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Investigating an outbreak in 10 steps ...opportunities to trace food

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Outline

- Learning objectives
- Types of outbreaks with focus on food borne outbreaks
- 10 steps of an outbreak investigation
- Wrap up

Learning objectives

- Get familiarized with
  - common sources for outbreak detection
  - the basic principles of field epidemiology

- How to investigate an outbreak in a structured manner
  - Starting from the public health side
  - Considering interfaces with food / feed safety side

- When would tracing make sense? In which not? Elaborate on the way

Some general remarks/definitions first…

- Epidemic = outbreak

- Prevalence of disease = number of diseased individuals

- Incidence = **new** cases of a disease within a defined population over an established **period of time**
  - ➢ Epidemic = excessive incidence in defined

  population,

  place and

  time
- Epidemics…
  - often evolve rapidly
  - are Public Health emergencies

Types of outbreaks

- Depend on transmission routes defined by
  - Pathogen characteristics
  - Host characteristics (behaviour)

Common source outbreaks

FBOs

- ➢ Single or point source
- ➢ Continuous or multiple exposure outbreaks

Propagated outbreaks

- ➢ Person to person (Influenza, HIV…)
- ➢ Arthropod vector (Malaria, Dengue…)
- ➢ Animal reservoir

Slow (modern) outbreaks

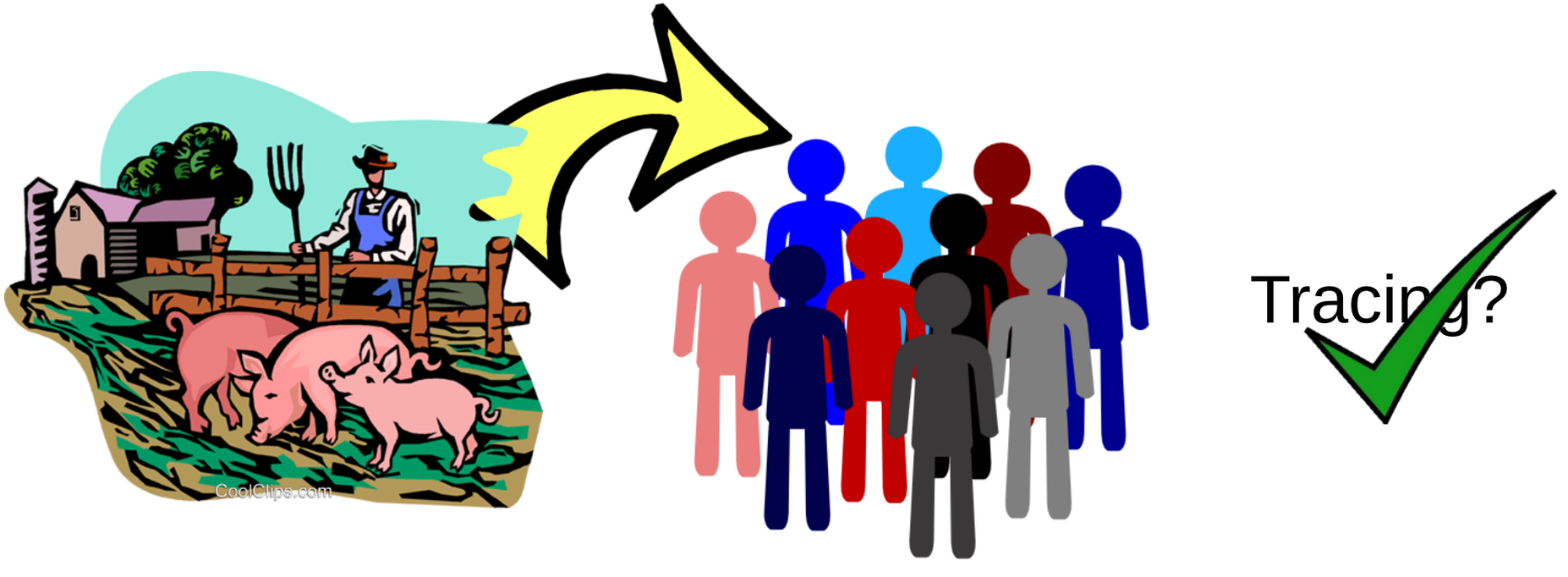
- ➢ …of non-communicable diseases: eg. diabetes, heart attacks, depression

Types of outbreaks related to food

- **Common source & single exposure** outbreaks
  - Single source exists for a short time period
  - All cases have a common exposure a that particular time
    - First and last case within incubation period
    - Rapid rise and rapid decline in epicurve
  - Examples: food poisoning (street vendors, feasts, etc)

Types of outbreaks related to food

- **Common source & multiple exposure** outbreaks
  - Single source exists which provides intermittent exposure
  - Rapid or moderate peaks during extended time periods
    - Multiple foci / disease clusters
  - Example: pig farmer producing intermittently contaminated pork (eg. Salmonella)



Why investigate outbreaks?

They won´t go away if we ignore them

- Ebola, HIV…

- To gain **practice**: what happened once may happen again
  - Natural experiments we can use for training
- To define the **magnitude**
- To determine conditions & **factors** responsible
- To identify the **source**
- To recommend **prevention** measures

Who investigates outbreaks?

- In DE described within the infection protection law:
  - Federal states are in charge of public health & safety
  - If >1 state affected national authorities take over, primarily to coordinate!
- Outbreak investigation team (OIT)
  - Epidemiologists
  - Representatives of affected jurisdictions / health care facilities
  - Microbiologists, clinicians, veterinarians
  - …other specialists as required
- Similar applies to multinational outbreaks (COM coordinates)

- **Before start:**
  - Briefing of members of OIT on roles & responsibilities

10 steps of an outbreak investigation

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2. Confirm the diagnosis
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With potential dead ends at many stages!

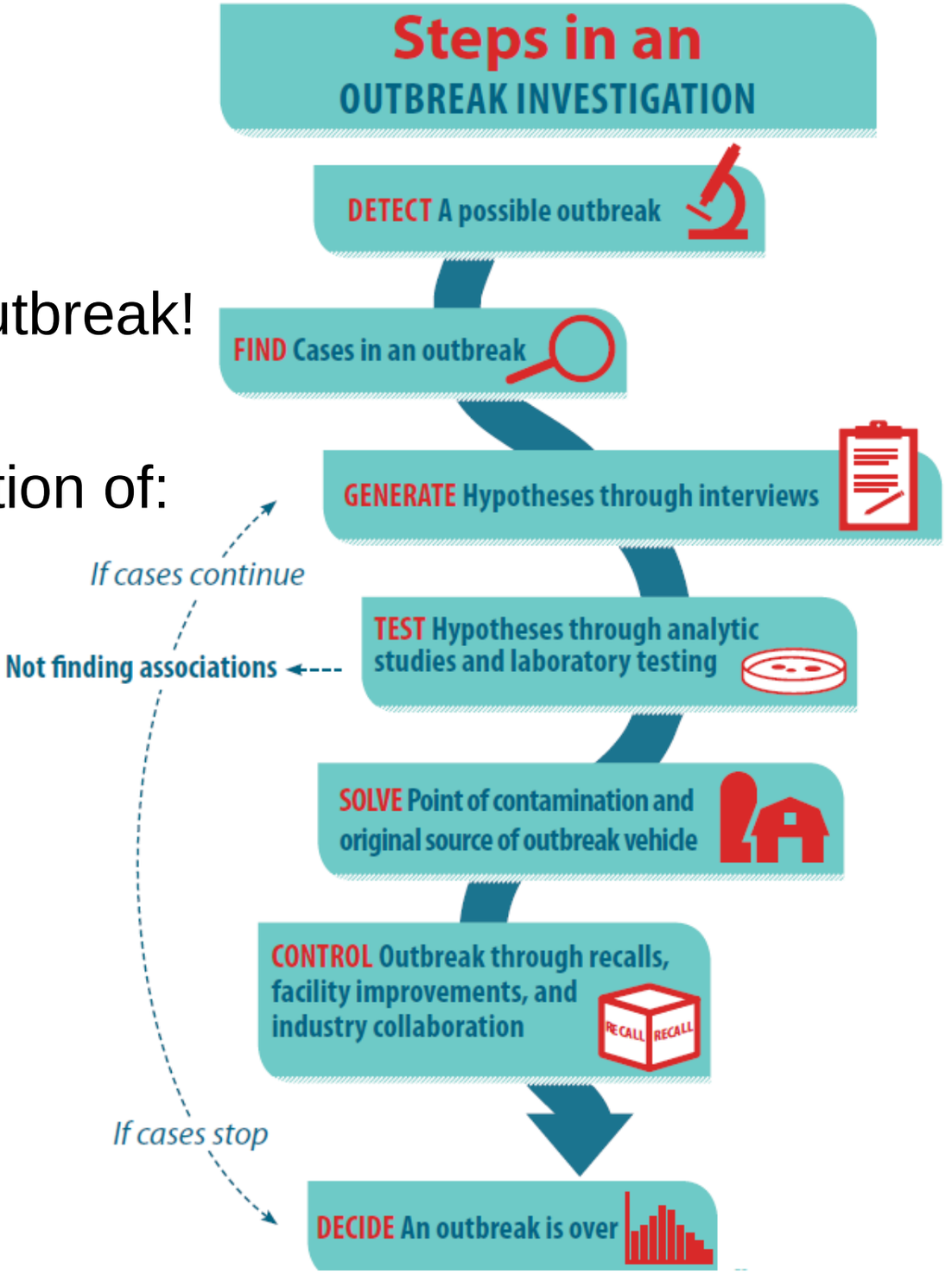
Is it really 10 steps?

Many ways lead to Rome

It´s important to stop the outbreak!

Many steps require interaction of:

- Epidemiologists
- Microbiologists
- Veterinarians
- Caterers
- Managers
- …



CDC Centers for Disease Control and Prevention
CDC 24/7: Saving Lives, Protecting People™

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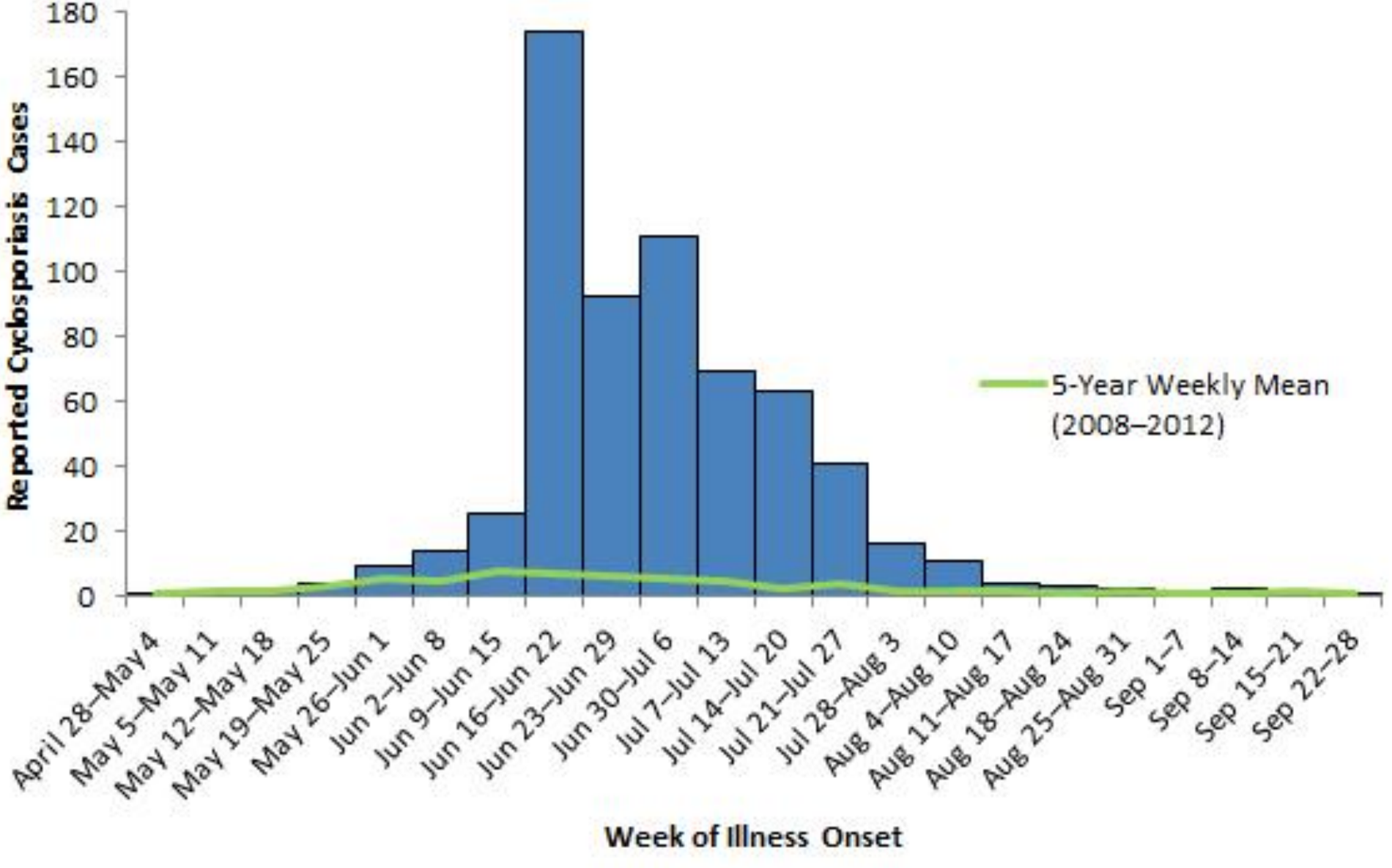
Step 1: confirm the outbreak

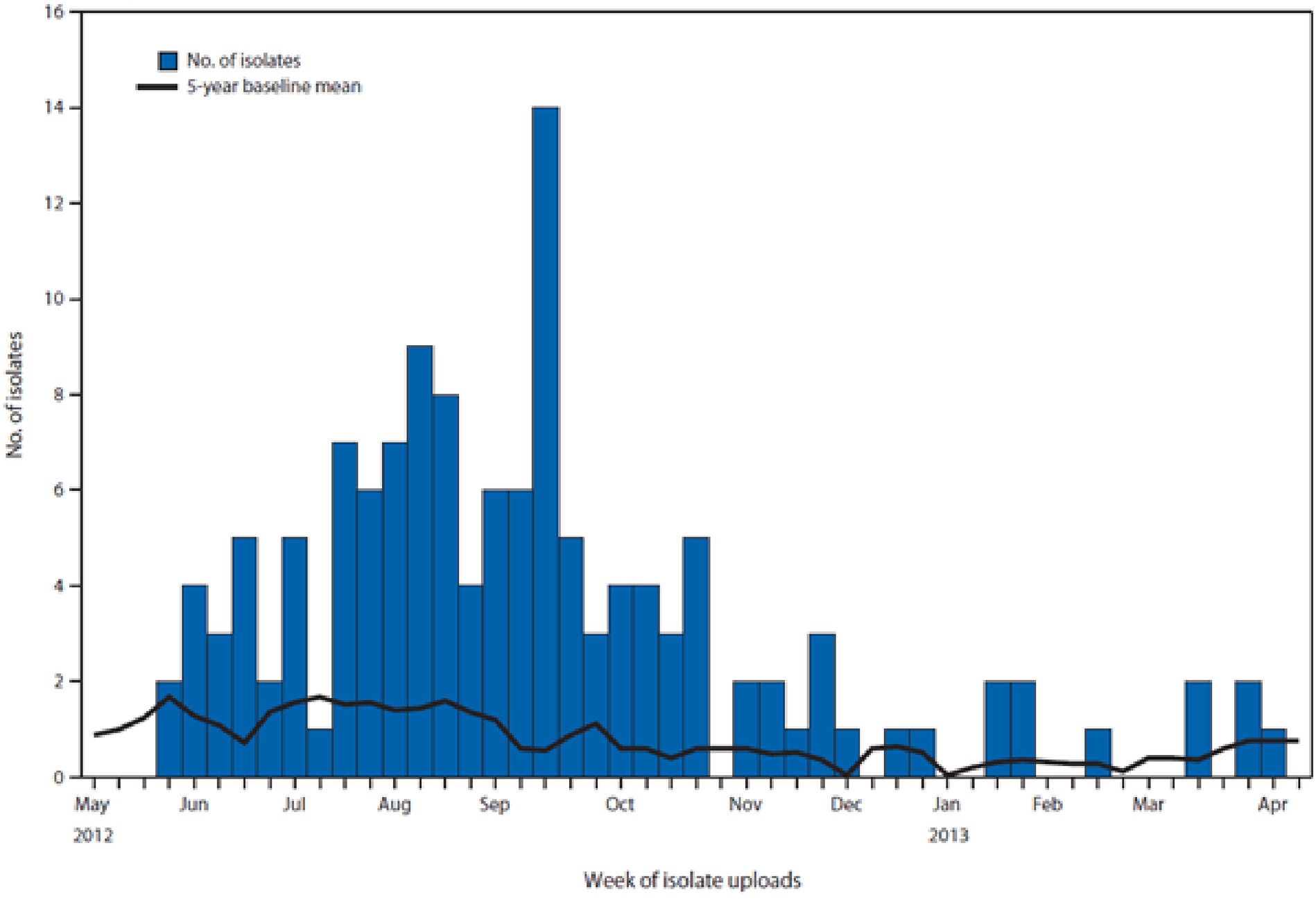
- Definition of an outbreak:
  - Increased incidence (new cases) in a place at a given time
  - i.e. more than you would expect

- Elements needed:
  - Numerator
    - Number of cases
  - Denominator
    - Size of the population where cases come from
  - Collection of this information over time
    - Baseline data

Outbreak of Cyclosporiasis, United States, 2013*



Outbreak of *Salmonella* Heidelberg Infections Linked to a Single Poultry Producer — 13 States, 2012–2013



Step 1: confirm the outbreak

- Pseudo-outbreaks
  - No recent increase of incidence

Any ideas?

Step 1: confirm the outbreak

- Pseudo-outbreaks
  - No recent increase of incidence
  - Artifacts in the numerator:
    - Increased awareness (Campylobacter 2011)
    - Change in surveillance practices (case definition)
    - Laboratory error
  - Variation of the denominator:
    - Rapidly changing population denominators
      - Hospital patients, migrants, refugees, mass gatherings

Step 1: confirm the outbreak

NOT

Most outbreaks are detected by routine surveillance

Outbreaks with hundreds of ill persons can be missed if they are spread out over a wide area

- Who might detect and report outbreaks?
  - Microbiologists (labs with bigger catchment area see more)
  - Directors of long term care facilities, schools, …
  - Clinicians
  - Public
  - Hotels, cruise ships …
  - Media
  - ?
- **Food/feed safety partners often not primarily involved at this step (public health competence)**

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Step 2: confirm the diagnosis

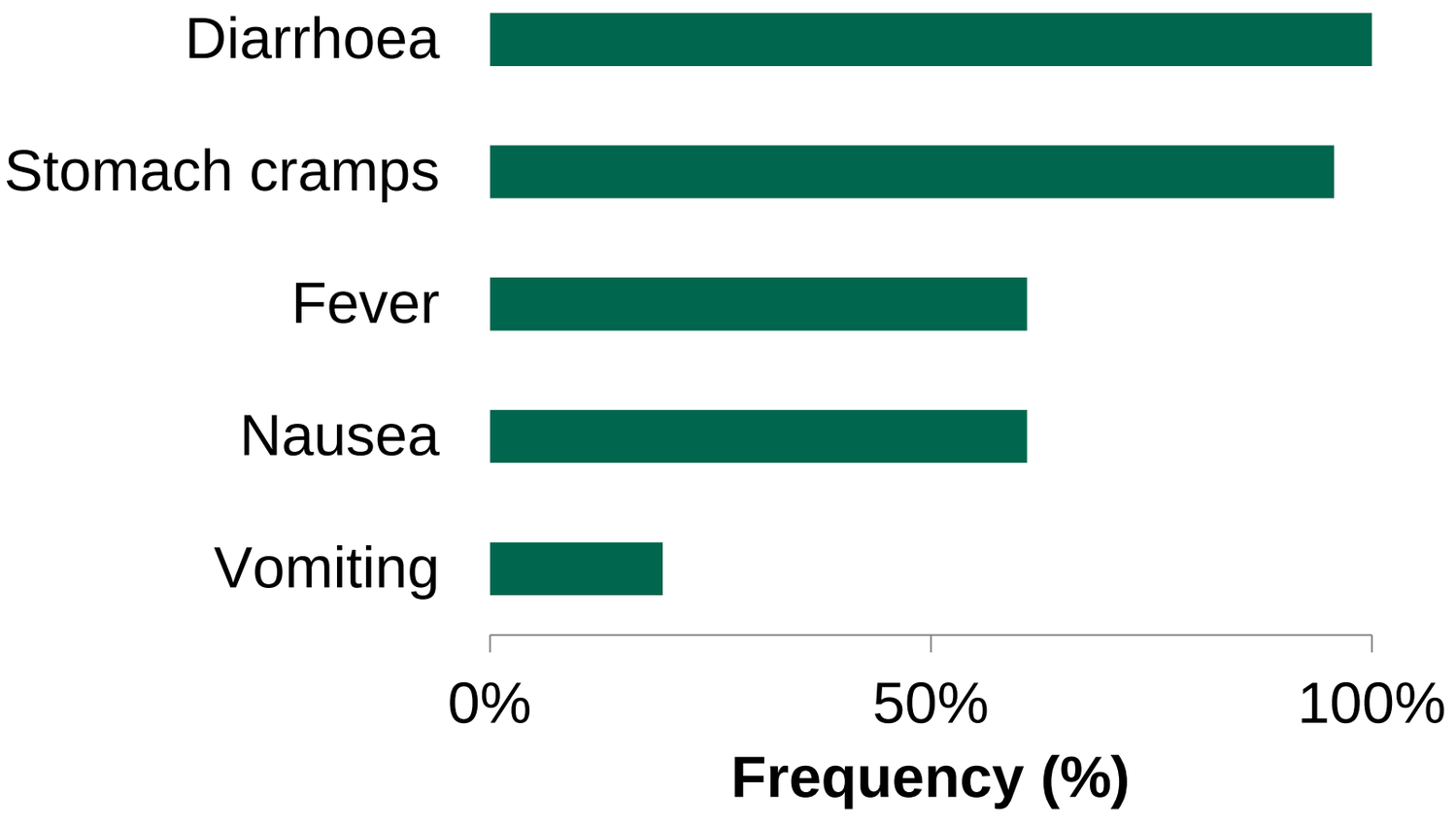
A 2-stage process

1. Clarify the syndrome and identify possible diagnoses
   - Communicate with clinicians, specialists
   - Examine the frequency of symptoms among cases
   - Outbreaks of the same nature may look different
2. Confirm diagnosis with laboratory tests
   - Discuss best tests to use with lab and clinicians

- Don´t test for everything because you might find everything
- Guidelines for Confirmation of Foodborne Outbreaks (eg. CDC)

- **Food/feed safety partners often not primarily involved at this step (public health & microbiologists competence)**

Symptoms reported by cases among wedding attendees, Camberley, 2011



- This could be anything
- At the end it was *C. jejuni*

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Step 3: define a case (by time, place, person)

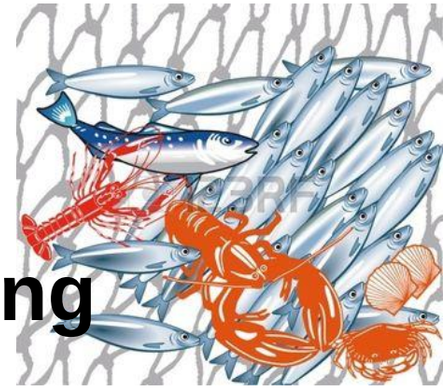
Standard case definition

A case is the occurrence of [spell out syndrome] in a resident of [spell out location] between [beginning date] and [end date] (+/- [lab confirmation])

- Use of standardized syndromic case definition
  - National reference
  - WHO
  - ECDC
  - Others (e.g., CDC)

- **Food/feed safety partners often not primarily involved at this step (public health & microbiologists competence)**

Step 3: define a case



Defining a case is like preparing to go fishing

- Different levels of case definition allow:
  - –Searching for potential cases widely
  - –Narrowing the search subsequently

- Case definitions may <u>differ at various stages</u>
  - –Descriptive stage (Case-finding)
    - More **sensitive** (e.g., diarrhoea and vomiting)
  - –Analytical stage (Hypothesis testing)
    - More **specific** (e.g., diarrhoea and vomiting + laboratory confirmed *Campylobacter jejuni*)

Example case definition: Multistate HAV-outbreak, Europe 2013 – 2014

- Stage of investigation: case finding
  - Aim: establish magnitude of outbreak (descriptive)

- Different levels
  - Confirmed case
  - Probable case
    - Exclusion criteria

- Additional definitions for food trace back
  - Secondary case
  - Travel-related case

Case definition with different levels: Multistate HAV-outbreak, Europe 2013 – 2014

- Confirmed case

a) EU/EEA resident with laboratory confirmed HAV genotype IA

and

b) date of symptom onset ≥ 01/01/2013

and

c) at least one of 3 conditions related to genotype of virus

- Probable case

a without genotype restriction) + b) + **exposure:**

Within 15-50 d before onset

c) having been in a country experiencing the outbreak during the indigenous outbreak period **and/or**

d) person-to-person contact with a confirmed case (secondary case)

Case definition:
Multistate HAV-outbreak, Europe 2013 – 2014

- Probable case exclusion criteria:
  a. other genotypes than IA outbreak strain
  b. travel outside EU within 15-50 d before onset

- Cases to exclude for **trace back** purposes:
  - A secondary case:

  a person with no reported exposure to berries (acquired infection via person-to-person or unknown)

  - A travel-related case:

  a person with a history of travel abroad 15 to 50 days prior onset of symptoms.

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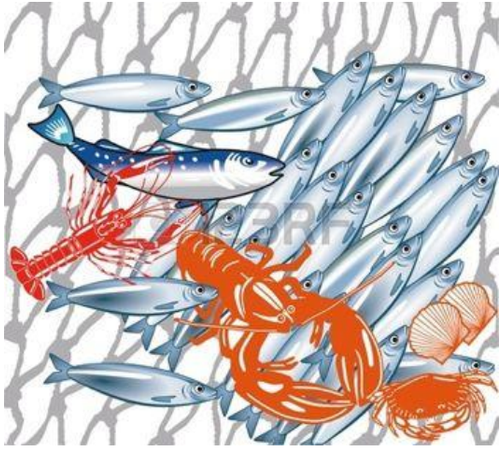
Step 4: search for cases



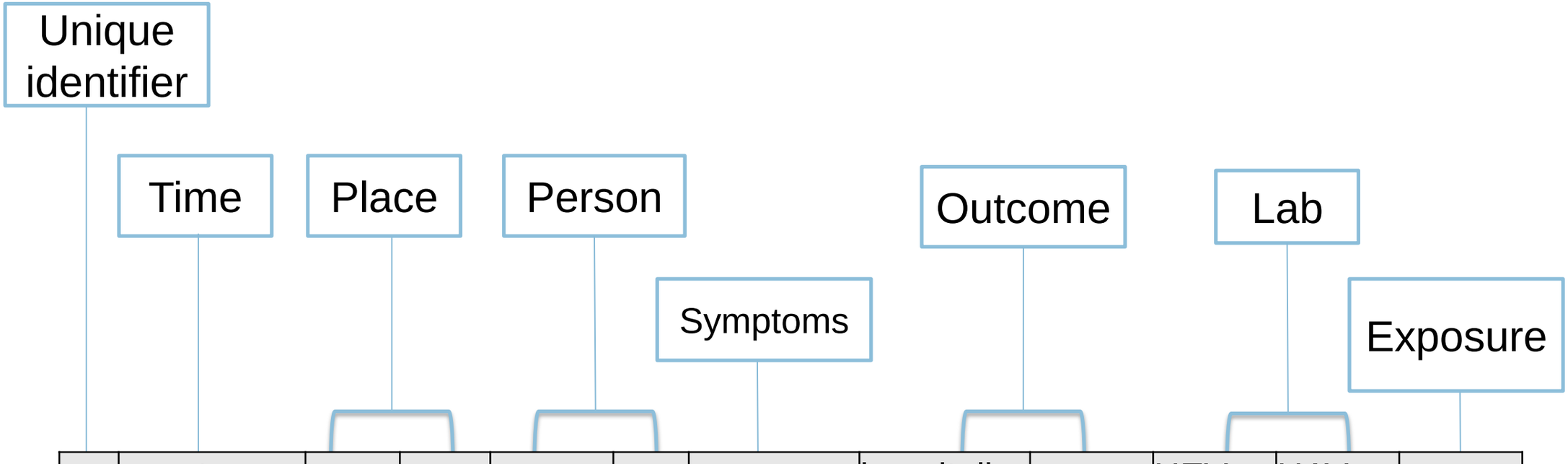
Now you actually go fishing

- Time, place and person criteria
  - From case definition (for case searching stage!)
- Chose a uniform strategy to search for cases
  - Passive (routine) surveillance
    - Reports coming to surveillance unit (eg. public health institute)
  - Stimulated passive surveillance
    - Alert clinicians, microbiologists, known **members** of population at risk to trigger reporting
  - Active surveillance
    - Direct search of medical records
  - Door-to-door/media case search

Genuine competence of public health authorities

The line listing

- ✓ Constitutes and updates a **database of cases**
- ✓ Protects the **confidentiality** of the patients
- ✓ Prepares automated **descriptive analysis**



ID	onset date	street	city	age years	sex	diarrhoea	hospitalization	death	HEV IgM	HAV IgM	berries
1	01.03.2015	18	HYD	12	1	1	1	2	1	9	1
2	05.03.2015	22	HYD	25	2	2	1	2	2	1	1
3	05.03.2015	23	HYD	36	1	1	2	9	9	9	2
4	07.03.2015	-	SEC	23	2	1	1	1	1	2	9

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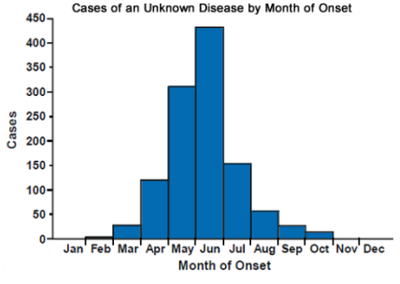
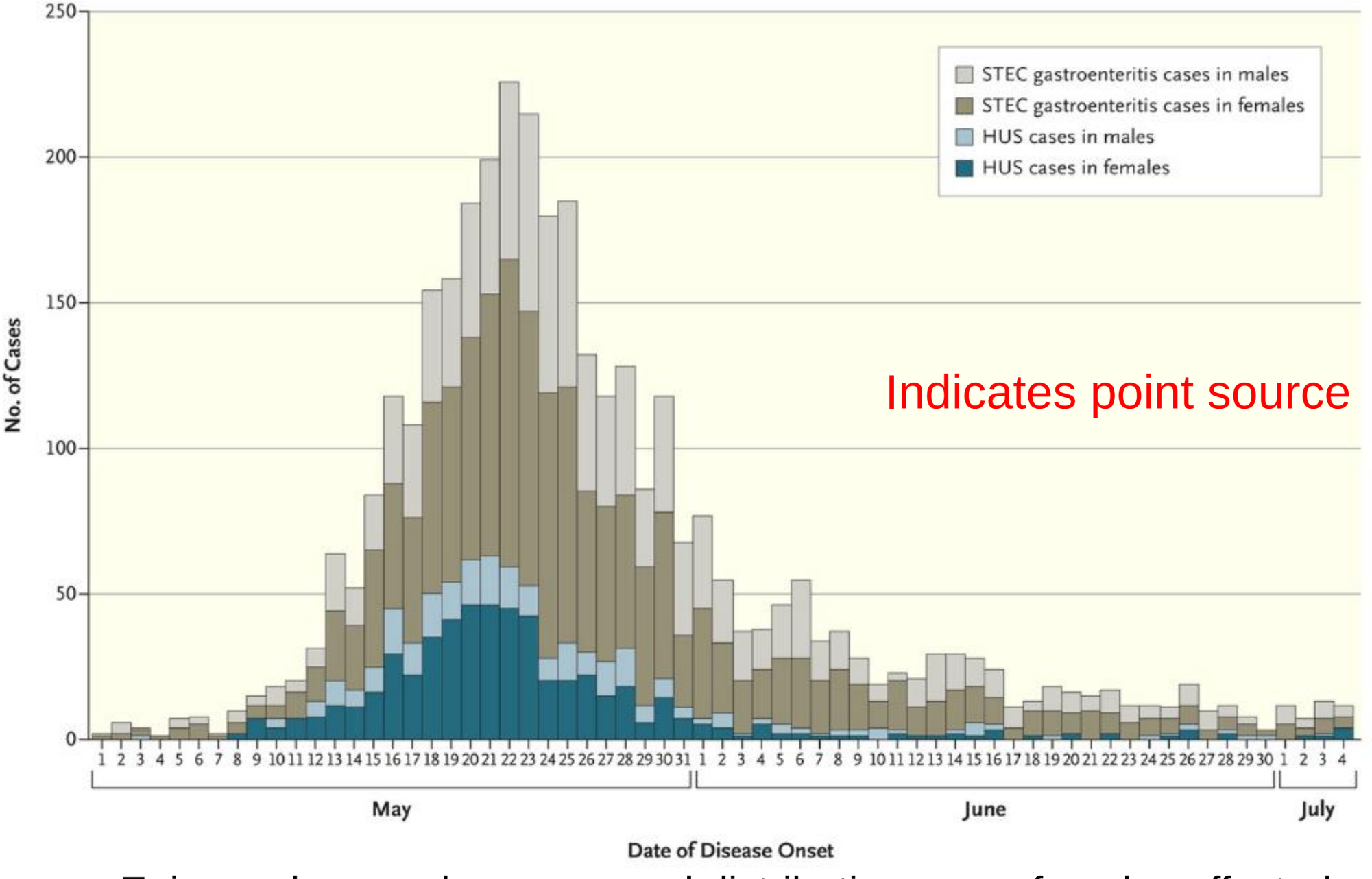
Step 5: generate hypotheses

…by using time, place, person

- Time
  - –Epidemic curve
- Place
  - –Spot map
  - –Incidence by area
- Person
  - –Incidence by age, sex, etc.
  - –Trawling questionnaire of cases
  - –Interview of outliers



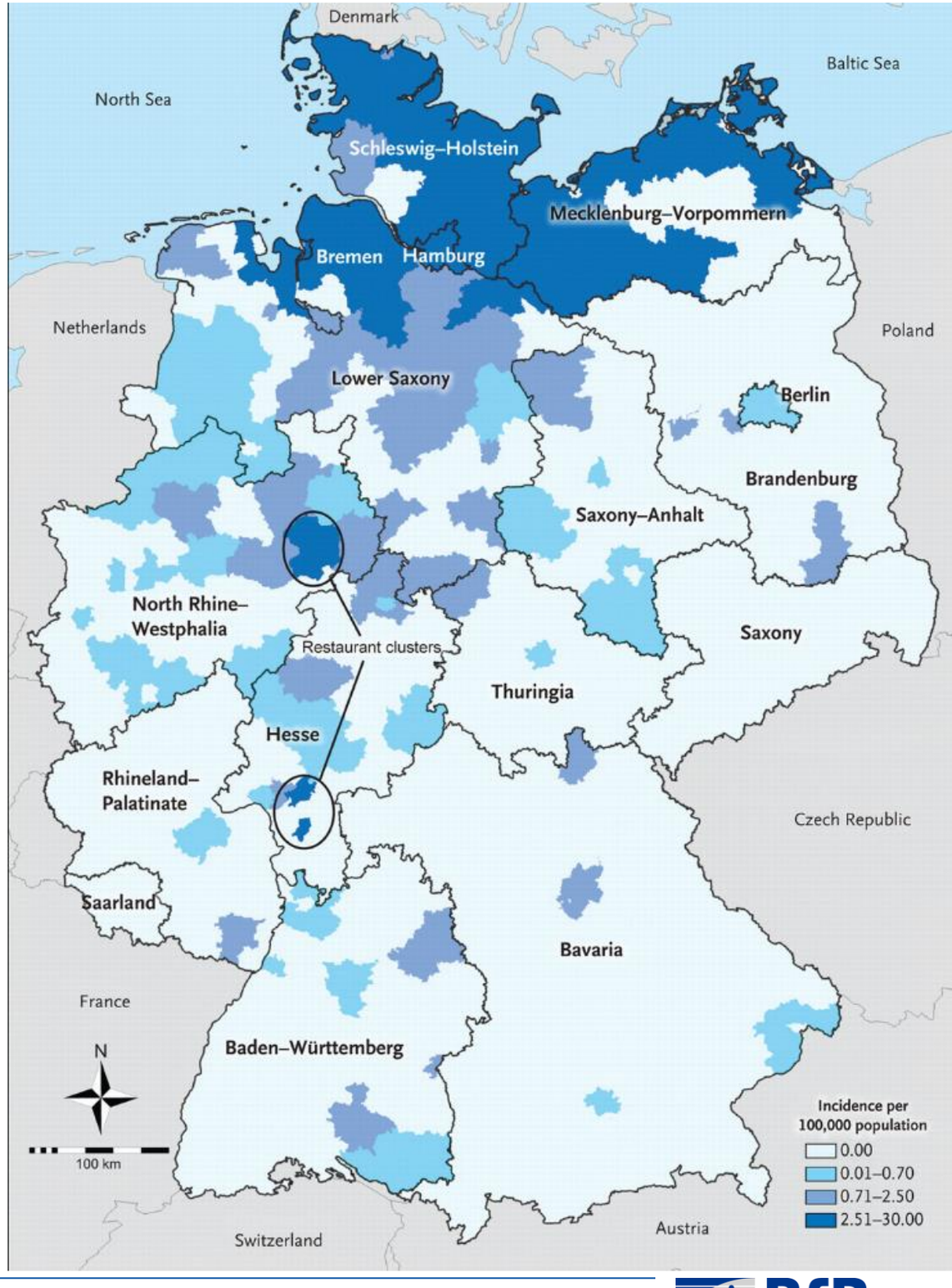
The epidemic curve: EHEC outbreak, DE 2011



- Epicurve by sex shows unequal distribution: more females affected

Incidence map: EHEC outbreak, DE 2011

- Epicentre of outbreak in northern Germany



Step 5: Generate hypotheses

…by using time, place person

- **Trawling interviews** of cases:
  - –open ended, generic questionnaires for case-patients
  - –objective: Identify what is **common** to all the cases
    - Event they participated in?
    - Place they visited?
    - Behaviour they have in common? Eg. exposure to food
    - **Don´t generate risk associations → investigators decide**

- ➢ via telephone or in person by trained interviewers
- ➢ very time consuming
- ➢ **Crucial**: investigation will focus on the outcome!

Step 5: Generate hypotheses

Hypothesis testing example:

- **Trawling interviews** of patients in Hamburg, 2011 yielded
  - **Food item** contaminated with *E. coli* O104:H4 is probably the vehicle
  - Normally with EHEC associated food items as row meat, raw milk or sprouts are **unlikely vehicles**
  - **Information points towards fresh produce as vehicle**

Food/feed safety partners involved as soon as food is suspected as the vehicle of infection

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Step 6: Test hypotheses

…by using analytical studies to sort out characteristics:

- common to all individuals
- specific to cases

- Typical studies:
  - Case-control
  - Cohort
  - Questionnaires used to collect information on exposure
  - Generate odds and risk ratios
    - Indicating association between disease and exposure

- Remember dead ends → investigation may involve several types of studies

Step 6: Test hypotheses

- Hypothesis testing examples from EHEC, 2011:
  - Initial hypothesis from trawling interviews pointed towards fresh produce

a. Early case control study in Hamburg, early May

- Leafy salads, cucumbers and tomatoes associated with disease

b. Matched case control study in 3 hospitals focussed on fruits and vegetables, May – June 2011

When would you trace what?

Multistate HAV outbreak 2013-2014

Standardization is key!

4.1 FRESH BERRIES:

Q. In the seven weeks prior to your illness, were you likely to have eaten fresh berries either on their own or as a garnish with desserts and salads, these include strawberries, raspberries, blackberries, blueberries, cranberries and also blackcurrants and redcurrants (re-emphasise it is either on their own or as a garnish)

Yes ☐ **No** ☐ **Not sure** ☐

If YES, which of the following fresh berries were you likely to eat?

(Please go through each of the items listed; if respondent answered "No" or "Not sure" above, go through each of the items listed to verify this is definitely the situation)

Fresh Berries/Currants	Yes	No	Not sure	If yes, how often (frequency)								Place of Purchase (name and location of shop, supermarket, café, restaurant, market etc. where fruit purchased)	Brand
				5 or more times/ week	3-4 times/ week	1-2 times/week	2-3 times/month	Once/month	Once in the 7 week period	Never	Don't remember		
Strawberries													
Raspberries													
Blackberries													
Blueberries													
Cranberries													
Blackcurrants													
Redcurrants													
Other, specify													
Notes:													

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Step 7: Draw conclusions

Interpreting example from EHEC, 2011:

b. Matched case control study in 3 hospitals focussed on fruits and vegetables, May – June 2011

Table 1. Vegetables or Fruits Evaluated in a Case–Control Study in the German Outbreak.*

Food Item	Case Subjects Exposed	Control Subjects Exposed	Matched Odds Ratio (95% CI)	P Value
	no./total no. (%)			
Sprouts	6/24 (25)	7/80 (9)	4.35 (1.05–18.0)	0.04
Cucumbers	22/25 (88)	52/79 (66)	3.53 (0.96–12.9)	0.06
Apples	22/24 (92)	57/81 (70)	3.91 (0.86–17.7)	0.08
Peppers	16/24 (67)	35/80 (44)	2.66 (0.90–7.9)	0.08
Strawberries	19/26 (73)	43/81 (53)	2.33 (0.90–6.0)	0.08

What food item would you like to trace?

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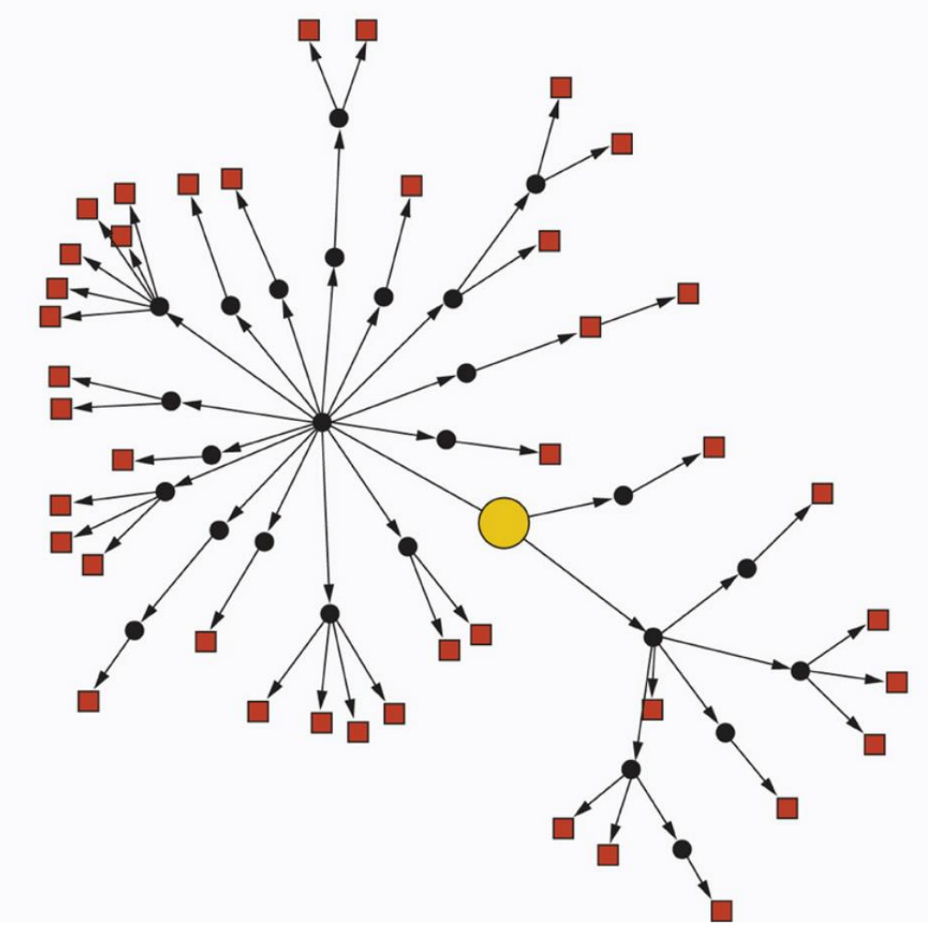
Step 7: further investigations

- To support evidence
- Microbiological
  - Typing (MLST, PFGE, MLVA, …)
    - Identical isolates among cases
    - Identical isolates in source and case
- Other studies
  - Environmental
    - e.g., test the water
  - **Food (and feed) tracing**
    - Will be subject of the next few hours



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Will be subject of the following 2 days!

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Thank you!

Katja, Armin & Olaf