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Background

The ECDC Fellowship Programme is a two-year competency-based training with two paths: the field epidemiology path (EPIET) and the public health microbiology path (EUPHEM). After the two-year training, EPIET and EUPHEM graduates are considered experts in applying epidemiological or microbiological methods to provide evidence to guide public health interventions for communicable disease prevention and control. The Administrative Decisions <u>ECDC/AD/2023/23</u> and <u>ECDC/AD/2023/06</u> govern the EU-track and MS-track, respectively, of the ECDC Fellowship Programme, field epidemiology path (EPIET) and public health microbiology path (EUPHEM).

Both curriculum paths provide training and practical experience using the 'learning by doing' approach at acknowledged training sites across the European Union/European Economic Area (EU/EEA). This final report describes the experiences and competencies the fellow acquired by working on various projects, activities, theoretical fellowship training modules, other modules or trainings, and international assignments or exchanges during the fellowship.

Pre-fellowship short biography

Ilse Hazelhorst studied health sciences at the Vrije Universiteit in Amsterdam. She was always intrigued by the epidemiology of infectious diseases. After reading the books, *And the band played on: Politics, People, and the AIDS Epidemic* by Randy Shilts and *The Wisdom of Whores: Bureaucrats, Brothels and the Business of AIDS* by Elizabeth Pisani, she decided that she was ready for a career in public health and infectious diseases. Following the completion of her master's degree in Infectious diseases and public health and International public health, she worked in the field for some years, as infection control specialist. After being accepted for the EPIET fellowship, she got a position as epidemiologist at the local public health authority – GGD (De gemeenschappelijke gezondheidsdienst) Twente, the Netherlands. Ilse took the Member State track, also known as MS-track of the EPIET fellowship, whereby she combined the fellowship with her regular job duties as epidemiologist at GGD.

Results

The objectives of the core competency domains were achieved partly through project and activity work and partly by participating in the training modules. Results are presented in accordance with the EPIET/EUPHEM core competencies, as set out in the ECDC Fellowship Manual¹.

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¹ European Centre for Disease Prevention and Control (ECDC). European public health training programme. Stockholm: ECDC; 2020. Available from: <u>https://www.ecdc.europa.eu/en/publications-data/ecdc-fellowship-programme-manual-cohort-2021</u>.

1. Epidemiological investigations

1.1. Outbreak investigations

Outbreak of puerperal sepsis in Twente, 2023

Supervisors: Marieke Dimmendaal, Margreet te Wierik, Mirjam Knol

Category: Respiratory diseases

Aim: To confirm the outbreak, to identify the source, to implement the control measures

Methods: Outbreak investigation with descriptive epidemiology, laboratory investigation by culture and emm-typing.

Results: Eleven cases were diagnosed with puerperal sepsis, of which 10 met the case definition for this outbreak. The median age was 32 years. Seven cases gave childbirth in the same hospital and nine received care from the same neonatal care organisation. From five cases, culture samples were available that could be typed, resulting in four different *emm*-types. Additional information obtained from the hospital and care organisation did not show any overlapping healthcare workers between the cases. A single source could be excluded.

Public health implications: Reference laboratories should share their typing results with local public health authorities, in order to support timely outbreak investigations.

Role: Ilse was the main investigator in this outbreak, extracted the data from the system, collected information about the laboratory investigation, did the analysis and wrote the outbreak report. The report was shared with the stakeholders involved. In May 2024, in collaboration with the reference laboratory, an abstract was submitted for the European Scientific Conference on Applied Infectious Disease Epidemiology (ESCAIDE 2024). The abstract had good reviews, but was unfortunately rejected. The manuscript is about to be written and submitted for the *Infectieziektenbulletin* (Dutch), see 4.1.

Routine outbreak activities

Regional outbreak activities in the Netherlands

Activities and role: During the fellowship, Ilse was involved in routine outbreak activities at the national and local level. She was involved in confirming outbreaks (*legionella*, Shigatoxigenic *Escherichia coli* (STEC), hepatitis B, whooping cough), constructing case definitions (measles, rabies), case finding and line listing (*legionella*), developing questionnaires (*campylobacter*), performing hypothesis testing and when necessary, conducting additional investigations such as laboratory investigations (hepatitis b). She was also involved in communicating the results by writing reports (puerperal sepsis) or communicating with the media (whooping cough).

1.2. Surveillance

Setting up a surveillance system for Urinary Tract Infections in nursing homes, the Netherlands, 2023–2024

Supervisors: Kati Halonen, Anja Haenen, Mirjam Knol

Type of project: Setting up a surveillance system

Aim: To set up an in-depth sentinel surveillance system to monitor the incidence of urinary tract infections (UTI) in residents of nursing homes, the diagnostic methods for UTI, the treatment of UTI, and provide information for UTI prevention strategies.

Methods: The surveillance system was developed in collaboration with the National Institute for Public Health and the Environment (RIVM) and the Surveillance Network for Infectious diseases in Nursing Homes (SNIV) by using the Osiris software (web application to notify diseases to the RIVM). The surveillance system will be available for all nursing homes in the country as an optional module within the SNIV network.

Results: The surveillance system will provide feedback to nursing homes about the incidence of UTI which can be used locally to implement accurate diagnostic methods and treatment. The national data may provide data to improve guidelines and develop prevention strategies.

Public health implications: Residents of nursing homes are among the most vulnerable groups of society. As UTI are very common and incorrectly diagnosed, it may result in an overuse of antibiotics and increase the risk of antimicrobial resistance.

Role: Ilse was the coordinator in setting up this surveillance system. The available literature and national guidelines on this topic were used to design the system in the most useful way. Ilse wrote the surveillance protocol, the data specifications, tested the questionnaire in the Osiris software, and implemented the surveillance system in one nursing home as a pilot. The data available up to July 2024 was too limited to start an analysis, but it will surely be analysed and evaluated to improve the system before making it available for the whole country.

Routine surveillance activities

Regional surveillance of notifiable infectious diseases in Twente, the Netherlands

Activities and role: As epidemiologist, Ilse was responsible for the monitoring and reporting of the epidemiological situation for the local public health authority in the Twente region for all notifiable diseases, scabies, rabies exposure, and outbreaks in closed settings. Surveillance activities included: supporting routine operations for the information system; automatisation of data analyses and reporting with R, regularly analysing surveillance data and producing health information products for diverse audiences (general public, experts, decision makers, journalists) such as monthly situation reports, monitoring of mortality and epidemiological situation, sharing information and collaborating with other agencies and stakeholders. Besides these regular duties, Ilse was also involved in improving the local surveillance by designing a local surveillance system based on the information available (indicator-based passive surveillance, syndromic surveillance, event-based surveillance). A draft surveillance protocol was made available by August 2024, and the retrieved surveillance information will be available through a Business Intelligence tool/dashboard.

2. Applied public health research

Risk factors for iGAS in children aged six months to five years

Supervisors: Brechje de Gier, Mirjam Knol

Aim: In 2022, an increase in invasive Group A Streptococcal infections (iGAS) was observed in the Netherlands. In response, all invasive disease manifestations became notifiable by 2023, and post-exposure prophylaxis was indicated for household contacts. A particularly strong increase was seen among children. Therefore, the aim was to assess risk factors for iGAS in children aged six months to five years.

Methods: A prospective case–control study was conducted between February and May 2023. Parents of notified iGAS cases, defined as invasive disease with *Streptococcus pyogenes* cultured from the normally sterile site, were approached to complete an online questionnaire on exposures during four weeks prior to disease onset. Controls were recruited via social media. Whenever a case was notified, 10 controls were invited to complete the same questionnaire. Cases and controls were matched on sex and birth year. Logistic regression was performed to estimate odds ratios (OR) of exposures.

Results: Eighteen cases and 103 controls were included in the final analysis. A varicella zoster infection prior to the onset of iGAS disease was reported in two (11%) cases and one (1%) control (OR: 12.0, 95% CI: 1.1–139.0). Exposure to GAS-like illnesses, impetigo, pharyngitis and scarlet fever, was reported in eight (44%) cases and 15 (15%) controls (OR: 7.1, 95% CI: 1.8–29.0).

Public health implications: The findings of this study are in line with previous studies by identifying varicella as a risk factor for iGAS among young children and highlight the association with non-invasive GAS infections in the community as a possible source of transmission.

Role: Ilse was involved as co-author of the study protocol and the design of the questionnaire. Ilse performed the data cleaning and analysis. For ESCAIDE 2023, an abstract was submitted which resulted in an oral presentation, see 4.3. Ilse was the first author of the manuscript that was submitted to the journal, *Eurosurveillance*. Unfortunately, the manuscript was rejected at *Eurosurveillance*, so a submission at another journal, *Epidemiology & Infection* will be prepared, see 4.1.

COVID-19 vaccine effectiveness in long-term care facilities

Supervisors: Mirjam Knol, Susan Hahné

Aim: To describe the severity of SARS-CoV-2 infection in unvaccinated and vaccinated nursing home residents during outbreaks, to estimate vaccine effectiveness of COVID-19 vaccines against SARS-CoV-2 infection and death.

Methods: A retrospective cohort study was conducted by collecting data during SARS-CoV-2 outbreaks in nursing homes in the Netherlands. Data was collected according to ECDC's study protocol, 'Data collection on COVID-19 outbreaks in closed settings with a completed vaccination programme: long-term care facilities'. For every outbreak the attack rate and case fatality rate were calculated. Vaccine effectiveness was calculated by 1 minus relative risk, comparing vaccinated and unvaccinated residents.

Results: In total, 333 residents were exposed to SARS-CoV-2 during 28 outbreaks, of which 183 tested positive (AR: 55%). Of the residents with a SARS-CoV-2 infection, 13 (7%) had a saturation level <92% or needed oxygen therapy and three (2%) died. For the estimation of the vaccine effectiveness, 258 residents of 21 outbreaks were included, of which 252 (98%) were vaccinated, 36 (14%) with the primary series vaccine only and 216 (86%) also received one

booster dose. For the primary series, vaccine effectiveness against infection was 50% (95% CI: 15–70). Vaccine effectiveness for the primary series and one booster dose was 29% (95% CI: -3–52). Vaccine effectiveness for severe COVID-19 and death could not be calculated, because there were no events in the unvaccinated group.

Public health implications: Despite the high vaccine coverage in nursing homes, the AR in outbreaks is still high. There is little data available about the effectiveness of COVID-19 vaccines in the elderly population. Due to the closed setting in which the elderly live in, the information often escapes from the national surveillance system. This study serves as a strong example of the significant impact that field epidemiology can have on a more comprehensive understanding of the effectiveness of COVID-19 vaccines. Monitoring of vaccine effectiveness among residents of nursing homes is necessary to take preventive measures on time to protect the most vulnerable groups in society.

Role: Ilse was involved in the study protocol, data collection, preparation and analysis. Ilse was the first author of the manuscript that was written in Dutch and published in the *Infectieziektenbulletin* journal, see 4.1.

Legionnaires' disease and cooling towers

Supervisors: Henk Broekhuizen, Mirjam Knol

Aim: To investigate whether living in the proximity of a cooling tower increases the risk of getting Legionnaires' disease and how that is related to temperature and humidity.

Methods: In this case–case study surveillance data of notifiable Legionnaires' diseases cases in the Twente region were used. First, incidence rates of Legionnaires' disease per 10,000 people within different radii of a cooling tower were calculated. The cases were divided in two groups: cases with and without travel history. After calculating incidents rates, a Poisson regression was performed to determine if there is an association with living in the proximity of a cooling tower. Next, a time series was created by making an epicurve of the cases over the years, and temperature and humidity data were added in the graph. A time series analysis was conducted to assess the association between weather conditions and Legionnaires' disease.

Results: Data cleaning and analysis still have to be done, but it is expected that people who live closer to a cooling tower have a higher exposure to Legionnaires' disease, especially when a period of drought is followed by heavy rains.

Public health implications: Due to climate change, more extreme weather conditions are expected in the Netherlands. The results of this study will advocate for more research to improve the safety of cooling towers around cities.

Role: Ilse wrote the study protocol during the EPIET fellowship and is now coordinating the research. She will be continuing this research after the fellowship.

3. Teaching and pedagogy

Teaching 10 steps of outbreak investigation, Zeist, the Netherlands, 2023 and 2024

Outbreak investigation is one of Ilse's favourite topics to teach. She translated the 10 steps of outbreak investigation in Dutch and trained her own infectious disease team at the local public health office, which included medical doctors, nurses and infection control specialists. She also developed an exercise on a potential hepatitis A outbreak where the participants needed to practise the first few steps of an outbreak investigation.

This topic was also taught during the epidemiology course for regional infectious disease epidemiologists in Zeist, the Netherlands.

Another amazing experience was the recording of the masterclass about this topic in a professional studio. Ilse prepared and conducted this masterclass together with Katja van Ewijk (EPIET Cohort 2021). Katja was responsible for the theory while Ilse explained all the steps through practical examples from the field. After editing the recording, the masterclass was made available via YouTube on the channel, 'GGD GHOR Nederland' (the association of all local public health authorities).

Teaching epidemic curves, Utrecht, the Netherlands, 2023

This lesson was part of the training for medical doctors working on infectious diseases at the Netherlands School of Public and Occupational Health (NSPOH) in Utrecht, the Netherlands. The slides were in English, but the lecture was given in Dutch.

Teaching surveillance, Utrecht, the Netherlands, 2023 and 2024

Ilse also taught surveillance at the education programme for nurses, 'From cell to notification' at the Netherlands School of Occupational and Public Health (NSPOH) in Utrecht, the Netherlands. The lesson was previously in English, but Ilse translated it to Dutch, using the original version. The lesson was complemented by an exercise where the participants needed to describe a surveillance system. Ilse gave the lecture to three different nursing cohorts during the fellowship.

Workshop infection control, Enschede, the Netherlands, 2022

This face-to-face workshop was organised for healthcare professionals. During the workshop, the web application 'Infectionary' was used for an interactive meeting about infection control in a healthcare setting. The workshop was in Dutch. It was organised by the local public health authority in Enschede, the Netherlands.

Facilitating a case study, 'Trichinosis in Paris', Nijmegen, the Netherlands, 2023

The case study, 'Trichinosis in Paris' was part of the international epidemiology Master's programme at Radboud University Medical Center in Nijmegen, the Netherlands. Ilse facilitated the case study in English at a face-to-face meeting.

Facilitating a case study, 'Giardia in Bergen', Utrecht, the Netherlands, 2023

The case study, 'Giardia in Bergen' is part of the training for medical doctors working on infectious diseases at the Netherlands School of Public and Occupational Health in Utrecht, the Netherlands. The material of the case study was in English, but Ilse delivered it in Dutch.

Ilse also facilitated this case study during an epidemiology course for regional infectious disease epidemiologists in Zeist, the Netherlands.

Facilitating a case study, 'GI in Sweden', Utrecht, the Netherlands, 2023

The case study, 'GI in Sweden' is also part of the material of the previous case study. It was in English but the Ilse delivered it in Dutch.

4. Communications related to the EPIET/EUPHEM fellowship

4.1. Manuscripts published in peer-reviewed journals

Published

Hazelhorst EI, Verstraten C, Haenen A, Afrian A, Biesheuvel M, Hahné SJ, et al. COVID-19 in verpleeghuizen: besmettingskans, ernst en vaccineffectiviteit bij 28 uitbraken in 2022. Infectieziektenbulletin. 2024; april. Available at: <u>https://www.rivm.nl/weblog/ib/covid-19-in-verpleeghuizen-besmettingskans-ernst-en-vaccineffectiviteit-bij-28-uitbraken-in</u>

Submitted

Hazelhorst EI, Van Ewijk CE, Wielders CCH, Te Wierik MJM, Hahné SJM, De Melker HE, et al. Risk factors for invasive Group A Streptococcal infection in children aged 6 months to 5 years, a case-control study, the Netherlands, February-May 2023. Eurosurveillance. Publication pending.

Draft

Hazelhorst EI, Winters JAS, Te Wierik JMJ, Helou RI, De Wit L, Van Sorge NM. Increase of puerperal sepsis between April and September 2023 in public health region Twente, the Netherlands, outbreak or not?

Planned

Hazelhorst EI, Tackenkamp A, Haenen A, Halonen K. Setting up a urinary tract surveillance in nursing homes in the Netherlands.

Hazelhorst EI, Helou RI, Blanford J, Broekhuizen H. Legionnaires disease, cooling towers, temperature and humidity.

4.2. Other reports

Hazelhorst EI. Outbreak investiation report purerperal sepsis. Enschede: GGD Twente; 2023. Not public, but disseminated amongst the hospital and neonatal care organization involved.

4.3. Conference presentations

Presented

Hazelhorst EI, Van Ewijk CE, Wielders CCH, Te Wierik MJM, Hahné SJM, De Melker HE, et al. Risk factors for invasive Group A Streptococcal infection in children aged 6 months to 5 years, a case-control study, the Netherlands, February–May 2023. Presented at: ESCAIDE; 23-11-2023; Barcelona, Spain.

Submitted

Hazelhorst EI, Winters JAS, Te Wierik JMJ, Helou RI, De Wit L, Van Sorge NM. Increase of puerperal sepsis between April and September 2023 in public health region Twente, the Netherlands, outbreak or not? Submitted at: ESCAIDE 2024; Stockholm, Sweden.

5. EPIET/EUPHEM modules attended

- Introductory Course, 26 September–14 October 2022, Spetses, Greece
- Outbreak Investigation, 5–9 December 2022, Berlin, Germany
- European Scientific Conference on Applied Infectious Disease Epidemiology (ESCAIDE) 2022, 23–25 November 2022, Stockholm, Sweden
- Multivariable Analysis, 22–26 May 2023, Frankfurt, Germany
- Rapid Assessment and Survey Methods, 19–23 June 2023, Stockholm, Sweden
- Project Review Module 2023, 28 August–1 September 2023, Lisbon, Portugal
- European Scientific Conference on Applied Infectious Disease Epidemiology (ESCAIDE) 2023, 22–24 November 2023, Barcelona, Spain
- Time Series Analysis, 11–15 December 2023, Rome, Italy
- Vaccinology, 4–8 March 2024, virtual
- Qualitative Research Elective course, 19 and 22 March 2024, virtual
- Management, Leadership and Communication in Public Health, 24–28 June 2024, Stockholm, Sweden
- Project Review Module 2024, 26–30 August 2024, Lisbon, Portugal
- European Scientific Conference on Applied Infectious Disease Epidemiology (ESCAIDE) 2024, 20–22 November 2024, Stockholm, Sweden

6. Other training

- Fundamentals of R Course, 28 November–1 December 2022, virtual
- Tidy-R Course, 31 March 2023, Bilthoven, the Netherlands
- Vis-R Course, 12 May 2023, Bilthoven, the Netherlands
- United Nations BSAFE, 15 June 2023, virtual
- Cursus R voor GGD'ers, 19 October, 2, 10 and 17 November 2023, Utrecht, the Netherlands
- Media Training, 9 November 2023, Enschede, the Netherlands
- Scholing Infectieziekte-epidemiologie, 27–30 November 2023, Zeist, the Netherlands
- Data Storytelling, 4 July 2024, Utrecht, the Netherlands

7. International assignments

- Application GOARN: Diphtheria Outbreak in Guinea, Guinea, September 2023, not accepted
- Application GOARN: Diphtheria Outbreak in Nigeria, Nigeria, November 2023, not accepted
- Application GOARN: Cholera in Zambia, Zambia, January 2025, not accepted

8. Other activities

- During the fellowship, Ilse was promoted as the first infectious disease epidemiologist at her local public health authority. There was no job description, so she needed to start epidemiology from scratch.
- Ilse was, together with Andrea Parisi, cohort representative for EPIET Cohort 2022. During the fellowship, she
 collaborated with the representatives from EUPHEM, PAE, MEDIPIET and the Epiet Alumni Network (EAN) and
 was involved in organising career series for the current cohort. In the role as representative, she also attended
 the NFPT/TSF meetings, organised by the fellowship office.
- Ilse set up an infrastructure for in-house training for the infectious disease team at the local public health authority.
- Together with other local public health authorities, Ilse applied for a grant to design a practical tool for local public health authorities to investigate outbreaks, also called a REC-project. The application was accepted.
- Ilse attended multiple national conferences on infectious diseases such as the Transmissiedag, One Health Symposium, multiple network days for infectious disease epidemiologists based at the local public health authority, supra-regional meetings to intensify collaboration within regions, multiple meetings to evaluate and improve infection control in the Netherlands after the COVID-19 pandemic.
- Ilse was member of the regional Antimicrobial Resistance and Infection Control Network (Euregio-Zwolle), where she collaborated with external stakeholders such as hospitals, long-term care facilities, general practitioners and laboratories.
- Ilse is member of the regional zoonosis network in Twente, whereby she collaborates with external stakeholders such as veterinarians, laboratory food authority and an animal welfare organisation (Dierenbescherming).

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