- The Next Frontier in Risk Assessment in Food -

Quantitative Viral Risk Assessment

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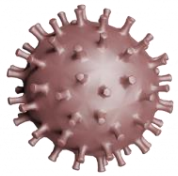

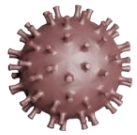
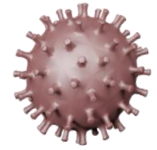

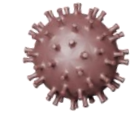

European Food Risk Assessment Fellowship Programme

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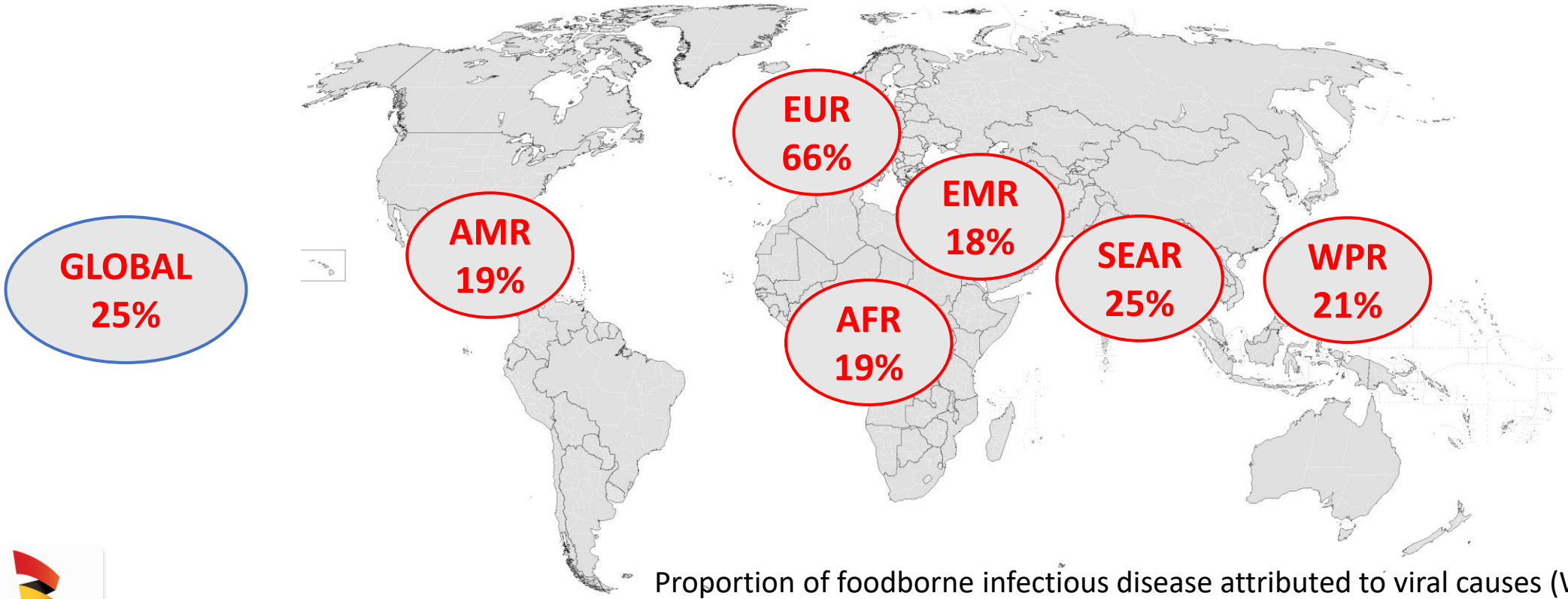
Munich
4 May 2022, 08.30

Introduction

Foodborne infectious diseases cause an estimated **600 million cases of illness** and **420,000 fatalities** every year. The WHO attribute **25%** of global foodborne infectious diseases to enteric viruses (mainly norovirus), and **over 60%** for cases in Europe (WHO, 2015).

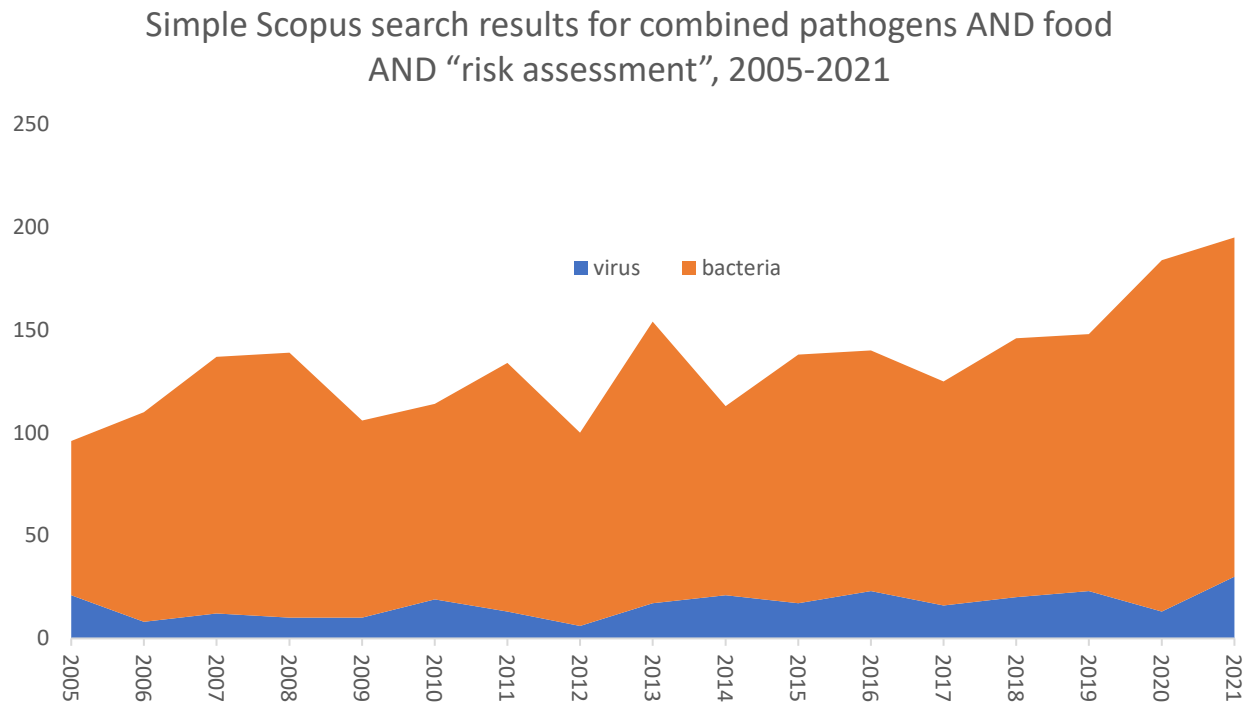


Proportion of foodborne infectious disease attributed to viral causes (WHO, 2015)

Kirk, M.D., Pires, S.M., Black, R.E., Caipo, M., Crump, J.A., Devleesschauwer, B., Döpfer, D., Fazil, A., Fischer-Walker, C.L., Hald, T., Hall, A.J., Keddy, K.H., Lake, R.J., Lanata, C.F., Torgerson, P.R., Havelaar, A.H., Angulo, F.J., 2015. World Health Organization Estimates of the Global and Regional Disease Burden of 22 Foodborne Bacterial, Protozoal, and Viral Diseases, 2010: A Data Synthesis. PLOS Med 12, e1001921. https://doi.org/10.1371/journal.pmed.1001921

Introduction

But risk assessments (and scientific opinions) for foodborne **virus hazards** are much less common than **bacterial hazards**.



Introduction

Objectives of presentation

To **explain** why quantitative virus risk assessment (QVRA) is less common

To **explore** the future of QVRA.

Outline of presentation

1. The **difficulties** in applying QRA to viruses

2. The main **differences** between bacteria and viruses as hazards

3. Future **challenges and opportunities** for QVRA

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Timeline of QMRA

1970s

Risk assessment

In relation to aerospace and nuclear disasters

1983

First virus risk assessments

Stemming from Haas, C. N. 1983. Estimation of risk due to low doses of microorganisms: a comparison of alternative methodologies. Am. J. Epidemiol. 118:573–582

1990s

Formalisation of Microbial Risk Assessment

Publication of Principles and guidelines for the conduct of microbiological risk management, Codex Alimentarius Commission

2000s

FAO/WHO organize Expert Consultation on Foodborne Viruses

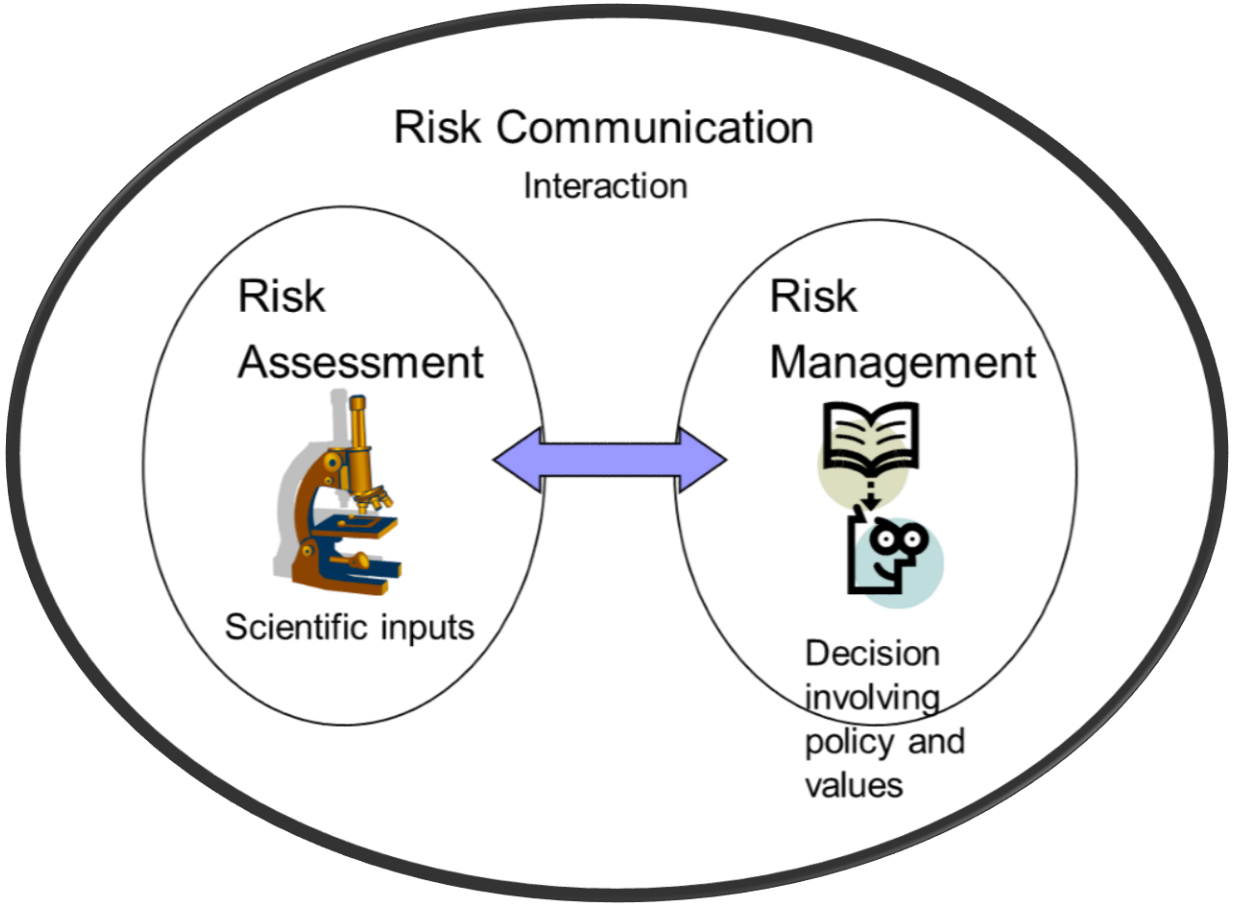
Publication of Viruses in food: scientific advice to support risk management activities: meeting report. Microbiological Risk Assessment Series, No. 13..

Future

QVRA developing?

Bradshaw, E., Jaykus, L.-A., 2016. Risk Assessment for Foodborne Viruses, in: Goyal, S.M., Cannon, J.L. (Eds.), Viruses in Foods. Springer International Publishing, Cham, pp. 471–503. https://doi.org/10.1007/978-3-319-30723-7_17

Risk assessment is the **scientific component** of risk analysis



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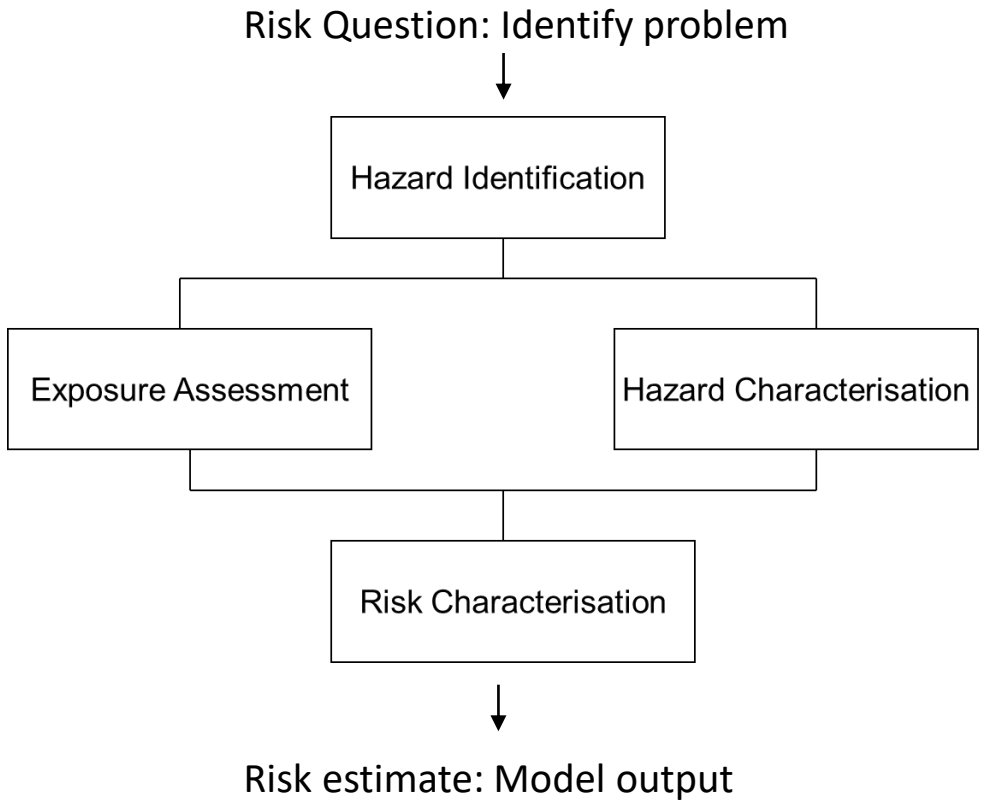
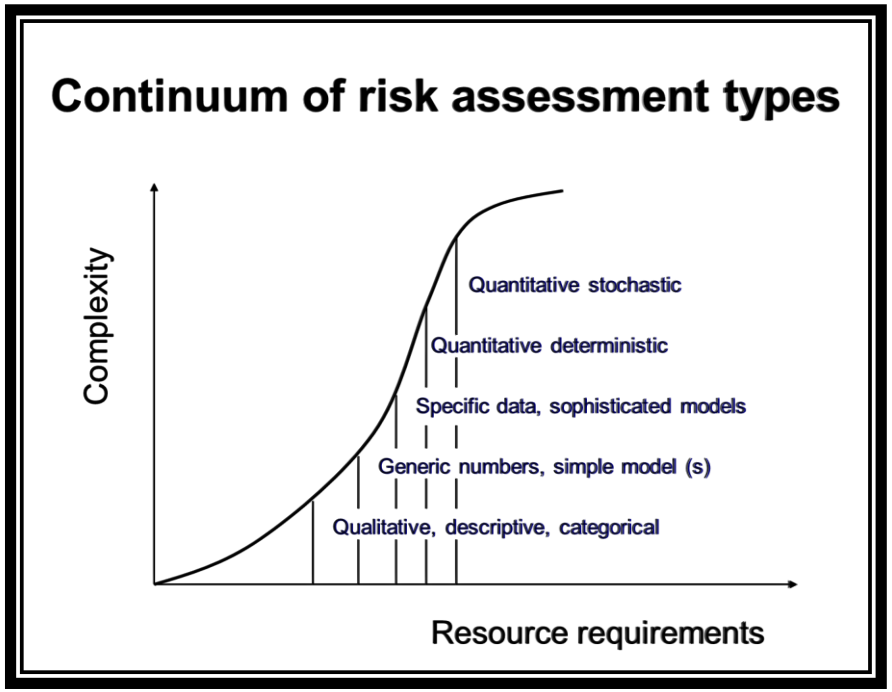
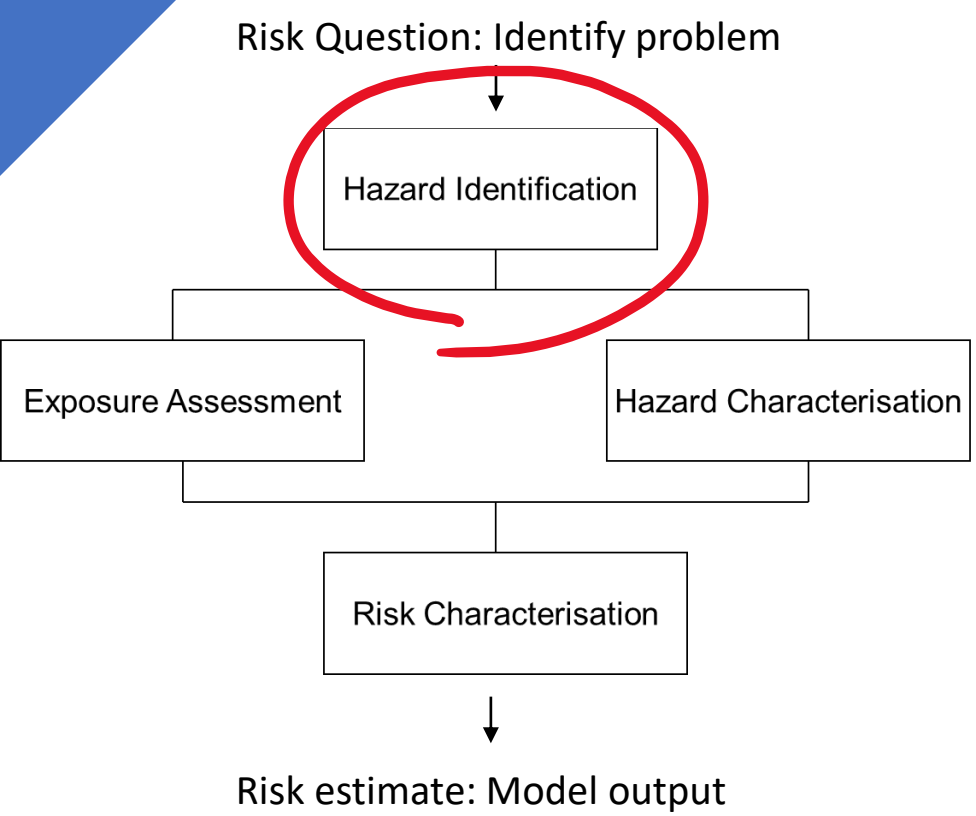




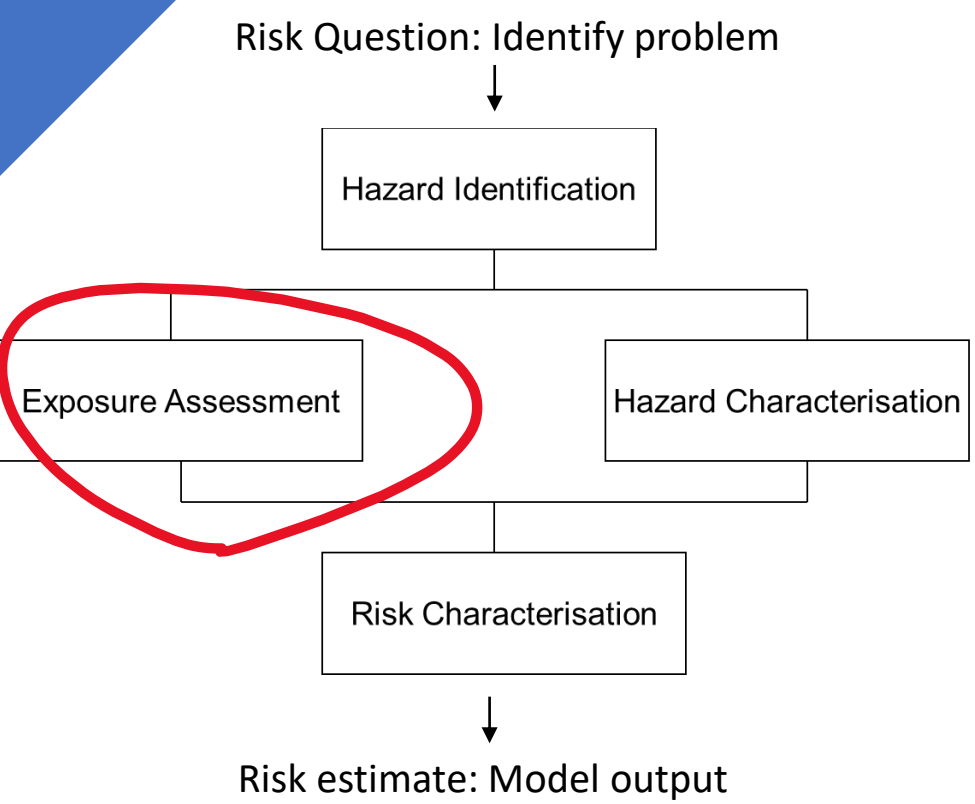
Risk is a function of **exposure** and **hazard**; risk assessment estimates this function



Hazard identification

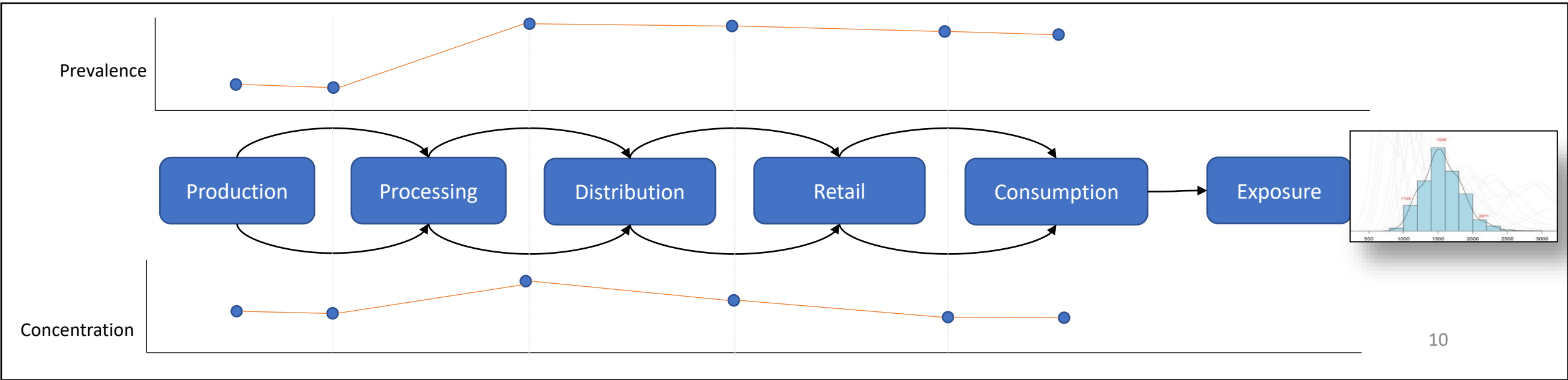
- ”A biological, chemical or physical agent in, or condition of, food with the potential to cause an adverse health effect”
- For viruses, main hazards are Norovirus, Hepatitis A and Hepatitis E
- Main sources are contaminated shellfish, fresh produce, ready to eat foods, and (for HEV) undercooked pork -most raw or lightly cooked

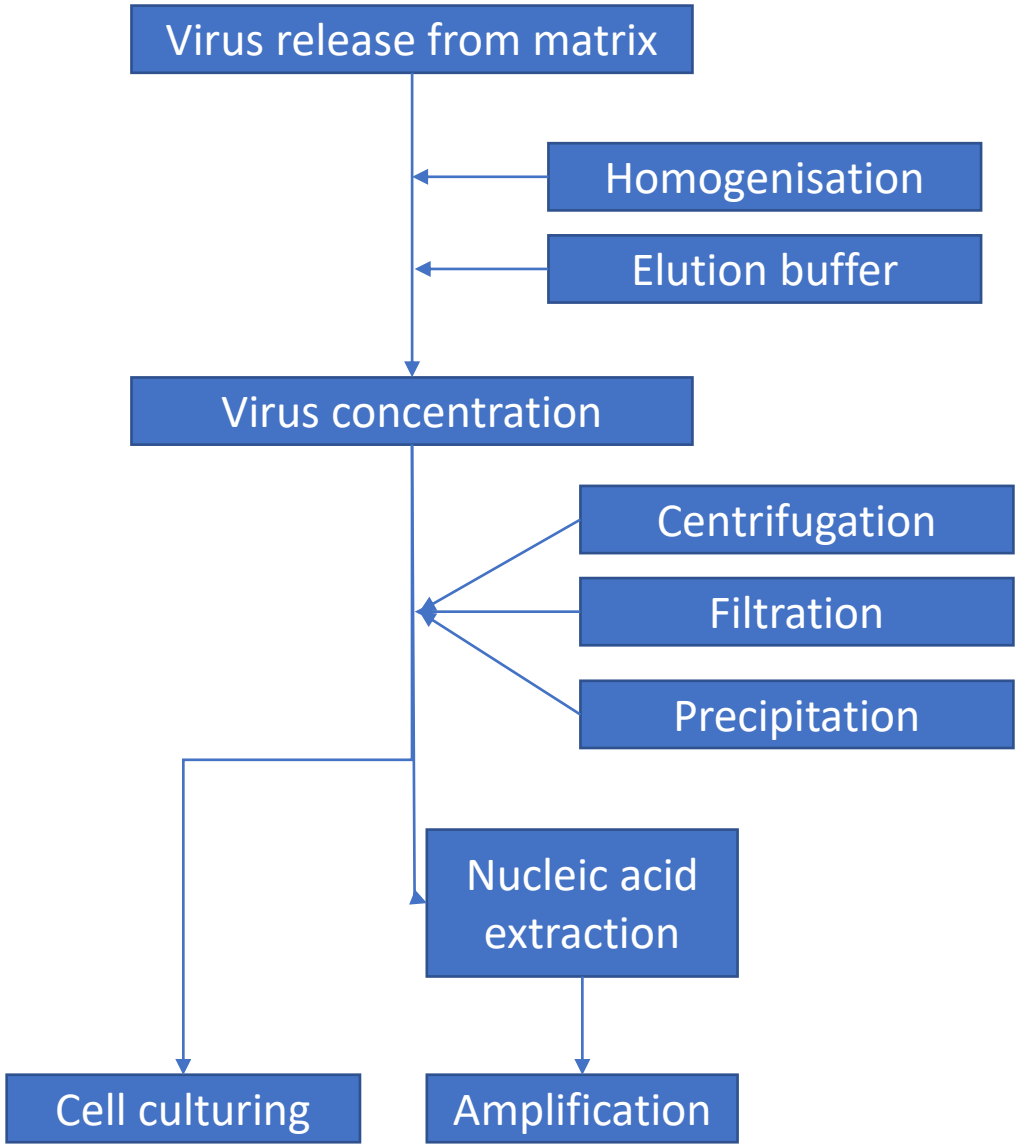
- Genetic diversity of common viruses can affect different populations – transmission pathway affects strain prevalence.
- Different health outcomes following infection in vulnerable populations
- Epidemiological data can be incomplete or uncertain, given high prevalence



Difficulties in **Exposure assessment**

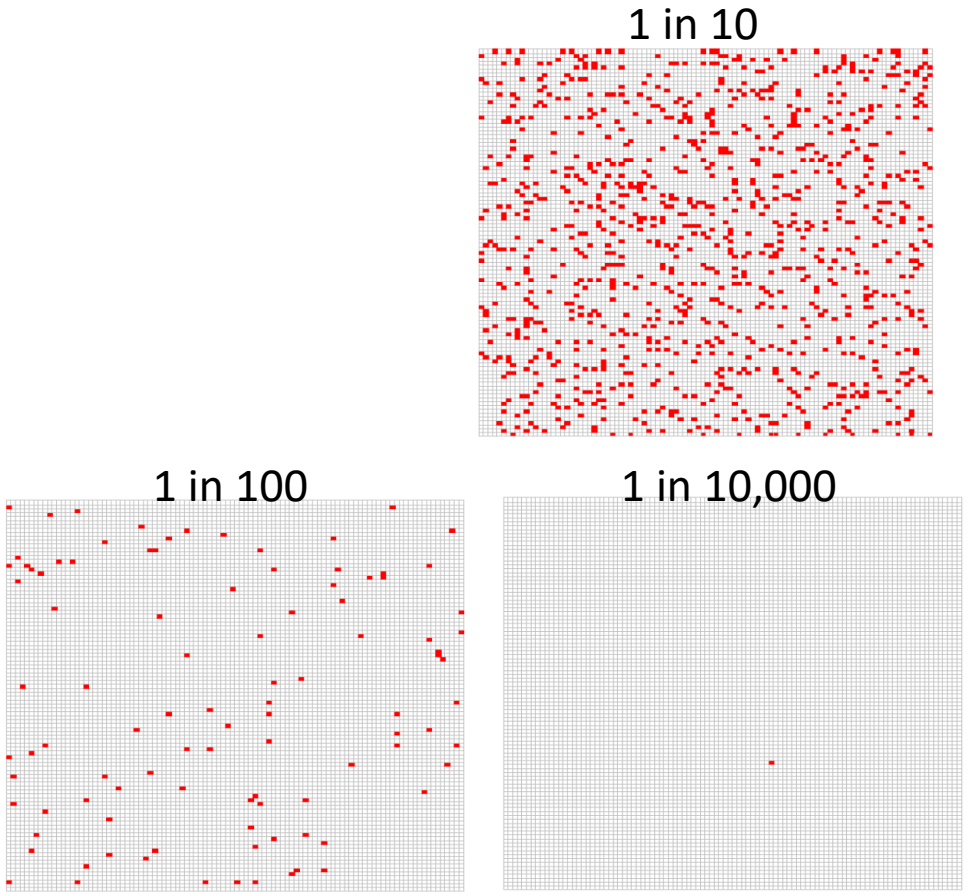
- Modelling transmission pathways, including cross-contamination
- Data on persistence of virus in food
- Data on inactivation of virus in food
- The efficacy of surrogates



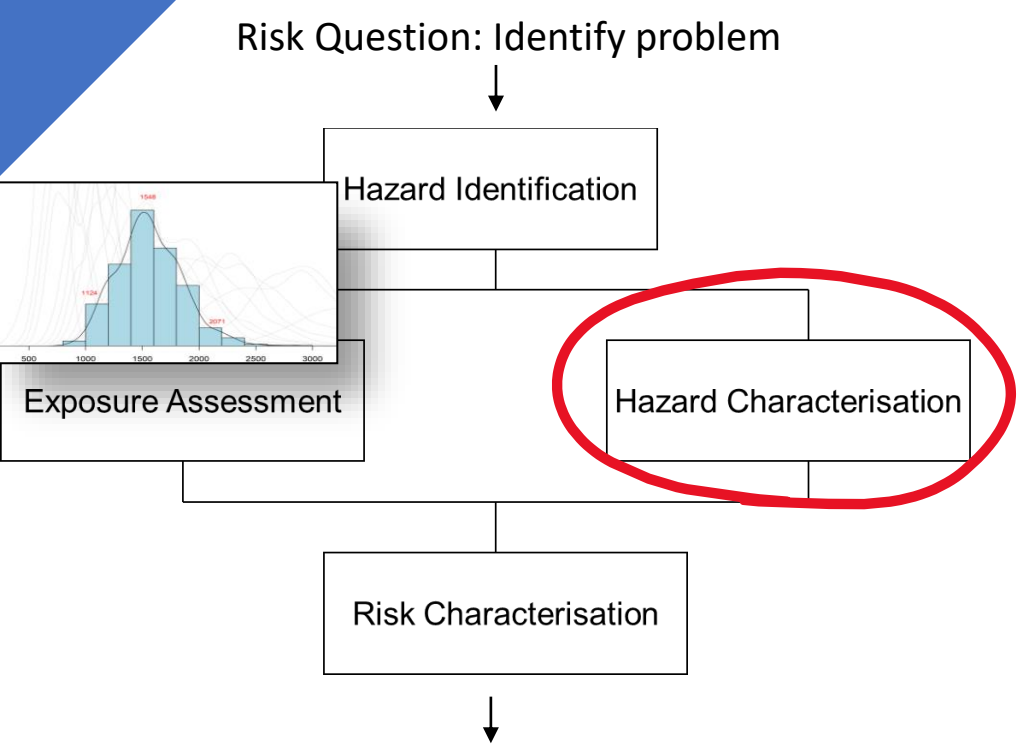


Difficulties in **Exposure assessment**

- Detection of virus in food
- Effect of binding to food matrix unclear

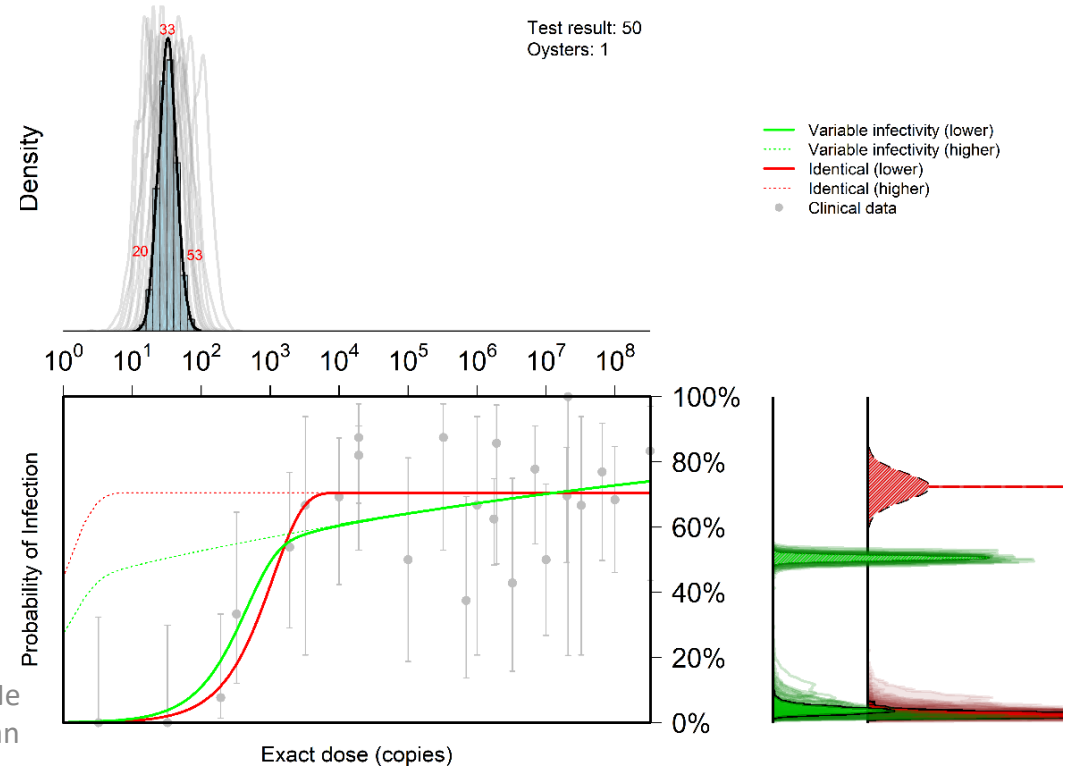


Potential infectivity ratios



Difficulties in **hazard characterisation/dose response**

- Understanding mechanisms of infection for accurate modeling
- Availability of data and interpretation of available data
- Surrogate virus efficacy again



Key points from part one

The main difficulties preventing wider virus risk assessments largely relate to **detection**

Data gaps mainly for

- **infectivity** of detected copies
- **Challenge studies** at lower concentrations
- the efficacy of **surrogate viruses**
- Survival, inactivation, persistence

Important takeaway: If virus copies enter the production chain, a significant proportion are likely to survive until consumption.

Objectives of presentation

To **explain** why quantitative virus risk assessment (QVRA) is less common

To **explore** the future of QVRA.

Outline of presentation

1. The **difficulties** in applying QRA to viruses

2. The main **differences** between bacteria and viruses as hazards

3. Future **challenges and opportunities** for QVRA

Major Differences

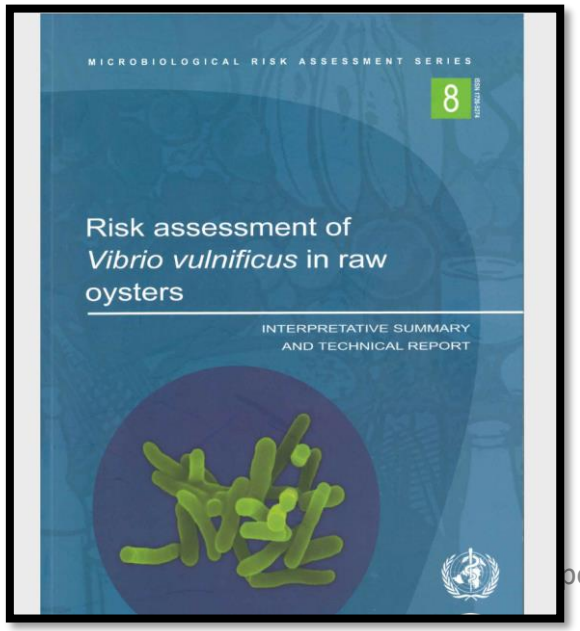
- Unlike bacteria, viruses do not grow or metabolise during production (excluding HEV in livestock)
- Viruses are more persistent, with high survival rates over time. They tend also to be more resistant to removal and inactivation.
- Viruses have lower infectious doses, and potentially higher loads at point of contamination, especially with high shedding
- This puts greater emphasis on prevalence and prevention of contamination.

Example

Comparing two risk assessments for **bacteria** and **virus** hazard in same product (**raw oysters**)

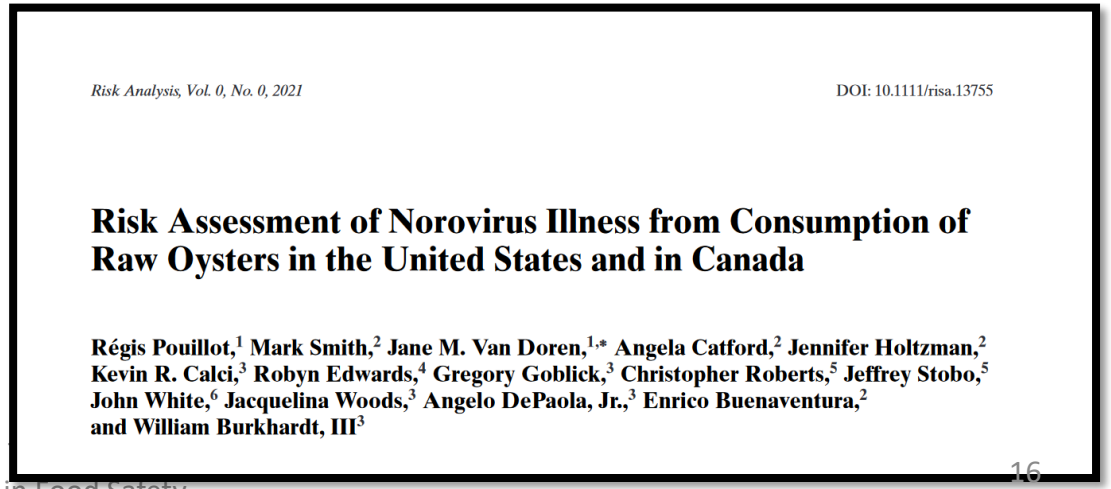
Vibrio Vulnificus

Risk Assessment of *Vibrio Vulnificus* in Raw Oysters (FAO/WHO, 2011)



Norovirus

Risk Assessment of Norovirus Illness from Consumption of Raw Oysters in the United States and in Canada. (Pouillot et al., 2021)


Risk Analysis, Vol. 0, No. 0, 2021 DOI: 10.1111/risa.13755

Risk Assessment of Norovirus Illness from Consumption of Raw Oysters in the United States and in Canada

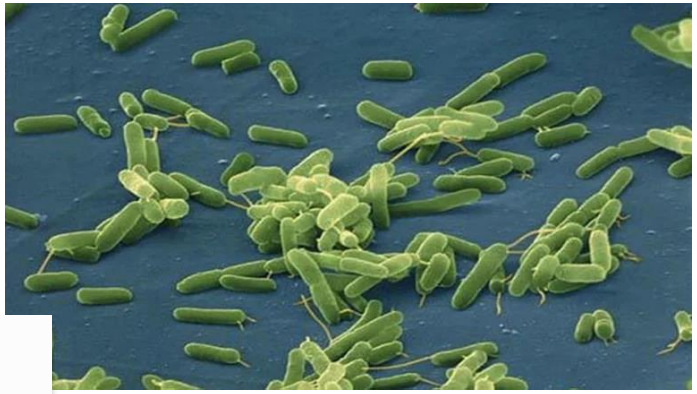
Régis Pouillot,[1] Mark Smith,[2] Jane M. Van Doren,[1,*] Angela Catford,[2] Jennifer Holtzman,[2] Kevin R. Calci,[3] Robyn Edwards,[4] Gregory Goblick,[3] Christopher Roberts,[5] Jeffrey Stobo,[5] John White,[6] Jacquelina Woods,[3] Angelo DePaola, Jr.,[3] Enrico Buenaventura,[2] and William Burkhardt, III[3]

Example

Hazard identification

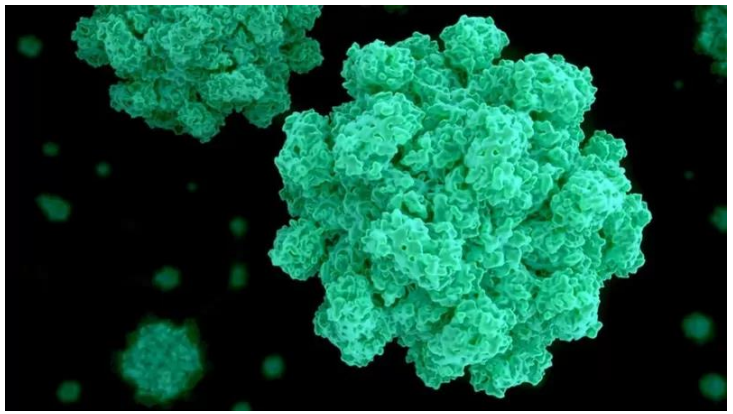
Vibrio Vulnificus

- Indigenous to warm estuarine waters
- Infections rare but severe (30-40 foodborne cases per year as of 2011)
- Optimal growth between 20-35°C
- Population at risk: those with chronic liver conditions and other immunocompromised status



Norovirus

- Transmitted by wastewater contamination
- Infections common (70,000 oyster cases estimated per year) but usually mild
- No growth, but high survival in environment
- No stratification of population in this risk assessment

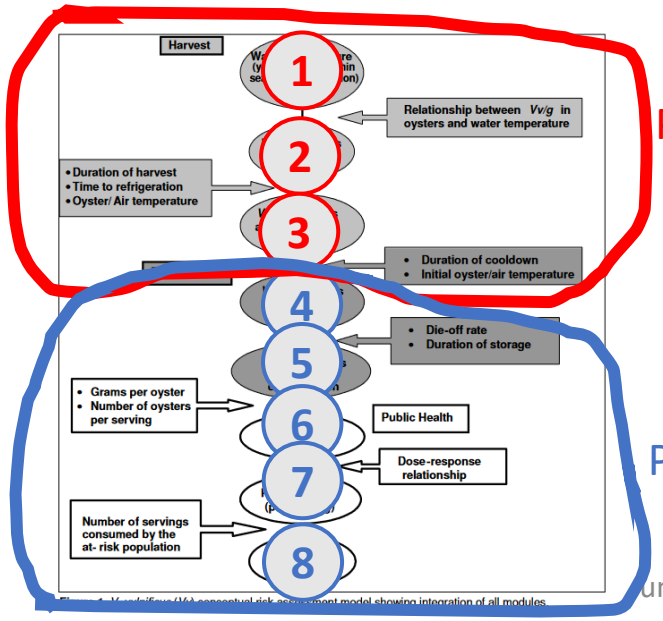


Example

Exposure assessment

Vibrio Vulnificus

- Focus on growth post-harvest
- Simple environmental model – water temp. and salinity
- Evidence for seasonal effect during summer

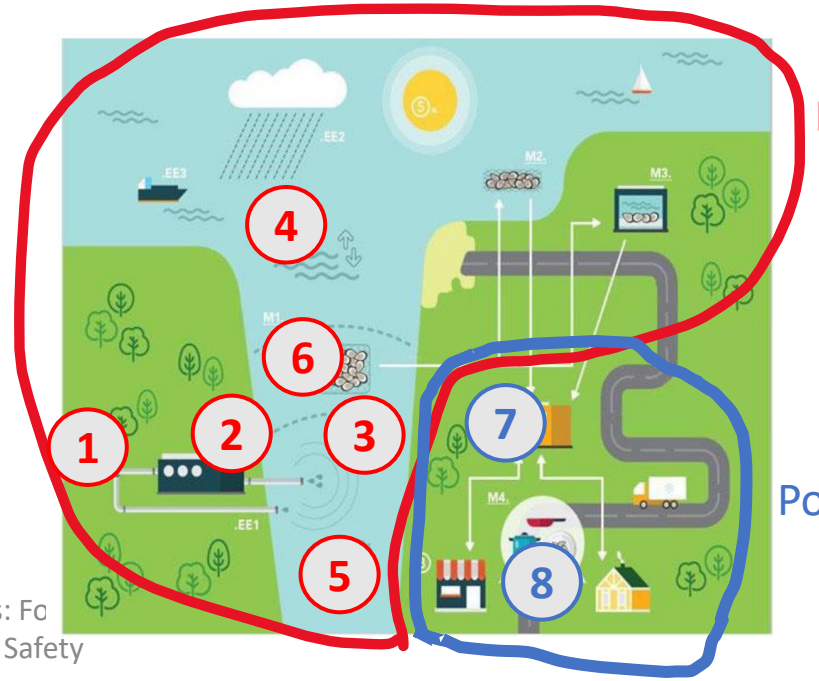


Pre-harvest

Post-harvest

Norovirus

- Focus on accumulation pre-harvest
- More complicated environmental modelling
- Evidence for seasonal effect during winter
- Removal steps more strongly considered



Pre-harvest

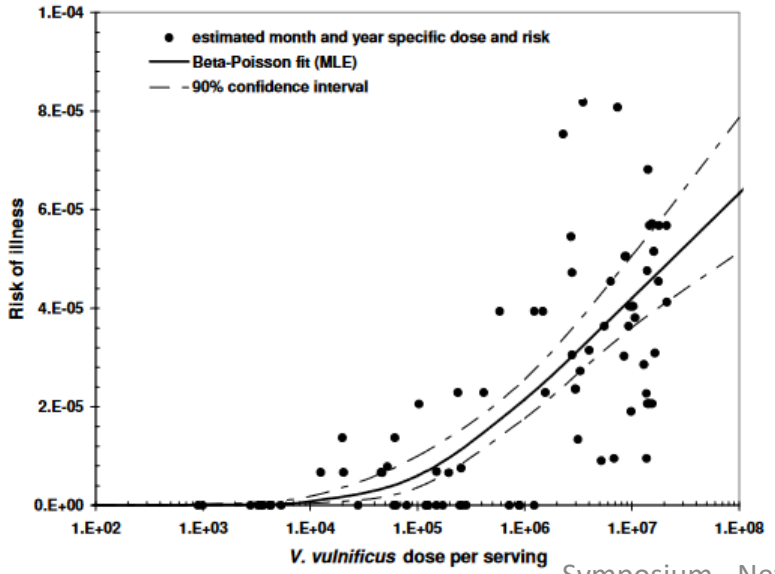
Post-harvest

Example

Hazard characterisation / dose-response

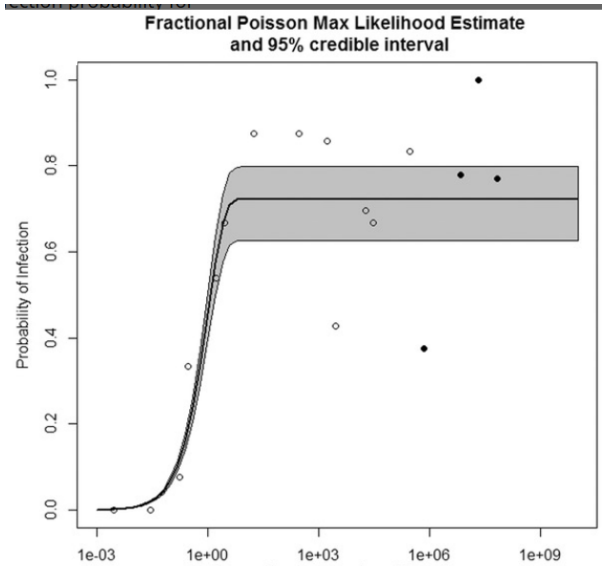
Vibrio Vulnificus

- Beta-Poisson dose response model – fit using epidemiological data
- High dose needed to cause infection (10,000+)
- No immunity modeled



Norovirus

- Modified “fractional Poisson” model
- Very low infectious dose, a single copy if susceptible
- High rate of genetic immunity (28%)



Example

Conclusions

- Growth post-harvest is much more important for bacterial hazards
- Initial concentrations are more important for viral hazards
- Risk assessments for bacterial hazards are more transferrable across species and strains.
- Viral infection is more dependent on host genetics
- Removal through mitigation methods is more important for the viral hazard, given the low infectious dose
- Higher uncertainties for virus conclusions, given the detection difficulties.

Key points for part two:

The combination of

- No growth in food
- lower infectious doses
- Transmission through human contact
- Higher persistence or survival

are the main differences between viruses and bacteria as hazards

This is especially significant for control strategies and inactivation

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Challenges and opportunities

The major challenges for the future:

- Emerging viruses, mutations
- Detection of infectious copies
- Detecting presence at low levels
- Data needed for dose response
- Efficacy of surrogates

Opportunities

There have been promising developments in detection, with cell culturing for major viruses and more sophisticated PCR methods

Virus cell culturing

- Human Norovirus Cultivation in Nontransformed Stem Cell-Derived Human Intestinal Enteroid Cultures: Success and Challenges. (Estes et al., 2021)
- Replication of human noroviruses in stem cell–derived human enteroids (Ettayebi et al., 2016)

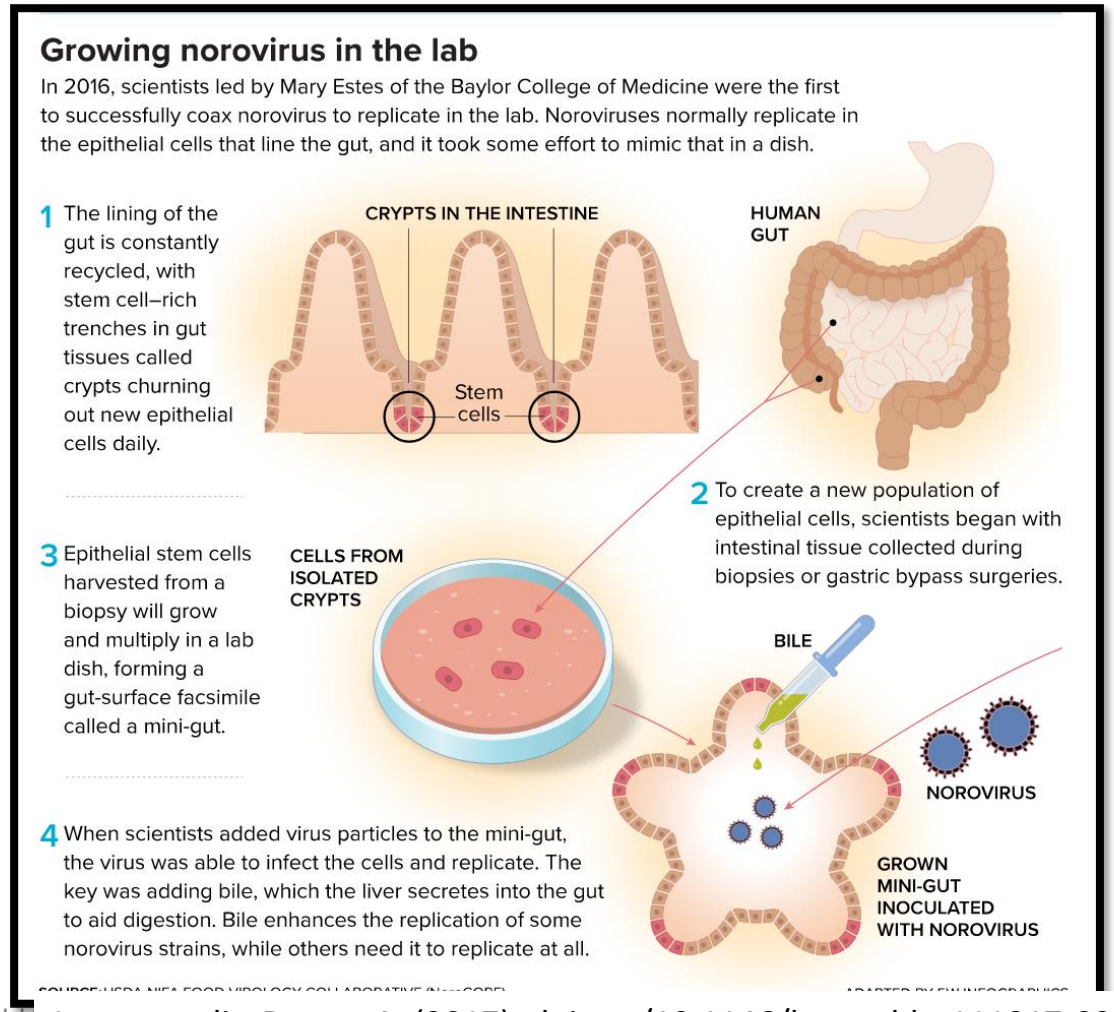


Image credit: Dance, A. (2017). doi.org/10.1146/knowable-111017-093400

Opportunities

There have been promising developments in detection, with cell culturing for major viruses and more sophisticated PCR methods

Viability PCR

- Viability RT-qPCR to detect potentially infectious enteric viruses on heat-processed berries. (Chen et al., 2020)
- Application of viability PCR to discriminate the infectivity of hepatitis A virus in food samples. (Moreno et al., 2015)
- Recent developments in the use of viability dyes and quantitative PCR in the food microbiology field. (Elizaquível et al., 2014)

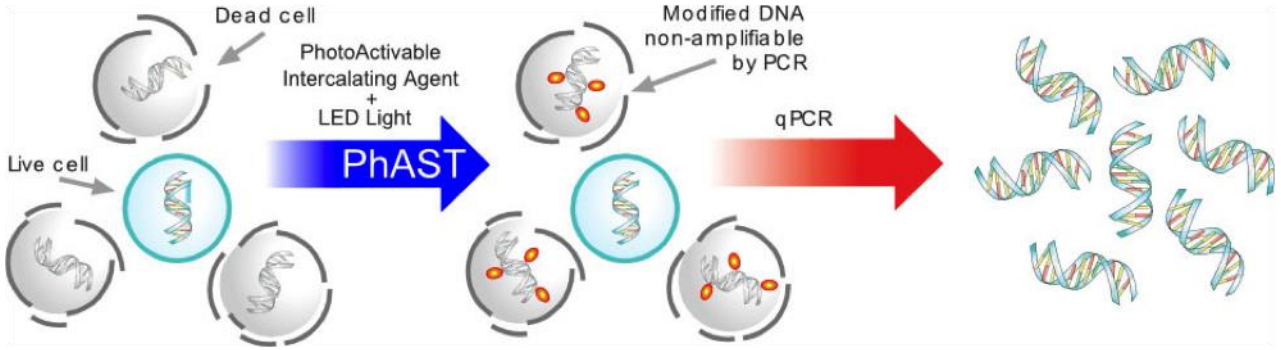


Image credit: FCI1971, CC BY-SA 4.0 via Wikimedia Commons

Opportunities

There have been promising developments in whole genome sequencing, and –omics approaches for all microbial hazards ("next generation" risk assessment).

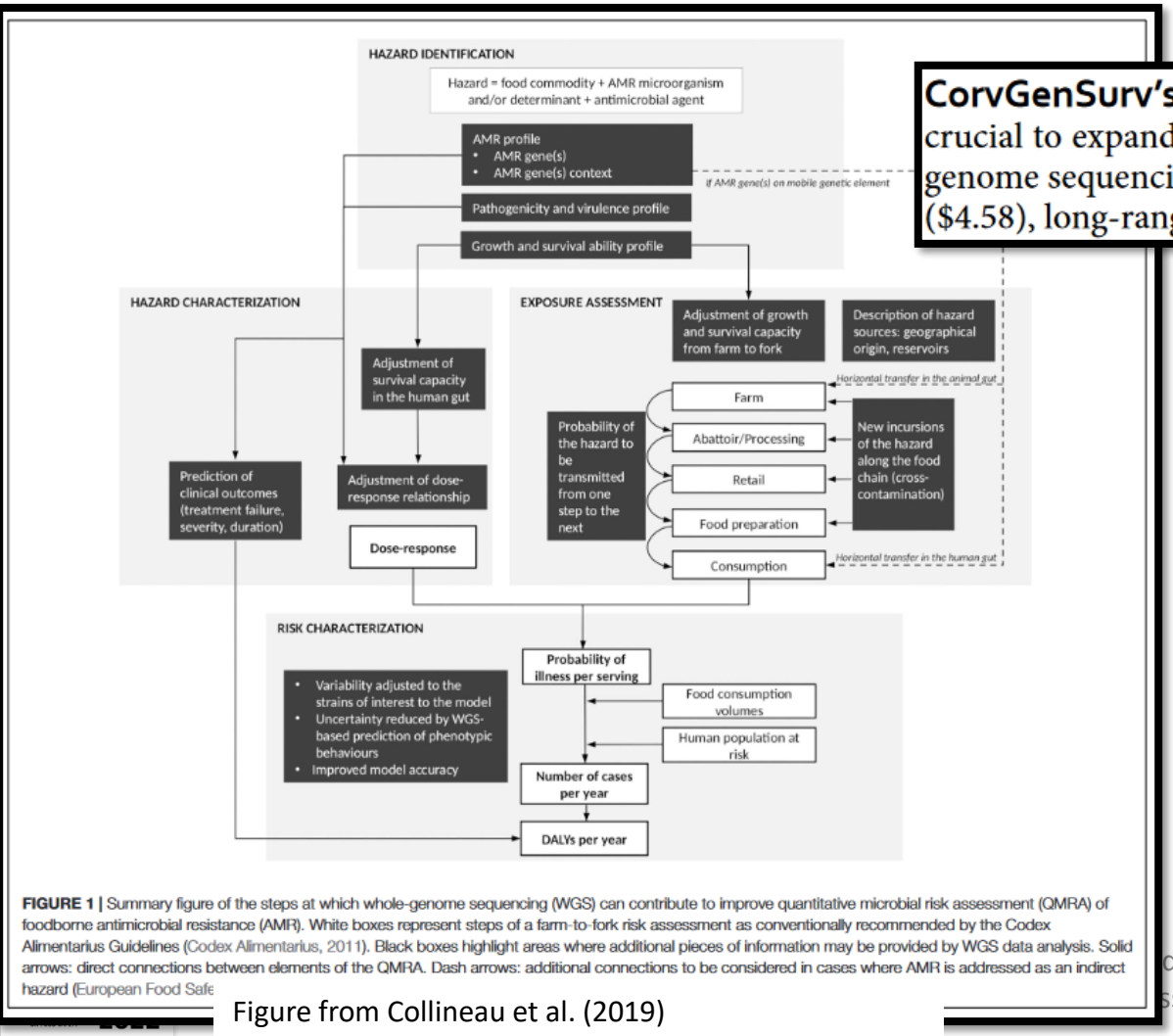


FIGURE 1 | Summary figure of the steps at which whole-genome sequencing (WGS) can contribute to improve quantitative microbial risk assessment (QMRA) of foodborne antimicrobial resistance (AMR). White boxes represent steps of a farm-to-fork risk assessment as conventionally recommended by the Codex Alimentarius Guidelines (Codex Alimentarius, 2011). Black boxes highlight areas where additional pieces of information may be provided by WGS data analysis. Solid arrows: direct connections between elements of the QMRA. Dash arrows: additional connections to be considered in cases where AMR is addressed as an indirect hazard (European Food Safe

Figure from Collineau et al. (2019)

Park et al. (2021) https://doi.org/10.1038/s41598-021-93145-4

CorvGenSurv's supply cost. The development of a cost-effective SARS-CoV-2 genotyping protocol crucial to expanding COVID-19 surveillance efforts. The per-specimen supply cost of our SARS-CoV-2 who genome sequencing method was estimated to be $33.8. This includes RNA extraction from NP/OP swab med ($4.58), long-range RT-PCR ($25.8), index PCR ($2.6), and long-read high-throughput sequencing ($0.82).

Representative publications

- Collineau et al., (2019). Integrating Whole-Genome Sequencing Data Into Quantitative Risk Assessment of Foodborne Antimicrobial Resistance: A Review of Opportunities and Challenges
- den Besten et al., (2018). Next generation of microbiological risk assessment: Potential of omics data for exposure assessment.
- EFSA BIOHAZ, (2019) Whole genome sequencing and metagenomics for outbreak investigation, source attribution and risk assessment of food-borne microorganisms.
- Franz et al., (2016). Significance of whole genome sequencing for surveillance, source attribution and microbial risk assessment of foodborne pathogens.
- Fritsch et al., (2018) Next generation quantitative microbiological risk assessment: Refinement of the cold smoked salmon-related listeriosis risk model by integrating genomic data.
- Haddad et al., (2018) Next generation microbiological risk assessment—Potential of omics data for hazard characterisation.
- Rantsiou et al., (2018) Next generation microbiological risk assessment: opportunities of whole genome sequencing (WGS) for foodborne pathogen surveillance, source tracking and risk assessment.

Opportunities

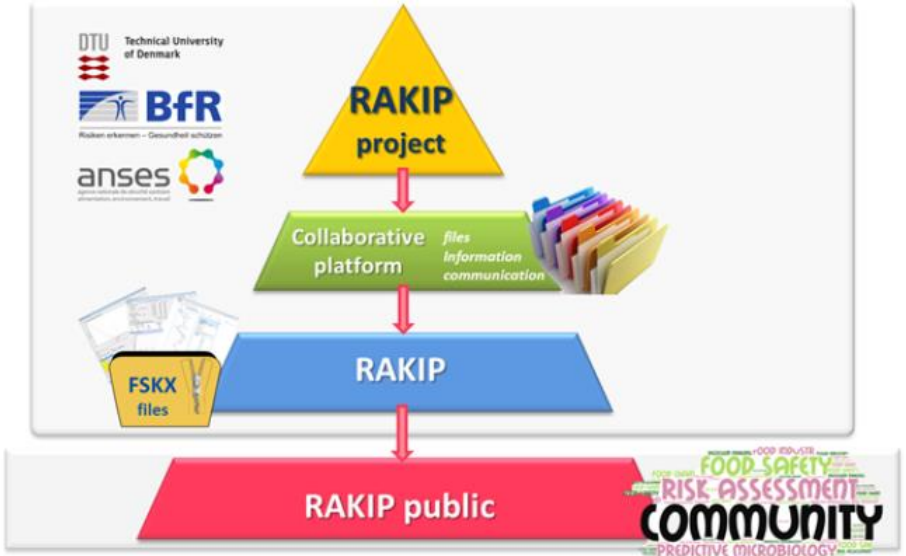
There have been promising developments in data sharing, data harmonisation, and the publication of expert guidance documents

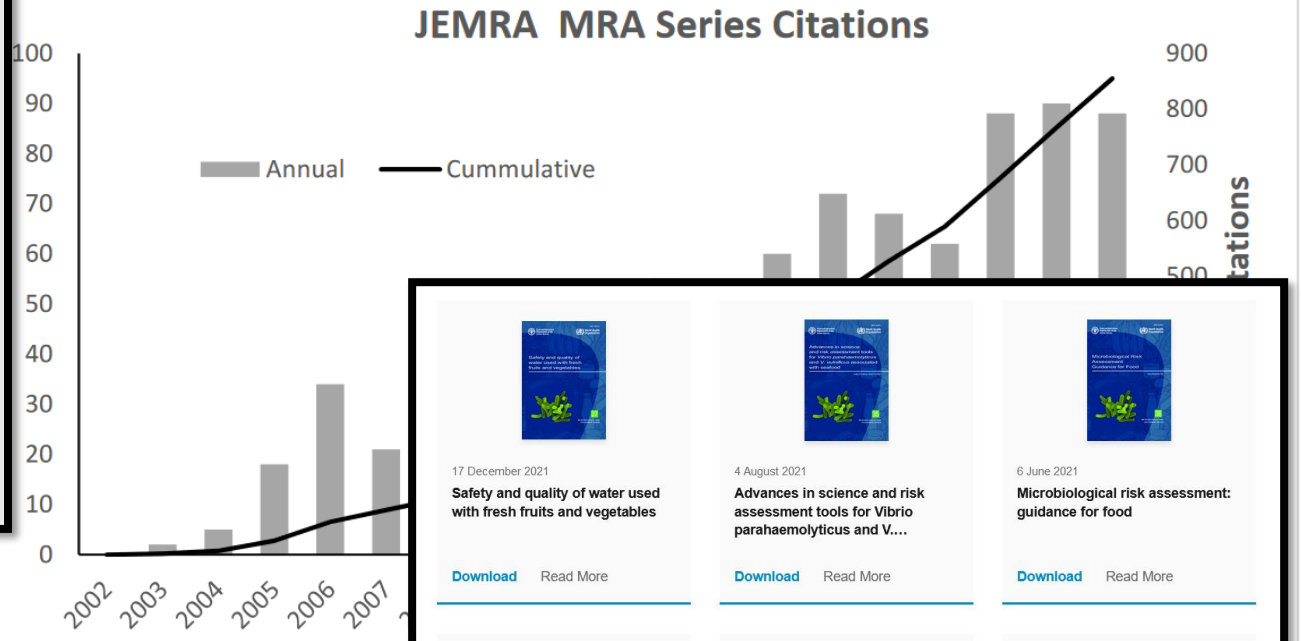
FoodRisk.org is a metadatabase of tools and models for food safety professionals in industry, academia, and government

We feature 197 total food safety resources listed in 5 different categories.

TOOLS | DATABASES | RISK ANALYSIS | MODELS | TRAININGS

Do you have a





Key points

Challenges

- emerging viruses
- detection and infectivity
- dose-response data

Opportunities

- culturing methods
- WGS and–omics
- greater data sharing, harmonisation on databases, expert groups meeting

Conclusion

- Background
  - Foodborne virus contributes large percentage to foodborne illness
  - Quantitative risk assessment is an important tool for tackling this
  - But there is a lack of data and modelling for foodborne virus hazards
- Main difficulties are with detection
  - And a lack of data for necessary modelling of exposure and dose-response
- Differences
  - Absence of growth
  - Greater persistence in environment – antibacterial measures can even improve persistence
  - Lower infectious doses
  - Different responses to inactivation methods, more resistant in most cases
- Opportunities
  - Better detection methods for determining infectivity – more data for modelling
  - “Next generation” of risk assessment already here
  - Main objective is to control risk – discussed in next presentation

Conclusion

- Foodborne virus is a significant problem
- Risk assessment will be part of the solution
- The differences of virus hazards mean that ‘QVRA’ is emerging as a distinct sub-category of QMRA
- Many promising recent developments contributing to next generation of QMRA