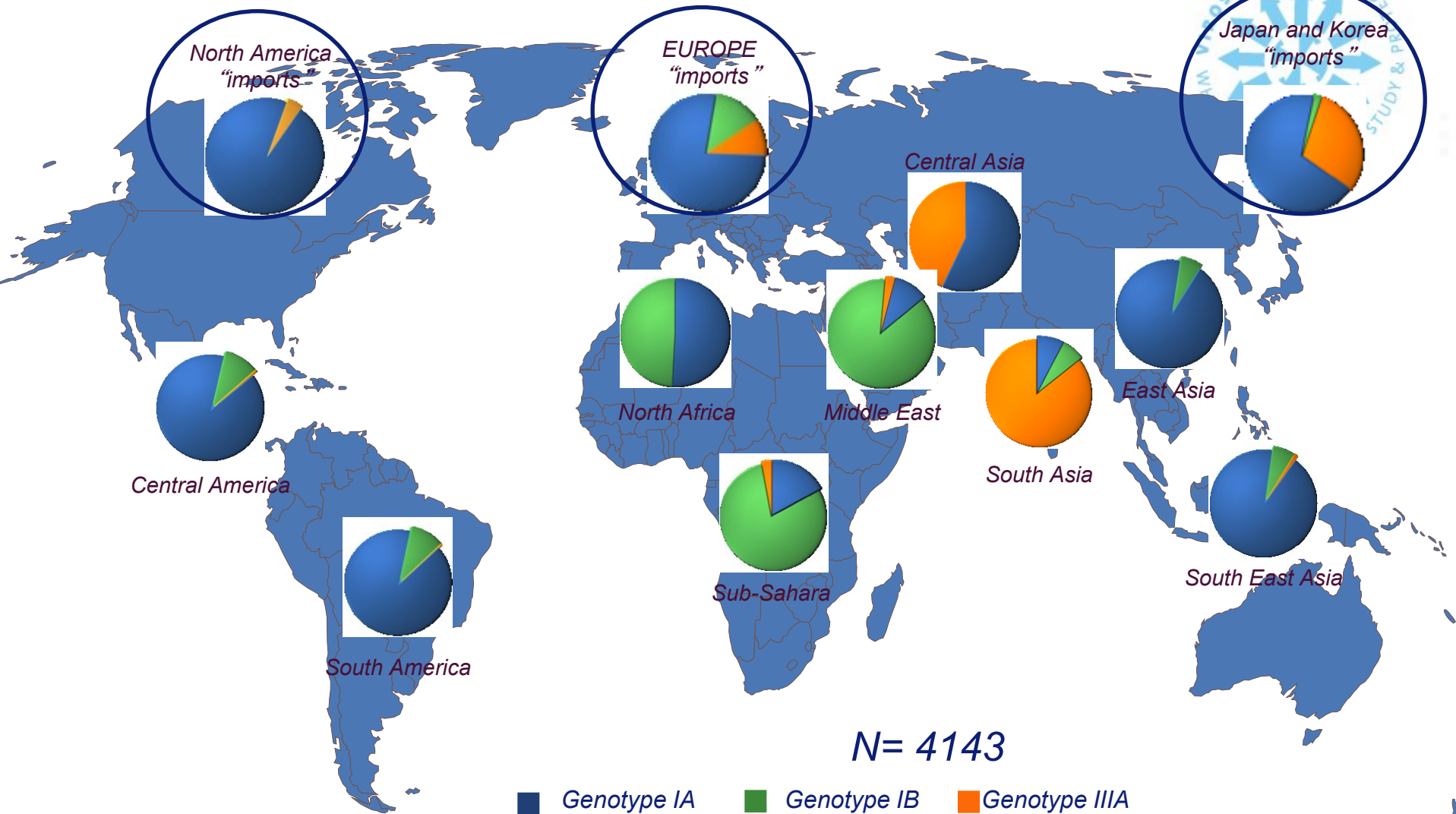


*Handwritten signature or mark in blue ink.*

# Effects of strain diversity of FB disease estimates



*Great fluctuations in estimated foodborne illness*



# Sequence based cluster detection, HAV example

France: Jan 2010

N = 59 cases HAV infections

The Netherlands: Jan 2010-2011

N = 14 cases HAV infections



Semi-Dried tomatoes



Frozen Berries

Nordic countries: Oct 2012 - 2013

N = 103 cases HAV infections

Australia: May 2009

N = 250 cases HAV infections

## Hepatitis warning on semi-dried tomatoes

Posted Fri May 22, 2009 3:36pm AEST  
Updated Fri May 22, 2009 3:47pm AEST

Health authorities in Victoria and South Australia say semi-dried tomatoes have been linked with a spike in the number of hepatitis A cases.

People are being warned not to eat loose semi-dried tomatoes sold in oil with herbs and garlic at IGA, Foodland, Foodworks and independent delis and cafes.

Victoria's acting Chief Health Officer, Rosemary Lester says the move is precautionary.

"Although the links between the product and a recent increase in hepatitis A cases in Victoria are still under investigation, we have taken this measure in collaboration with our colleagues in SA," she said in a statement.

"We are also working with the Victorian manufacturers to remove this product from these stores across Victoria."



Semi-dried tomatoes have been linked to a spike in hepatitis A cases. (www.flickr.com: Allerina and Glen MacLarby, file photo)

# Hurdle: getting robust evidence for foodborne outbreaks

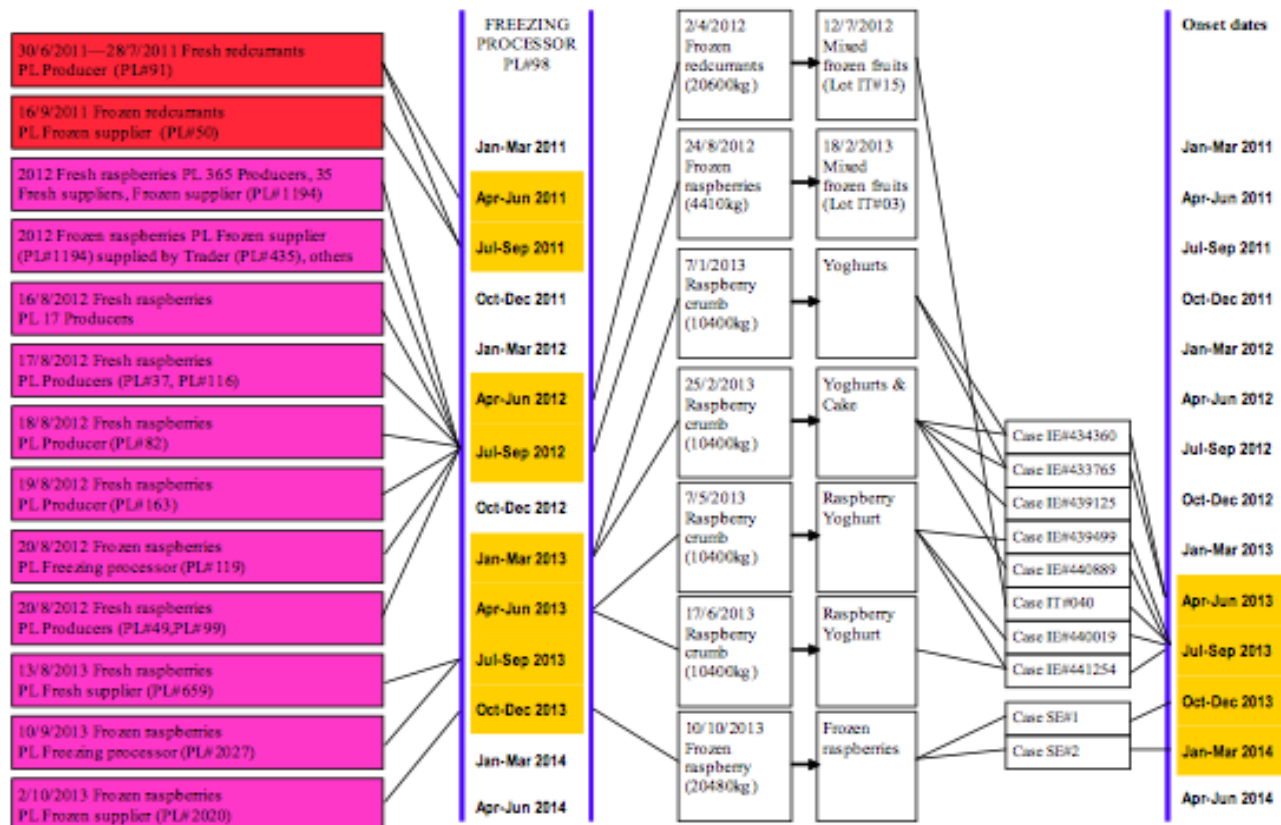


Figure 24: Time line of deliveries from “hotspot” PL#98 to lots and cases in Italy, Ireland and Sweden (only confirmed cases are represented)

## Intensive farming under scrutiny as French oysters face viral wipeout

From Hugh Schofield in La-Trinité-sur-Mer, Brittany

6 Jun 2010

French oyster farmers are facing ruin after a viral epidemic – which many believe is linked to intensive farming methods – struck for the third year in a row, wiping out millions of the baby shellfish.

From the Mediterranean coast, up to the Bay of Arcachon on the Atlantic and now Brittany, farmers have watched in dismay in recent weeks as the virus once again moved northwards, keeping pace with the rising sea temperature.

In 2008 and 2009 the industry was ravaged by the same epidemic, with many farms losing 80% to 100% of their stocks of naissains – first-year baby oysters. Because it takes three years to grow a commercially viable oyster, so far the economic impact of the crisis has been limited.

But now all pre-2008 production has been depleted, so major shortages are predicted next winter when demand peaks around Christmas and New Year. In France that is when 90% of oysters are sold.

The Committee to Save Oyster-Farming – an ad-hoc group set up in answer to the crisis – has warned that 40% of the country's 4,800 mainly family-run businesses could be forced to close, with the loss of thousands of jobs.

“Unofficially everyone thinks the hatcheries are to blame, even if no-one says so openly”

Jacques Cadoret



Oysters have been hit by the OsHV-1 virus

Ifremer – the state marine research agency – described the situation as “one of the worst crises in the history of French oyster-farming”.

Last month, hundreds of farmers staged a much-publicised protest in central Paris, dumping lorry-loads of oyster shells on one of the Seine River bridges. Their pressure paid off, because the French government has now promised a €150 million rescue package to tide the industry over the next three years.

Low tide on the sand flats at Le Po – a hamlet near Carnac in southern Brittany – exposes the poches or bags of oysters being cultivated by Bruno Lemoine. Last week he detected the first signs of the epidemic, with many of the

Tools

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dining room **THE BUSINESS Herald** Market Menu £25 - 3 courses

*Oyster herpes virus*

*Massive die-out*

*Market shift*

*Top producers:  
China, Japan, Korea*

# Emerging viruses and the food chain



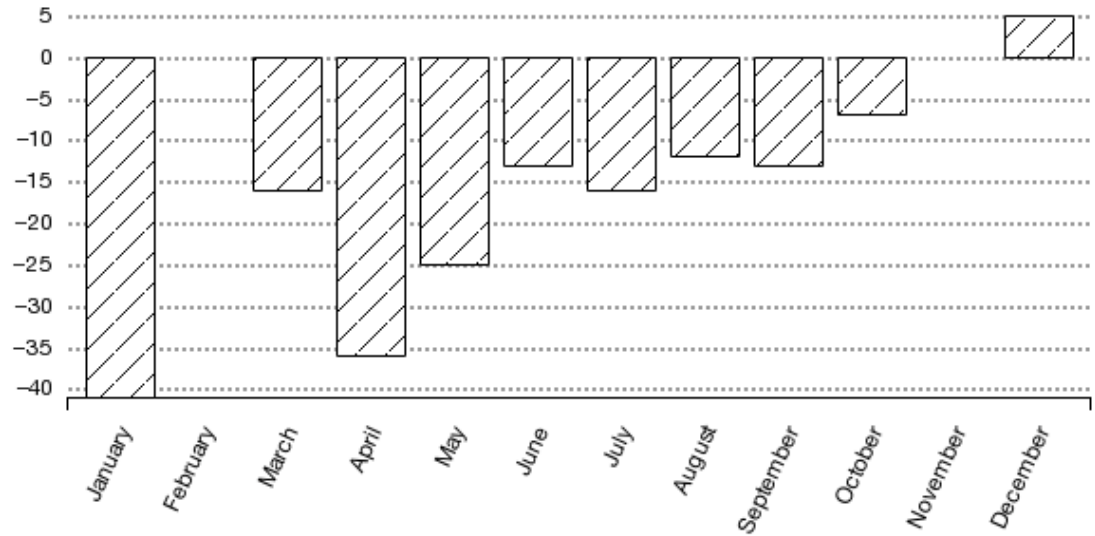
- Pig Hepatitis E – *immunocompromised*
- SARS – wild animal markets
- Nipah – fruits>pigs>people
- Avian influenza- food handlers, blood
- Rift valley fever – animal products, slaughter
- Ebola – bush meat
- MERS coronavirus: dromedary milk, slaughterers – *immunocompromised*
- .....



(2012)

# Impact of avian influenza H7N9 emergence

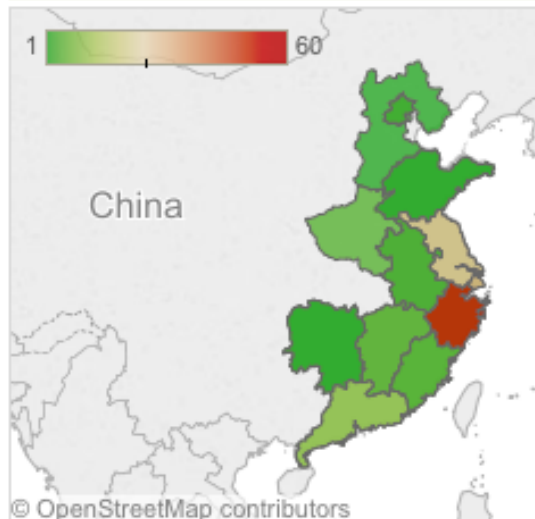
KFC China Same Store Sales (2013)  
% Change



Source: Yum Brands

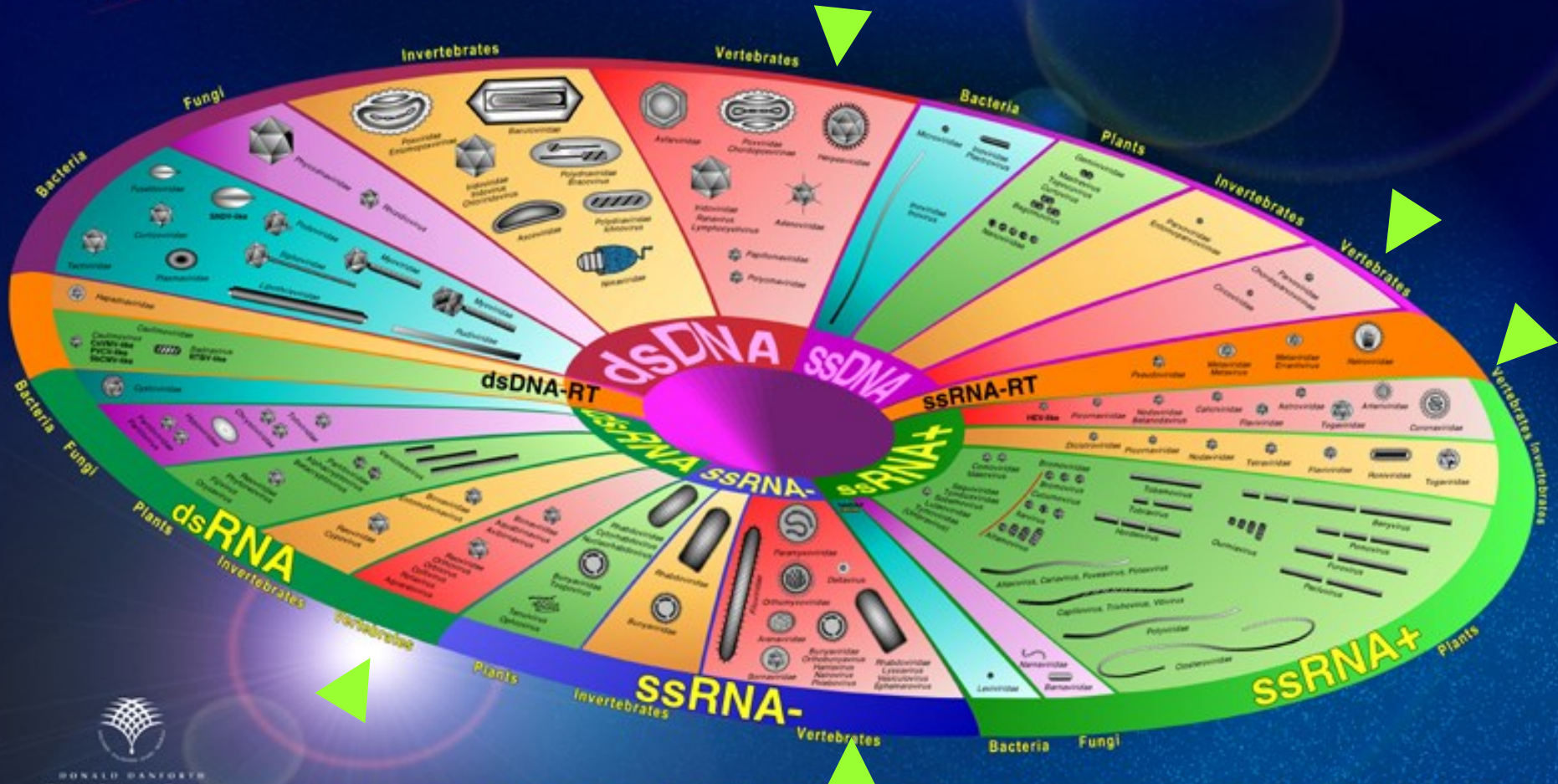
## 2013 MAP

By likely Province of acquisition, China





# Virosphere 2002



International Committee on Taxonomy of Viruses

A DEPARTMENT OF Erasmus MC

<http://www.ncbi.nlm.nih.gov/ICTVdb/Images/virosphere.htm>



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

*A global platform for the sequence-based rapid identification of pathogens  
- Start date December 1<sup>st</sup> 2014*

*Coordinated by*

*Frank M. Aarestrup (Technical University of Denmark)*

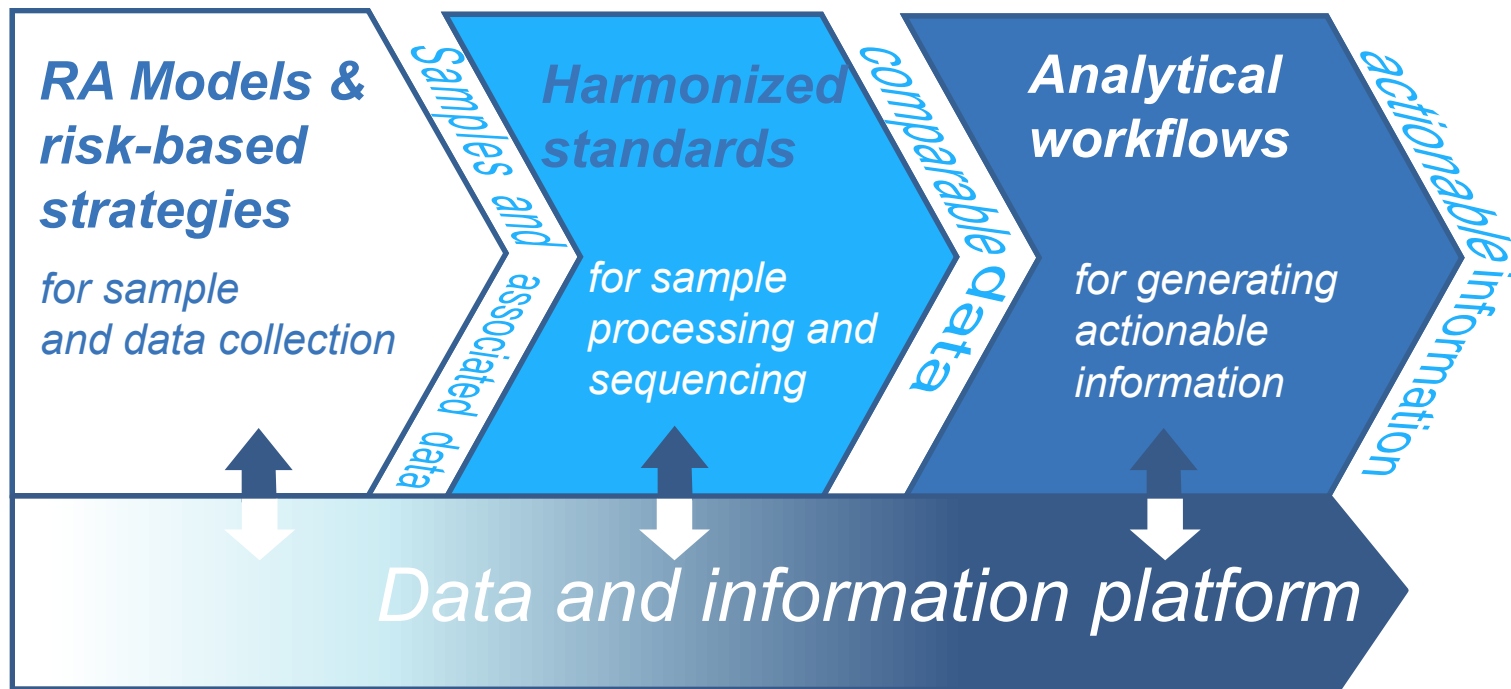
*Marion Koopmans (Erasmus Medical Center, the Netherlands)*

[www.compare-europe.eu](http://www.compare-europe.eu)

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*Analytical framework and globally linked data and information sharing platform.*



# The future of risk assessment science for viruses?



Develop capacity to deal with emerging diseases > agenda setting for research

Develop capacity to take stock of evolving data sources

