# Comparative and critical analysis

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# Outline

This session consists of the following elements:

1. Live discussion of the participant responses and aggregated poll results
2. Facilitators will explore different analytical paths and conclusions
3. Live discussions of the advantages and limitations of WGS-based and epidemiological outbreak investigations

# Live discussion of the participant responses and aggregated poll results

# Outbreak source and transmission

- The dataset represents a foodborne outbreak of *Brucella melitensis* occurring shortly after the Christmas period (December 2025 → January 2026).
- The most likely **transmission route is ingestion of unpasteurized sheep/goat cheese sold at a Christmas marke**t, with **cases arising through both direct consumption by market visitors and secondary exposure via food sharing after return from travel.**

- The outbreak primarily affects human cases, with **a single food isolate (Food_627)** acting as the **epidemiological and genomic bridge between cases**, consistent with a point-source exposure. **No sustained human-to-human transmission** is included in this scenario.

- Reports of livestock miscarriages and associated *Brucella abortus* detections reflect realistic background surveillance signals that are temporally related but epidemiologically and genomically unrelated to the human outbreak.

# Do you agree with the proposed outbreak source and transmission route? Why or why not?

# How confident are you in the identified outbreak source?

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# What evidence most strongly influenced your conclusion?

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# Which type of data was most critical for defining the outbreak cluster?

# Which transmission route do you think best explains the observed pattern of cases?

# At first, did the livestock miscarriage reports seem plausible as part of the outbreak?

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## Which piece of evidence most clearly ruled out the livestock miscarriages as the outbreak source?

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# Were there any isolates you found difficult to classify as outbreak or non-outbreak? Why?

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# Are you missing any information to make public health recommendations?

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# If this was a real outbreak, what would your immediate public health recommendation be?

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# Different analytical paths and conclusions

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# Which of the following analyses did you complete?

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# If you selected other, what analysis did you do?

# If you didn’t do a step, what made you decide it wasn’t necessary?

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**If you used cgMLST instead or in addition to SNP analysis, did you reach the same outbreak definition?**

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# Where did cgMLST and SNP analysis agree, and where did they differ?

# Would cgMLST alone have been sufficient to define this outbreak? Why or why not?

# Advantages and limitations of WGS-based and epidemiological outbreak investigations

# Advantages of WGS-based outbreak investigations

- High-resolution discrimination between isolates
- Objective, reproducible comparison of cases across settings
- Ability to confirm epidemiological links
- Detection of outbreaks across time and geography
- Supports integration across One Health sectors

# Limitations of WGS-based outbreak investigations

- Requires high-quality sequencing data and bioinformatics expertise
- Turnaround time may limit real-time decision-making (Illumina vs Nanopore)
- Start-up cost can be very high
- Interpretation depends on context and appropriate thresholds
- Cannot identify exposure routes on its own
- Risk of overconfidence without epidemiological support
- Metadata not properly recorded

# SNP analysis vs cgMLST in outbreak investigations

## SNP-based analysis

Advantages:

- Highest possible resolution between closely related isolates
- Well-suited for confirming or excluding outbreak membership
- Strong support for fine-scale transmission inference
- Often preferred for retrospective or confirmatory analyses

Limitations:

- More sensitive to reference genome choice and quality
- Requires greater bioinformatics expertise
- Results can be pipeline- and parameter-dependent
- Interpretation thresholds are not always standardized

## cgMLST-based analysis

Advantages:

- Standardised and reproducible across laboratories
- Easier to implement and interpret
- Many schemes available
- Well-suited for routine surveillance and rapid screening

Limitations:

- Potentially lower resolution than SNP analysis
- Closely related outbreak strains may appear indistinguishable
- Less suitable for fine-scale transmission questions
- May over-group isolates in highly clonal outbreaks
- Schemes may be missing or not well curated

# Advantages of epidemiological outbreak investigations

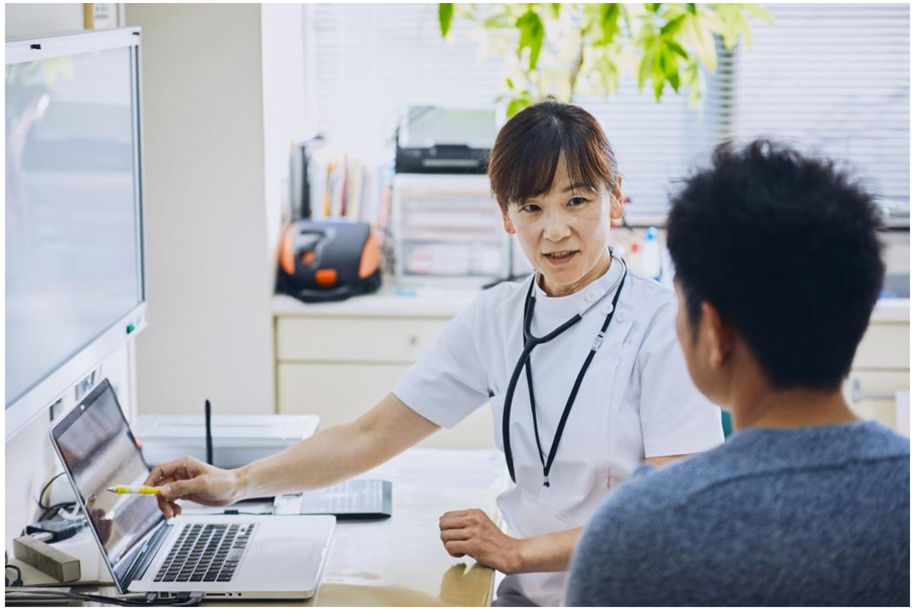
- Rapid hypothesis generation
- Provides exposure and behavioral context
- Directly informs public health action
- Can guide sampling and sequencing priorities
- Essential for risk communication and control measures

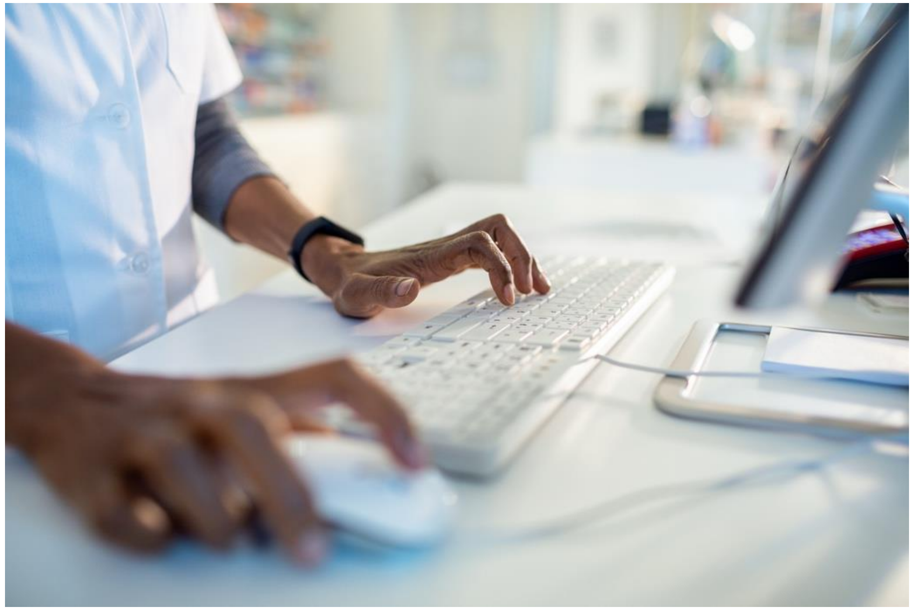
# Limitations of epidemiological outbreak investigations

- Time consuming (person-hours)
- Subject to recall and reporting bias
- Associations do not prove transmission
- Coincidental signals can mislead investigations
- Difficult to resolve complex or widespread outbreaks
- Limited ability to distinguish related vs unrelated cases

# Combining phylogenetics and epidemiology

- Epidemiology generates hypotheses
- WGS tests and refines those hypotheses
- Together, they reduce uncertainty and bias
- Integration supports evidence-based decision-making





# Thank you for listening! ☺

# Acknowledgements

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