The Next Frontier in Risk Assessment in Food -
Quantitative Viral Risk Assessment

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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)

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

Symposium: New Hazards and Old Threats: Foodborne Viruses and Risk Assessment in Food Safety
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Timeline of QMRA

1970s
Risk assessment

In relation to aerospace and nuclear disasters

1983
First virus risk assessments


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?

Risk assessment is the **scientific component** of risk analysis.
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Risk Question: Identify problem

- Hazard Identification

- Exposure Assessment

- Hazard Characterisation

- Risk Characterisation

Risk estimate: Model output

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

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Symposium - New Hazards and Old Threats: Foodborne Viruses and Risk Assessment in Food Safety

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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

- Virus release from matrix
  - Homogenisation
  - Elution buffer

- Virus concentration
  - Centrifugation
  - Filtration
  - Precipitation

- Nucleic acid extraction
- Cell culturing
- Amplification

Potential infectivity ratios
1 in 10
1 in 100
1 in 10,000
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.
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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**


**Norovirus**

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

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

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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)
Opportunities

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

Representative publications

Opportunities

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