ESGPHM
ESCMID STUDY GROUP FOR PUBLIC HEALTH MICROBIOLOGY
European Society of Clinical Microbiology and Infectious Diseases

# "An outbreak of gastro-enteritis in Kalundborg, Denmark"

ECCMID Educational workshop – exercise 1

**Sunday 14 April 2019, Amsterdam**

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Maastricht UMC+

Radboudumc

# Origin of this case study

- *European Program for Intervention Epidemiology Training*
  - *European Centre for Diseases Prevention and Control*
  - *Version Introduction course  Summer 2016*

- *Statens Serum Institute (Copenhagen, Denmark), invited by the authorities in Kalundborg*

- *Lieke van Alphen and Frédérique Dorléans  developed case study and conducted outbreak investigation*

# Learning objectives

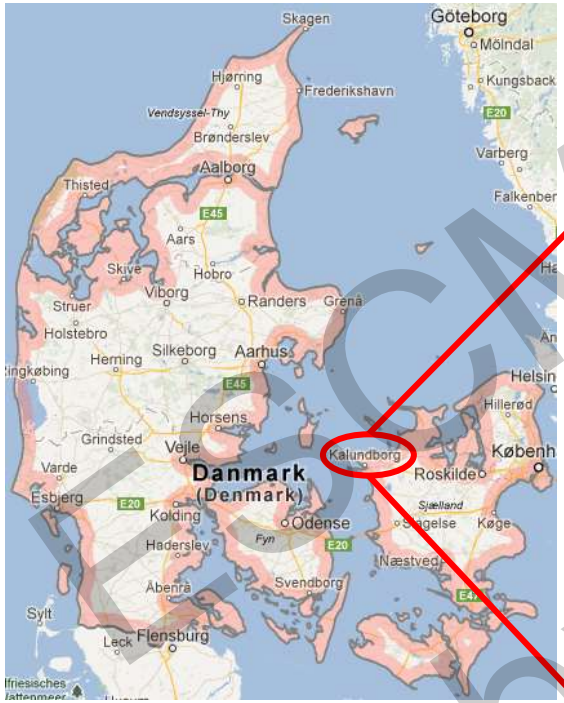
## Aim

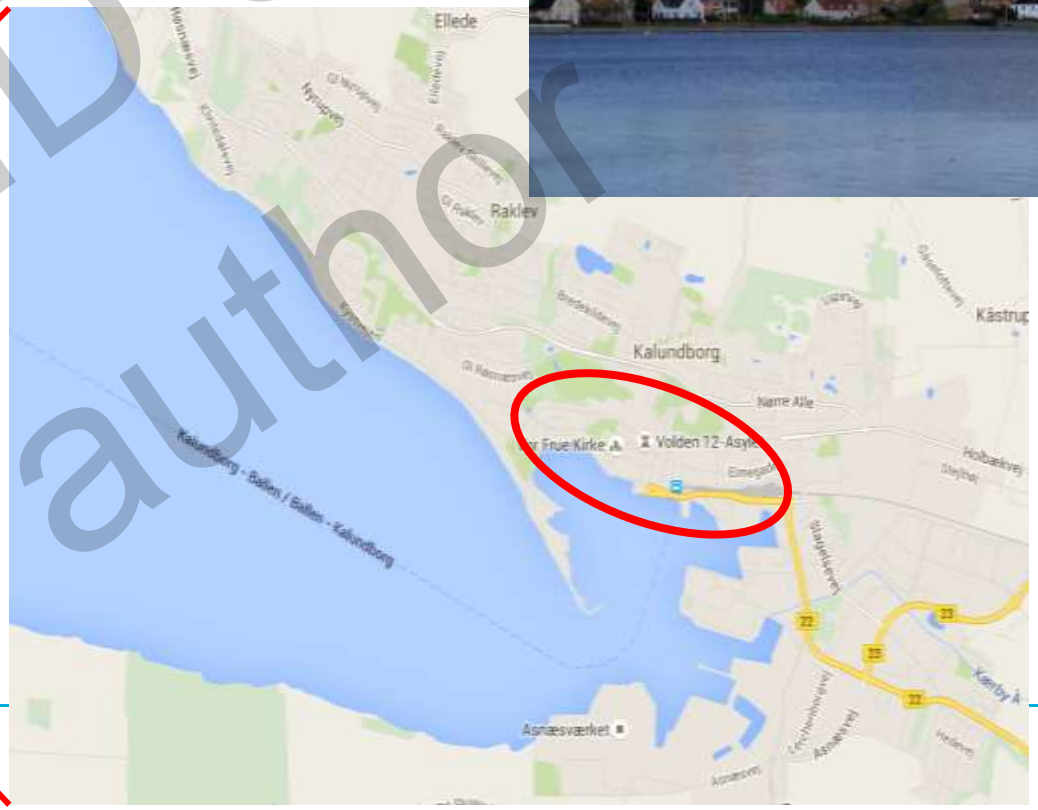
multi-disciplinary approach in an community outbreak investigation

Specific learning objectives

- **Shortlisting pathogens** in community outbreak of gastrointestinal illness
- Use of **case definition** for outbreak investigation purposes
- Generate **hypotheses** using different pieces of evidence
- Use **microbiological characterizations** of pathogens to demonstrate a common source
- **Combine epidemiological, microbiological and environmental data** to formulate conclusions and recommendations

# **Kalundborg, Denmark** (population ~50.000)



# Signal: 3 notifications of clusters of GE illness

| 13 Dec 2012 | 13 Dec 2012 | 14-15 Dec 2012 |
|---|---|---|
| a **day-care centre** | persons living in a single **apartment complex** | **clinician reports** 17 patients with watery diarrhoea, nausea and stomach pain , headache, vomiting and/or fever |

## Is this an outbreak?

***Definition outbreak: more cases of an illness than normally seen in a specific place / population / time period.***

"These reports >> average number GE illnesses reported in this particular area for the season" → this is an outbreak

*Causative pathogen and source are unknown. Do we need data on this?*

# The investigation starts

**14 December:**

- the local health authorities start to investigate

- As an investigator of this outbreak, who would you want to invite as collaborators in this investigation?

***Discuss with neighbour (1 min)***

- Collaborators:
  - Local authorities, municipal health services
  - Representative of GPs
  - Contact regional laboratory
  - Maybe: other parties (fire department/ waterworks etc)
  - National institute of public health (epidemiologist, microbiologist)

# The investigation has started

**17 December:**

- the local health authorities invited a team of the National institute of public health (Statens Serum Institute, SSI) to join the investigation.

- As an investigator of this outbreak, what are the next steps you would like to take?

***Discuss with neighbour (1 min)***

# Next steps in investigation (answer)

- **Confirm diagnosis**
  You need patient samples, but they are not hospitalised, how would you do this?

- **Case definition:**
  - For case finding
  - No lab yet, but based on symptoms, time (from xx December onwards) and place (area Kalundborg)

- **Case finding**
  - Contact the patients who were seen by the clinician (but: symptoms may be over)
  - More cases in the area? Via reported cases, contact GPs
  - Contact labs for results from patients that fit case definition

# Laboratory testing of patient samples

**17 December -** to confirm the diagnosis:

- randomly selected 15 households
- distributed 23 stool specimen collection kits to people with symptoms.
- collection kit : a stool sampling tube, lab form, questionnaire

**Questions:**

- What are the possible pathogens involved in such gastro-intestinal outbreak?

***Discuss with neighbour (1 min)***

# At the National Reference Laboratory in Copenhagen (SSI):

- 17 specimens from 14 separate households were tested for
  - **Bacteria**: *Campylobacter*, diarrhoeagenic *Escherichia coli*, *Salmonella, Shigella* and *Yersinia*
  - **Viruses**: Norovirus (Genogroup I and Genogroup II), Rotavirus, Sapovirus, Human Astrovirus and Human Adenovirus
  - **Parasites:** (*Entamoeba histolytica* or *E. dispar*, *Cryptosporidium* or *Giardia* and *Dientamoebe fragilis*)
  - **Toxins** could also be considered

# Cause of the outbreak: norovirus

**20 December**

- 16/17 patients: Norovirus (Genogroup II)

In the meantime, questions:

- What are **possible sources or causes** of community outbreaks of gastrointestinal illness and/or norovirus outbreaks?
- What could be the (updated) **case definition** in this outbreak investigation?
  - *Remember: case definition includes elements of place, person, time, symptoms*

***Discuss with neighbour (1 min)***

- **Possible sources** of GE outbreaks:
  - Food: e.g. restaurant, dinner/party/event, contaminated food in retail.
  - Water: recreational water, drinking water (waterworks)
  - Person-to-person: transmission in school, work, 'usual' winter outbreak.

- **Case definition**: a resident *(person)* of the affected area – part of Kalundborg *(place)* who presented with diarrhoea, vomiting, abdominal pain or nausea *(clinical symptoms)* from 10 December 2012 to the end of the month *(time)*.
  - Option: different levels of case definition (confirmed, probable, possible)

- **Generating hypotheses**
  - Describe cases to identify common characteristics or exposures
  - Then, compare distribution to that in non-cases

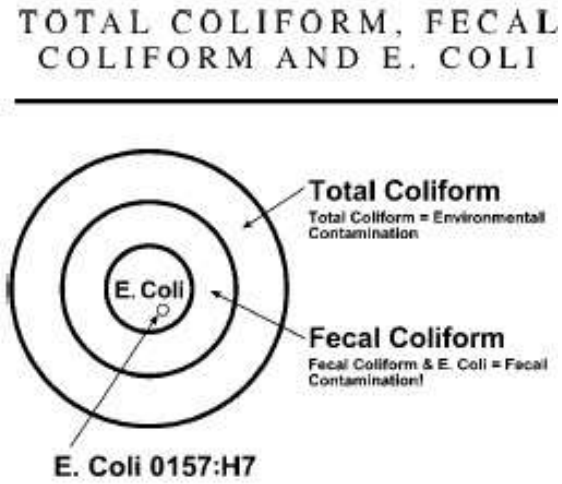
# Environmental investigation

**19 December**

- the team learned that the waterworks company had recently replaced old pipelines on the distribution network and that during the night between **11 and 12 December**, renovations had caused several drops in water pressure on one of the main pipelines supplying the affected area.

**Question**: Who would you contact to obtain and analyse the environmental samples?

***Discuss with neighbour (1 min)***



*Actually – Public Health was already in contact with water company from the beginning – and informed about water problems*

# Findings environmental investigation

- Authorities hypothesized a **waterborne outbreak**.
  - Renewal works
  - Drop in water pressure in the night of 11/12 Dec

- Water company: **intensified sampling** water (every 8 hours)
  - 19 households IN the affected area
  - 5 households OUT the affected area

- Interventions:
  - intensive flushing of the waterworks
  - Public health recommendations:

| Saturday 15-12-2012 | Sunday 16-12-2012 |
|---|---|
| Boil water before use | • Do not drink tap water + water distribution (3 water trucks )<br>• Closure of all restaurants, daycare and primary school |

# Cohort study – to estimate size outbreak

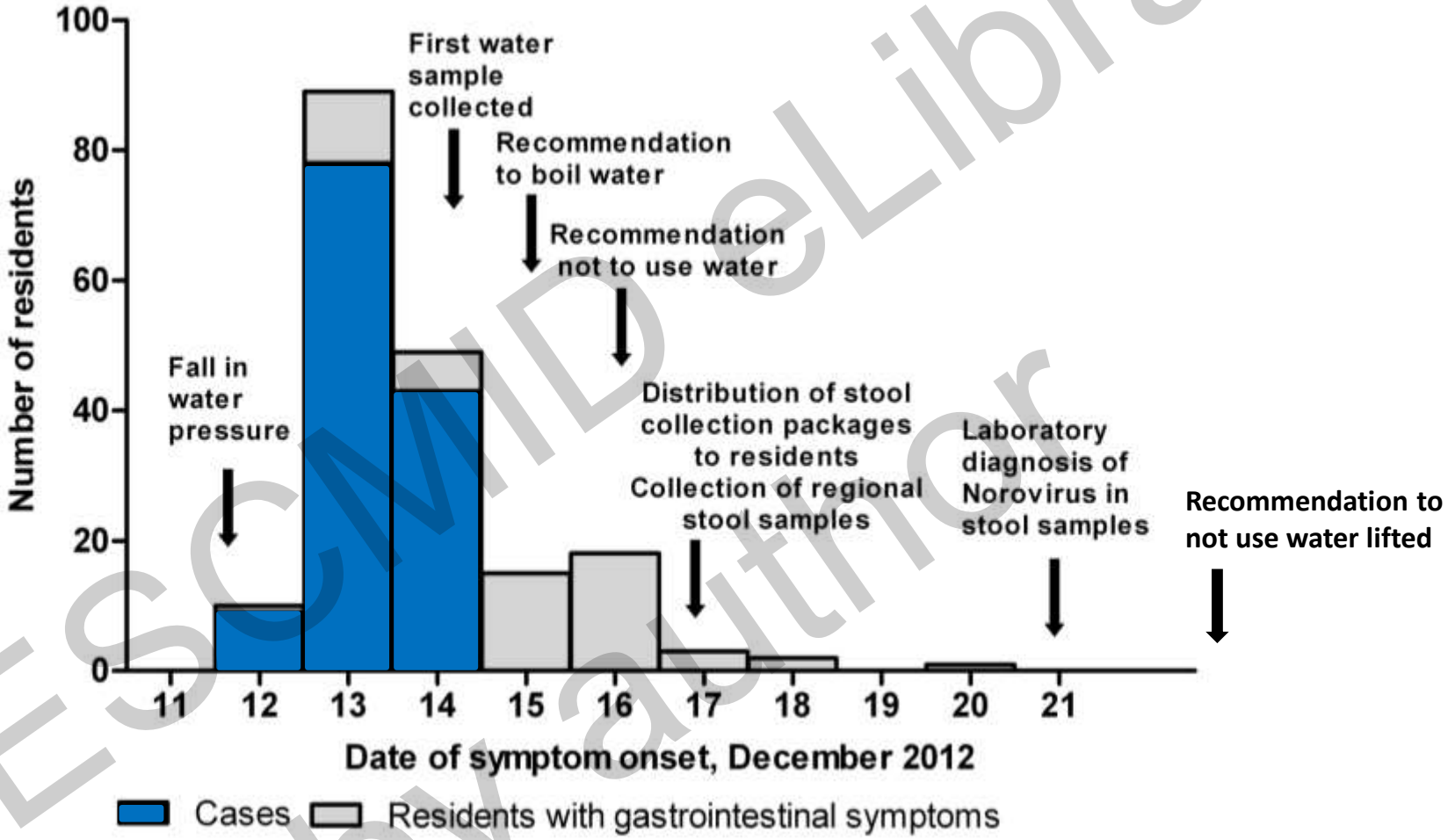



*Figure 1. Cases of gastrointestinal illnesses by date of symptom onset, 12-20 December 2012, Kalundborg, Denmark (N=183 cases)*

# Additional epidemiological & microbiological analysis

- descriptive epidemiology + isolation of norovirus among patients:
  - microbiological contamination of the water following pipeline incident.

- Next steps
  - Analytical epidemiological study
  - further microbiological testing.

- Compare attack rate between exposed and none exposed
  - Risk: universal exposure (i.e. no control group to use as comparison)

**Question**:

- What epidemiological approach could you use to increase the evidence for tap water as source of the outbreak?
- What microbiological evidence would you like to have?

***Discuss with your neighbour***

**Epidemiological**:

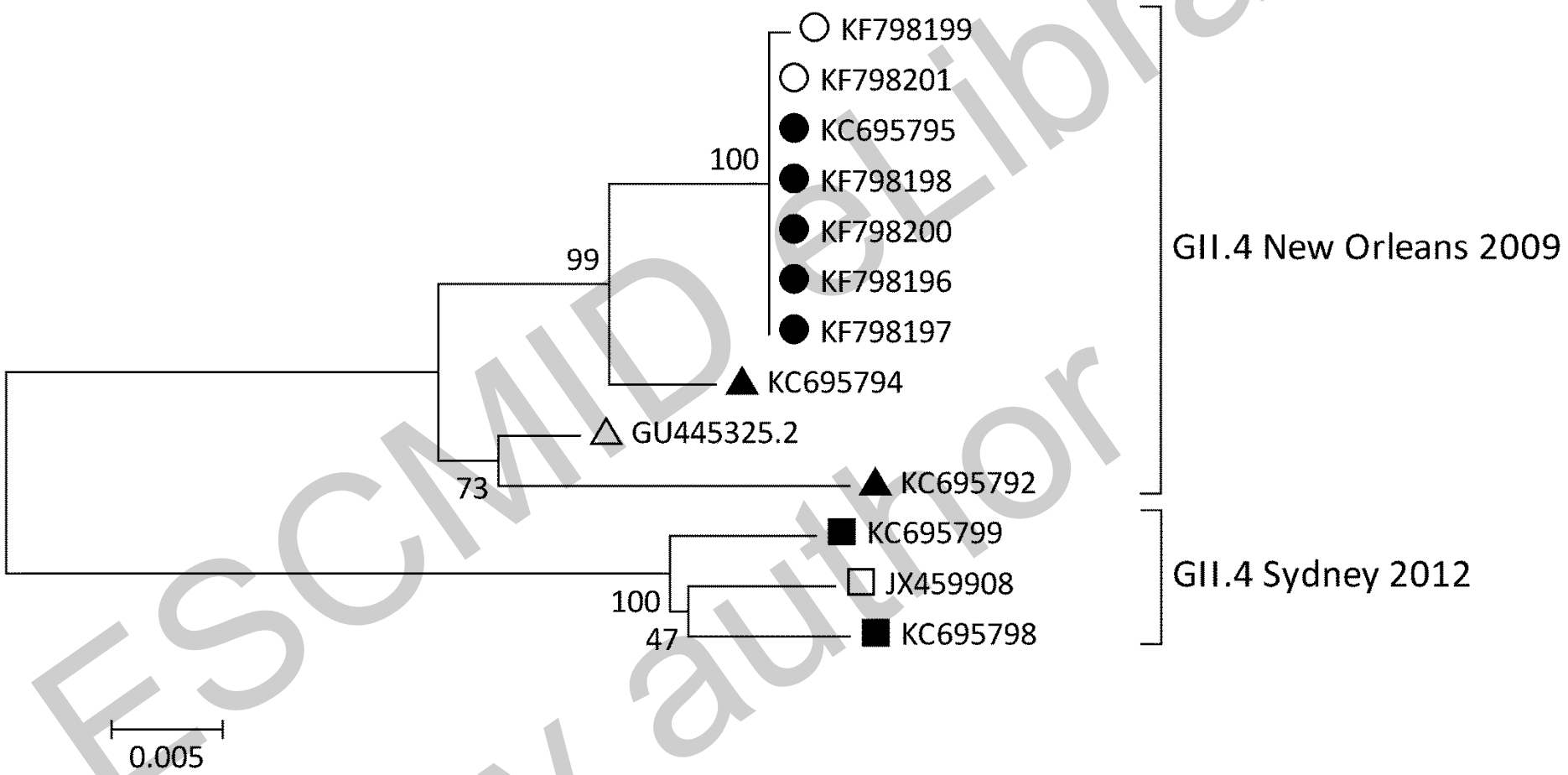
Dose response, with lowest exposure group as reference group.

**Table 6. Attack rate according to the number of glasses of water drunk each day, 12-20 December 2012, Kalundborg, Denmark (N=241).**

| Daily average number of glasses of tap water | Cases | Total | Attack rate (%) | Relative risk |
|---|---|---|---|---|
| **0 (did not drink tap water)** | 2 | 14 | **14 %** | *Reference* |
| **1*** | 16 | 27 | **59 %** ↑ | 4.2 |
| **2** | 20 | 26 | **77 %** ↑ | 5.5 |
| **3** | 36 | 45 | **80 %** ↑ | 5.7 |
| **≥4** | 86 | 103 | **83 %** ↑ | 5.9 |

*Estimation: 1 glass of water contained enough viral particles to cause disease

# Phylogenetic tree of NoV long capsid gene (1140 bp)



# Conclusions

- Outbreak of Norovirus in Kalundborg
  - Drinking water contaminated with fecal matter
  - 52% of people exposed developed diarrhoea / vomiting
  - Dose-dependent risk of illness
- Norovirus GII.4 New_Orleans_2009
  - Identical in water and patient samples

- Continuous interaction with outbreak management team
- Meeting with local population

- Collaboration between epidemiologists, microbiologists and water supply engineers → public health decision-making

# Epilogue

- On **23 December 2012**, the local health authorities lifted the water consumption ban.
- On **23 January 2013**, indicator bacteria were no longer detected and boiling water was no longer needed.
- On **24 January 2013**, the municipality organized a public meeting involving the waterworks company, local public health officials and SSI team members to inform citizens about the process and conclusion of the outbreak investigation and to address any questions and concerns about water safety and outbreak management.

*van Alphen LB et al. (2014) The application of new molecular methods in the investigation of a waterborne outbreak of norovirus in Denmark, 2012. PLoS One. Sep 15;9(9):e105053. doi: 10.1371/journal.pone.0105053. eCollection 2014.*

# More information

| Table. Online field epidemiology training resources |
| --- |
| **Textbooks**:<br>• From US CDC: Principles of Epidemiology in Public Health Practice, Third Edition. An Introduction to Applied Epidemiology and Biostatistics. https://www.cdc.gov/ophss/csels/dsepd/ss1978/index.html<br>• US CDC: Field epidemiology manual https://www.cdc.gov/eis/field-epi-manual/index.html<br>• Public health series: https://www.cdc.gov/publichealth101/index.html<br>• Having fun: Solve the Outbreak: https://www.cdc.gov/mobile/applications/sto/index.html |
| **Epidemiologic Case studies**:<br>• From US CDC, classroom and computer-based. https://www.cdc.gov/epicasestudies/index.html<br>• Case studies from the African Field Epidemiology Training Network AFANET, e.g. ebola, cholera and measles outbreaks. http://www.afenet.net/index.php/resources/training-materials |

# Acknowledgements

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# Questions for the panel

- Partners?
  - Who to include when
  - What to tell who, when? (public?)
- National level?
- What would be different in other
  - Sources: eg foodborne outbreak
  - More severe pathogen
  - Countries