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Epidemic
Disease
Detectives
Hamburg

An Epidemic of Haemolytic Uraemic Syndrome in Hamburg

Solution Guide

Please note:

The **EDDi Solution Guide** serves as a supporting document for lecturers, facilitators and also for self-study groups to verify their findings and answers:
(1) **Tabletop Exercise**: For each question/task of the case study, answers or possible solutions are presented, with some also allowing for discussion in the study group(s);
(2) **EDDi Serious Game**: The best-case and worst-case scenarios concerning the achieved game statistics are illustrated. The students can use the presented scenarios to assess their level of performance throughout the Serious Game.

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Based on a true event

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EDDi Serious Game – In-Game Statistics

Best Case Scenario (proxy)

Total EHEC = 363

Total HUS = 152

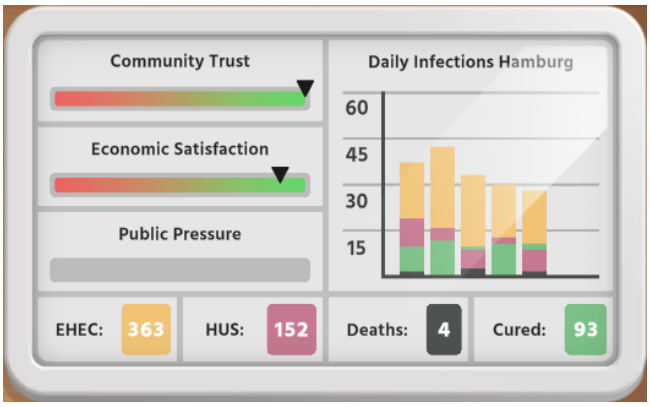
Total Death = 4

Total Cured = 93

Community Trust = max positive

Economy = almost max positive

Public Pressure = none



Worst Case Scenario (proxy)

Total EHEC = 439

Total HUS = 180

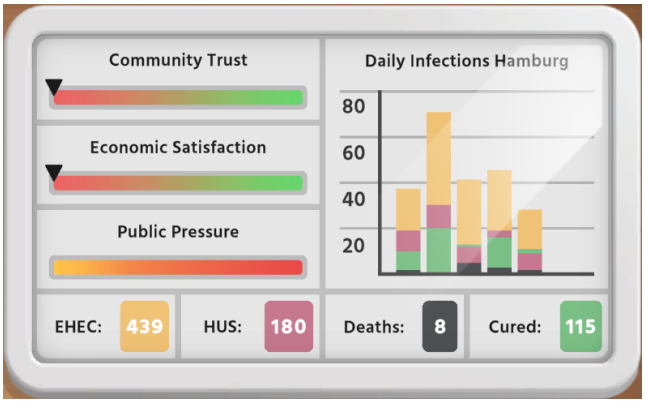
Total Death = 8

Total Cured = 115

Community Trust = max negative

Economy = max negative

Public Pressure = max



Note:

Outbreak numbers are automatically generated in the EDDi Serious Game. The case numbers and the different societal outbreak parameters change with your decisions.

For example, choosing an inappropriate subject line when answering an email may have caused mistrust in your community and newly infected cases. On the other hand, responding to emails correctly, e.g., by choosing the right evidence when responding to emails, can keep the number of cases down and keeps the community and the economy happy.

EDDi Tabletop Exercise

Q1. What could be the cause of this illness? What would be the next thing to do? Please discuss in your group.

Gathering first ideas:

- The disease is defined as *Haemolytic Uraemic Syndrome* and occurs mainly in children; it is characterised by bloody diarrhoea, pain of the lower abdomen, nausea, and vomiting, with only low or absent fever; a severe blood disorder may occur; no causative agent and mode of transmission have been identified
  → illness in children with severe complications may be a reason for concern and alert
  → disease could be food-/water-borne, environment-borne; most likely infectious disease
- Some cases are linked to the same family, but none had travelled outside Germany
  →it seems like a locally defined event, contact tracing may be required
- Laboratory diagnostics should be initiated, e.g., analysing stool samples or screening blood samples for common infectious agents in children under five years (e.g., noroviruses, rotaviruses, adenoviruses or diarrhoea-inducing bacteria)
- Cases should be closely monitored due to the risk of severe blood disorder; family and (close) relatives should be surveyed concerning diarrhoeal diseases or similar symptoms

Q2. Is this an outbreak? What would you do next? Please discuss in your group.

Gathering evidence:

- usually, 0-2 HUS cases per day are expected to occur in Germany; a maximum of 50-100 HUS cases is reported every year; especially children under five years are affected
- the number of reported cases in children (= 5 cases) exceeds the expected number per day; however, more details are needed → signs of an outbreak cluster to be investigated

Next steps:

- (i) developing a case definition considering the disease/outcome of interest, time and location to identify more cases experiencing similar symptoms/health complications (HUS) in Hamburg, especially in children, or rule out an outbreak cluster; (ii) identifying potential links between the paediatric cases; if linked, trying to find the common source of infection; (iii) interpreting laboratory findings once they become available; (iv) raising awareness about HUS among health care providers to ensure rapid detection of possible cases ; (v) reporting the incidence to the next surveillance level (federal/national level)

Q3. Who are you going to involve in your outbreak investigation team?

- Epidemiologist / Statistician
- Public Health Officer
- Public Health Nurses and Clinicians
- Laboratory Scientist / Microbiologist
- Media Officer
- Food and Environmental Safety Inspector
- If animals are involved: Veterinarians

Q4. How would you define a case? Please try to describe the following: (a) A suspected case, (b) a probable case, (c) a confirmed case

Suspected / Possible case indicators:

- Acute Diarrhoea: Acute onset of diarrhoea or bloody diarrhoea with laboratory criteria
  - detection of genetic load of shigatoxing stx2 in faeces with/out isolation of E.coli
- HUS: Typical symptoms include acute renal failure, haemolytic anaemia and thrombocytopenia (according to the textbook)

Probable case indicators:

- Individuals meeting the suspected case definition and having an epidemiological link, such as
  - close contact with a confirmed case
  - stay in Germany
  - consumption of a food product (or access to a water source) in Germany

Confirmed case indicators:

- Individuals meeting the characteristics of a probable case and isolation of shigatoxin-producing E.coli; as of now, no further classification of the infectious agent is available

Additional notes:

- cases must share a similar temporal description, i.e., the same duration of exposure
- no shigatoxin stx1 has been detected; thus, shigatoxin stx1 is an exclusion criterion

→ the final case definition is provided in *M.6 Investigation Notebook*

Q5. What information can you derive from the descriptive outputs? Interpret the findings in your group.

- the outbreak likely started in calendar week 18 (May 2-8)
- HUS seems to be a common complication in EHEC cases, according to the reports (see *Fig 2*)
- EHEC/HUS: age groups 20-34 years and 35-49 years are mainly affected; female individuals seem at higher risk of infection and complications
- Bloody diarrhoea is a significant symptom in most EHEC/HUS cases, along with abdominal pain
- The highest incidence per 100,000 population occurs in Hamburg Nord, followed by Hamburg Altona, Eimsbuettel and Wandsbek; the region most affected seems Northern and North-Western/Eastern Hamburg, with more cases close to the city centre
  → spatial distribution could provide clues for further investigation, e.g., common infection source

Q6. What steps would you follow in investigating the outbreak? Find the correct sequence and number each step of the outbreak investigation process.

[**6**] Deciding an outbreak is over

[**1**] Verifying a possible outbreak

[**4**] Testing hypotheses through analytical studies and laboratory testing of samples

[**5**] Application of control measures, including
(a) recall of products,
(b) removing the source of contamination,
(c) revision of the production process

[**2**] Defining and finding cases

[**3**] Generating hypotheses through interviews and surveys

Q7: Which hypotheses can you draw from the qualitative results?

- All interview partners/affected individuals have consumed vegetables or state consume vegetables regularly; salad is an often-stated meal/product
- Even though meat, including raw meat, was stated often, not all affected patients had meat or meals with meat (hint: one vegetarian)
- Both sexes and all age groups seem affected

→ meals including vegetables and/or fruits could be a potential source of infection exposure

Q8: How do you interpret the results? Which conclusions can you draw from the interviews and case-control study?

- Odds Ratio (OR) > 1 indicates increased odds of the event to occur
- Individuals experiencing EHEC/HUS were more likely to consume salad (OR 6.6) and raw fruits (OR 3.6.); in contrast, they were less likely to consume Hamburger meat, other undercooked or raw meat products, or raw milk or milk products
  → avoid interpreting the results like "Individuals consuming salad and meals with raw fruits were more likely to develop EHEC/HUS"; a case-control study focuses on the outcome (=EHEC/HUS) and compares the exposures of interest in the affected (case) and non-affected (control) groups

→ the results derived from the qualitative interviews and explorative case-control study support the hypothesis of vegetables and fruits being a potential source of infection; more studies are needed to confirm (or reject) this hypothesis

Q9: Which statements can you draw from the report?

- case numbers in Hamburg are increasing, indicating an active transmission and/or source of infection; cases in Germany are significantly higher than the usually expected number of cases per year (50-100 cases per year)
- HUS complications are still occurring, with the first fatal complications reported in Hamburg; about 30% of infected (suspected) EHEC cases experience HUS complications
- cases of EHEC and HUS are increasing not only in Hamburg but other Federal States, mainly in North-Western Germany, i.e., the neighbouring states of Hamburg; however, Hamburg seems to be the hotspot of the outbreak

Q10: In general: Which of the study designs is best suited to test your hypotheses? Can you give more specific suggestions on how to plan the investigation?

- overall, observational study designs, including case-control and cohort studies, are the most appropriate designs to test hypotheses on different disease-exposure relationships; however, both come with strengths and weaknesses (cf. *M11. Investigation Notebook*)
- at this stage of the investigation, a retrospective study design may be most appropriate as cases can be identified following the outbreak case definition → contrasting identified cases, control groups can be assigned, and different exposures (preferably derived from other assessments like surveys and qualitative approaches) can be studied in different study settings by comparing both groups
- cohort studies, on the other hand, would allow for investigating disease risks in larger samples; however, they require more resources, (usually) more time, a well-defined study population and more profound knowledge of potential exposures, all of which may apply at a later stage → this design observes the occurrence of an event in exposed and non-exposed groups

- for further investigation, case-control studies should focus on identifying specific vegetable and fruit ingredients in the meals consumed by affected individuals to narrow down the potential source of infection and apply targeted outbreak control measures; studies should aim for a larger sample to get more robust results and provide data for more advanced (multivariate) analyses

Q11: Which part of the case definition must be updated and why?

- with the new laboratory findings at hand, criteria of a confirmed case must be updated: identification of the serotype *O104:H4* should be included as this serotype has been identified as the outbreak strain in affected individuals, associated with high pathogenic potential
- consequently, cases linked to other serotypes can be excluded
- this update holds several advantages: (i) cases can be identified more effectively; (ii) guidance can be given for laboratory diagnostics and treatment of EHEC/HUS cases, especially with severe complications; (iii) the findings may inform an environmental investigation

Q12: What is the measure of association for this study? Please calculate and interpret the results.

- the measure of association is the *Odds Ratio* (OR) used in case-control studies
- the highest OR has been calculated for the exposure "salad consumption" (OR = 5.49), which helps rule out "consumption of fruits" (OR = 1.4); the list of potential exposures can now be narrowed down to vegetables in a larger study sample
  → the results can be found in *M13. Investigation Notebook*

Q13: What public health recommendations can you draw from the recent findings?

- An outbreak of EHEC, causing HUS complications, has been ongoing since calendar week 18, with Hamburg and Northern Germany being mainly affected
- females are at higher risk of developing severe symptoms, and, overall, the age group 20-49 years is primarily affected, unlike in previous outbreaks with children being the at risk-group
- Given the most recent findings: (i) public advice should be shared on standard hygiene measures concerning personal hygiene and food safety, e.g., washing food, hands, counters, and cooking tools appropriately, in line with WHO recommendations;
  (ii) visitors of restaurants, canteens, etc., shall be advised to refrain from eating raw vegetables, more specifically tomatoes, cucumber and green salads;
  (iii) individuals experiencing diarrhoea should apply strict hand hygiene; anyone experiencing bloody diarrhoea shall be advised to seek medical help immediately;
  (iv) food providers (restaurants, caterers, etc.) may be advised to reduce or refrain from serving raw cucumbers, tomatoes, and green salad;
- (v) however, though indication is given, confirmatory evidence is lacking to ban vegetable imports from Spain; more advanced studies, such as food sample analyses, are required to confirm

Q14: What is the measure of association for this study? Please calculate and interpret the results.

- the measure of association is *Risk Ratio* (RR), used in cohort studies
- the highest RR has been calculated for the exposure "Sprouts" (RR = 11.53), which further narrows down the list of potentially contaminated vegetables
  → the results can be found in M14. (Investigation Notebook)

Q15: ***What conclusions can you draw from the EHEC outbreak in Hamburg? Please summarise and discuss the main findings from your investigation and try to evaluate the implemented control measures critically.***

- an outbreak of EHEC/HUS started in Hamburg in early May (week 18), mainly affecting children
- the identified causative agent was shigatoxin-producing (stx2) E.coli, more specifically, the highly pathogenic serotype *O104:H4*; although detected in affected humans, the outbreak strain could not be confirmed in food samples
- unlike previous outbreaks, individuals aged 20-49 years were mainly affected, and more severe complications (including HUS) occurred in women than in men
- the outbreak peaked in Hamburg/Germany on May 20 (+/-), after which cases slowly decreased and continued to decline following a public health alert issued by the EDDi team on May 25, which included the communication of appropriate (personal) hygiene and control measures that proved effective in containing the outbreak
- the outbreak did not only affect Hamburg but spread to several federal states in northern/north-western Germany; later, other European areas (France, Sweden and Denmark) were also affected
- sprouts could be identified as the most likely source of infection considering (i) the results of the recipe-based restaurant cohort study, (ii) further studies conducted in Bremen, Luebeck and Bremerhaven, (iii) the results derived from the traceback analysis and (iv) testing of food samples, e.g., from the affected farm → a total of 18 epidemiological studies provided strong evidence for sprouts being the primary source of the current EHEC outbreak in Germany
- one farm could be identified as a producer of sprouts where the standard hygiene and safety measures were not adequately applied; a traceback analysis revealed that the farm was distributing its food products to some of the affected food providers (canteens and restaurants)
- comprehensive evidence gathered from different study approaches and investigation series could support (a) the contaminated food source (fenugreek sprouts) and (b) one potential farm as the main distributor of contaminated food products; corresponding control measures had to be taken, including suspension of sprout distribution in Germany and temporary closure of the identified farm
- … → further conclusions can be derived

If you want to learn more about the EHEC event in Hamburg in 2011, please check out the reference materials provided in the Investigation Notebook

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