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. Both curriculum paths provide training and practical experience using the ‘learning by doing’ approach at acknowledged training sites across European Union (EU) and European Economic Area (EEA) Member States.

This final report describes the output of the fellow and the competencies they 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

Dr Henrieke Prins graduated summa cum laude from University College, Utrecht with a Bachelor of Science in 2008 and obtained her medical degree at Utrecht University in 2012. During this period, she also studied at the University of California, San Diego and the University of Oxford. From 2012 to 2013, she conducted research in the field of HIV in Kenya at the KEMRI-Wellcome Trust. In 2013, she started her specialist training in internal medicine, followed by a sub-specialisation in infectious diseases, which she combined with a PhD on clinical HIV cure strategies, at the Erasmus University Medical Centre. Henrieke spent the final months of her specialist training at the Department of Infectious Diseases and Pulmonology of the Charité University Hospital in Berlin. In September 2021, she started her EPIET EU-track fellowship at the Robert Koch Institute (RKI) in Berlin under the supervision of Dr Sonia Boender and Nadine Zeitlmann as site supervisors, and Dr Zaida Herrador Ortiz, Dr Emily White Johansson and Dr Barbara Schimmer as frontline coordinators.
Results

The objectives of these 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 core competencies, as set out in the ECDC Fellowship Manual¹.

1. Outbreak investigations

1.1 Outbreak investigation of imported Corynebacterium diphtheriae among migrants arriving in Germany from 1 January 2022 to 30 September 2022

Supervisors: Wiebe Külp Schiek, Robert Koch Institute (RKI)
Category: vaccine-preventable disease

Diphtheria is a vaccine-preventable bacterial infection that is caused by toxigenic Corynebacterium species (C. spp.). C. diphtheriae is the classic C. spp. causing diphtheria, with humans being its only significant host. Previously, most diphtheria cases in Germany were caused by C. ulcerans, and diphtheria cases caused by C. diphtheriae were mostly imported. Since the end of July 2022, a notable increase in imported, mainly cutaneous diphtheria was observed among newly-arrived migrants in Germany. We initiated an outbreak investigation at RKI including analysis of migration routes and whole genome sequencing in collaboration with the specialised laboratory which is responsible for the diagnostics of notifiable infectious diseases. We established the existence of an outbreak by confirming 44 cases of C. diphtheriae among migrants predominantly from Afghanistan and Syria who had arrived in Germany between 1 January and 30 September 2022. The ongoing outbreak most probably originated from abroad, although a single epicentre was not identified. Presumably there are multiple origins, particularly along the refugees' travel route through the Balkans. Similar to Germany, cases have been reported in other European countries (Austria, Belgium, France, Norway, and Switzerland), constituting a multi-country outbreak in non-endemic countries. In Germany, local and federal health authorities were advised to follow the recommendations for the identification and management of diphtheria cases and contact persons, and the recommendation for outbreaks of infectious diseases in shared accommodation to facilitate intensified surveillance, and to monitor possible human-to-human transmission at reception centres. Vigilance, timely action and the sharing of data at national level via Epipulse, and internationally within the European Union/European Economic Area (EU/EEA) were vital for the rapid implementation of the necessary control measures to prevent further spread of this ongoing outbreak.

Educational outcome

Through her participation in this outbreak investigation, Henrieke was exposed to all the different stages of the process. After establishing the existence of an outbreak through intensified surveillance, Henrieke was part of the outbreak team that confirmed the diagnosis and formulated the case definition. She was then involved in case finding through line-listing, and collected data from the national surveillance system, as well as from intensified diphtheria surveillance questionnaires on the migration routes travelled and phylogenetic data. She performed descriptive epidemiological analysis to develop hypotheses, and actively exchanged ideas on possible hypotheses regarding migration routes with national and international colleagues. She worked on a line list used by the investigation team at RKI, and also collaborated on a line list used by ECDC. Henrieke participated in multiple weekly meetings related to the outbreak with colleagues at RKI, ECDC, and WHO Regional Office for Europe. Henrieke was involved in the communication of findings as publications in peer-reviewed journals and presentations to an international audience (see section 5.1.1).

2. Surveillance

2.1 International surveillance activities

2.1.1 HIV surveillance in Ukraine (WHO Regional Office for Europe remote mission 3–21 October 2022)

Supervisor: Dr Barbara Gansenheimer-Bartmeyer, RKI

As a WHO Collaborating Centre for HIV and viral hepatitis, the Robert Koch Institute took part in a remote mission organised by WHO’s Regional Office for Europe to evaluate the HIV surveillance system in Ukraine. The aim was to describe the current HIV situation in Ukraine using available surveillance data in Ukraine and to assess the progress of the national HIV response using available routine surveillance data, reports, study results and other relevant data or programmatic documents. Different stakeholders were also interviewed in order to identify challenges posed by the

COVID-19 pandemic and the military conflict in fulfilling the targets of the WHO’s Regional action plans for ending AIDS and the epidemics of viral hepatitis and sexually transmitted infections 2022–2030 and challenges measuring these targets.

On behalf of RKI, Henrieke worked on a desk review and started preparations for the mission on 9 August 2022. During the mission from 3–21 October 2022, she took part in all interviews with the different stakeholders on the assessment of epidemiological patterns, monitoring, evaluation and surveillance. Moreover, Henrieke participated in the daily debriefing meetings with the team during the mission. She also contributed to the presentation that was given to Ukraine’s Minister of Health on 19 October 2022. Henrieke wrote the first drafts of the report on the epidemiological assessment, including a performance review of Ukraine’s national HIV programme against national strategy targets, a description of key populations under surveillance and size estimations, assessment of the programme data collection and analysis system, and the availability of medical information systems. Finally, she suggested a number of recommendations on surveillance, monitoring and evaluation for the coming years. Henrieke helped integrate these findings into the final report ‘Review of the National HIV/AIDS, Opioid Agonist Therapy Programs, Ukraine’. She is currently still involved in the finalisation of this report (see section 5.1.3).

2.2 Routine national surveillance activities at the Robert Koch Institute

2.2.1 Screening the Rapid Alert System for Food and Feed (RASFF)

Supervisor: Dr Bettina Rosner, RKI

The Rapid Alert System for Food and Feed (RASFF) is an online warning system for reporting information on health risks derived from food or feed in the EU. Between October and November 2022, Henrieke screened all RASFF alerts on a daily basis. In the event of a notification relevant for German health authorities in order to solve food-borne infectious disease outbreaks, Henrieke summarised the available information, and subsequently alerted the respective federal states and local health authorities of potential sources of food-borne outbreaks.

2.2.2 Indicator-based surveillance of Toxoplasma gondii

Supervisor: Dr Hendrik Wilking, RKI

Henrieke was responsible for verification of the surveillance data on *T. gondii* reported to the RKI from across Germany. She also reviewed the chapter on congenital toxoplasmosis as part of RKI’s infectious disease epidemiology yearbook (annual report on notifiable diseases) in Germany for 2021 and 2022 (see section 5.1.3). The timely publication of these data and evaluations is an essential prerequisite for the development and assessment of health policy prevention concepts and effective control measures.

Educational outcome

Henrieke took part in routine surveillance activities, was responsible for selected categories of the German indicator-based surveillance, and was part of an international mission. This allowed her to familiarise herself with various aspects of surveillance both at the national and international level, to understand how event-based and indicator-based surveillance work, and to gain an insight into how different data sources are used for these purposes. Through these activities, and by participating in the weekly epidemiological teleconferences between RKI and the federal state epidemiologists on current infectious disease events, and methods and tools used in the public health services, she learned how the surveillance system in Germany is organised and operates.

3. Applied public health research

3.1 Determinants of intensive care admission and death among adults hospitalised with COVID-19 in 13 hospitals in Germany from 1 June 2021 to 31 January 2022

Supervisors: Dr Anna Stoliaroff-Pépin, RKI

Since 2020, COVID-19 has strained healthcare worldwide. It is important to understand which hospital- and patient-level factors are associated with a severe outcome of infection in order to optimise treatment and prevention strategies. Therefore, we performed a sub-study among 253 COVID-19 cases included in a case-control study at 13 hospitals throughout Germany. All cases were adults who were hospitalised with laboratory-confirmed SARS-CoV-2 between 1 June 2021 and 31 January 2022. In this study, we conducted univariable and multivariable logistic regression analyses to assess associations between 10 clinical and demographic factors (including age, sex and vaccination status) and severe COVID-19, defined as intensive care unit (ICU) admission or in-hospital mortality. Moreover, to assess whether potential clustering of data at hospital-level affected our outcome of severe COVID-19, we considered a multi-level modelling approach. We found that male sex was positively associated with severe COVID-19. However, contrary to our expectations, there were no other associated patient-related or hospital-level factors. Possible explanations for not finding associations previously reported in literature include selection bias due to enrolment being conditional on hospitalisation with COVID-19, and an insufficiently large sample size to detect significant differences.
Henrieke wrote the study protocol for this sub-study in May 2022 (see section 5.1.4). She accessed the data collected using the survey instruments programmed in VOXCO, and imported the data in R to perform regression analyses and multi-level modelling. Henrieke analysed, summarised and interpreted the results, wrote up the findings and presented them at a regional symposium on 30 August 2022, and during ECDC's site visit to RKI on 21 February 2023. She also submitted an abstract of this sub-study as the lead author to ESCAIDE 2022 (rejected) and to ECCMID 2023 (rejected).

3.2 Statutory health insurance-covered pre-exposure prophylaxis in Germany: changing trends in nationwide tenofovir disoproxil/emtricitabine prescriptions during the COVID-19 pandemic

Supervisors: Dr Daniel Schmidt, RKI, Dr Achim Dörre, RKI

In 2019, Germany introduced a national law to reimburse high-incidence populations for pre-exposure prophylaxis (PrEP), prescribed as tenofovir-disoproxil/emtricitabine (TDF/FTC), via statutory health insurance. In this study, we assessed changes in TDF/FTC prescriptions after implementation of the law and during the COVID-19 pandemic. To do so, we took an interrupted time series approach, involving regression models with monthly prescriptions per defined time period as the outcome. We modelled statutory health insurance-covered PrEP in September 2019 as an interruption, and considered four COVID-19 waves and two national lockdowns in 2020–2021 as explanatory variables. We extrapolated prescriptions on a linear basis, as if the lockdowns had not occurred, and compared this to the actual prescriptions during the same period. We performed sub-analyses based on stratification by the five federal states with the highest proportion of PrEP users (Berlin-Brandenburg combined, Bavaria, Hamburg, Hesse, North Rhine-Westphalia), and single-month prescriptions versus three-month prescriptions. We concluded that the introduction of statutory health insurance-covered PrEP resulted in a notable increase in TDF/FTC prescriptions nationwide. A drop was most apparent after the first lockdown, and particularly affected the initiation of PrEP prescriptions, possibly due to reduced healthcare access and behavioural changes. Ongoing monitoring of trends in TDF/FTC prescription is needed to safeguard access to preventive care such as PrEP, and particularly PrEP initiation, during public health crises such as the COVID-19 pandemic. This can guide efforts to expand PrEP coverage in Germany, and avoid lapses in access to PrEP in future health crises.

Henrieke started writing the study protocol for this study in July 2022 (see section 5.1.4). She performed an interrupted time series approach in R involving regression models using the monthly prescription data provided. She analysed, summarised and interpreted the results. Henrieke presented her EPIET project during the Project Review Module in Lisbon in August 2022. She wrote up her findings and submitted an abstract to ESCAIDE 2022 (accepted) and EACS 2023 (pending), and in June 2023 submitted a manuscript to a peer-reviewed journal (under review).

3.3 Evaluation of mpox contact tracing data collection in EU/EEA Member States during the 2022 multi-country outbreak in non-endemic countries (ECDC remote assignment)

Supervisors: Dr Daniel Cauchi, ECDC, Dr Agoritsa Baka ECDC, Dr Stefania De Angelis, ECDC

Contact tracing is an important component of outbreak response since it can facilitate the control of transmission as well as providing important information on the infectious agent (e.g. secondary attack rates, risk factors for transmission and infection), particularly for emerging pathogens. During the 2022 multi-country mpox outbreak, several EU/EEA countries reported that contact tracing was difficult and often only possible for a small proportion of cases. In this study, we collated mpox contact tracing activities, data collection, and experiences by conducting a survey among EU/EEA countries. We found that the vast majority of the 139 respondents from 27/30 EU/EEA countries performed case investigation, backward and forward contact tracing and follow-up of outcomes for contacts. Sixty percent used a standardised contact tracing data collection form and two-thirds used databases for recording. The highest-rated enablers were clear guidelines, quick access to laboratory results, and sufficient expertise. The highest-rated barriers were inability to contact contacts or cases, and lack of time or staff. The improvements most needed were improved expertise on the affected populations, and availability of staff and time.

To improve contact tracing of mpox and other diseases with similar transmission patterns, EU/EEA countries need common contact tracing guidelines, data collection tools, and harmonised surveillance and reporting systems, alongside preparedness for staff capacity during surges and better knowledge of the affected communities.

This study initially began in August 2022 as part of an ECDC remote international assignment to investigate mpox secondary attack rates in the 2022 multi-country outbreak. Henrieke collaborated on this assignment with another EPIET-EU track fellow, Liza Coyer. However, by the time the team was assembled, the mpox outbreak was already declining and there appeared to be too little data available to calculate secondary attack rates. Therefore, the team wrote the study protocol to investigate enablers and barriers to contact tracing activities in the EU/EEA, and drafted a questionnaire using REDCap software. Henrieke cleaned, organised, interpreted and analysed the data. The fellows are currently writing up the results, which are intended to be submitted for presentation to ESCAIDE 2023 (late breaker), and as a manuscript to a peer-reviewed journal.
Educational outcome

The different projects allowed Henrieke to develop her competencies with regard to the writing of study protocols, and communicating in the form of abstracts and manuscripts submitted to peer-reviewed journals. Moreover, she performed statistical analyses and other types of data analyses for all projects, ranging from univariable and multivariable logistic regression, to multi-level modelling, and interrupted time series analyses involving regression models. This helped to deepen her understanding of different types of data analyses, when to use the different methods, and how to draw conclusions based on the results of the different statistical methods. By conducting all analyses in RStudio, she improved her programming skills. Finally, through her hands-on experience with these projects, Henrieke observed how concepts such as vaccine effectiveness and time series analysis are put into practice in operational research. Moreover, she learned how routine (pharmacy) prescription data can be used for surveillance purposes, the importance of international collaboration during multi-country outbreaks and how this can lead to applied research that can also help future responses to infectious disease outbreaks.

4. Teaching and pedagogy

4.1 EAN mini-module on media and infodemic management, 21–22 November 2023, Stockholm, Sweden

Organising committee: Dr Charlotte Hammer, Dr Sonia Boender, Dr Liza Coyer, Dr Eftychia Kotronia

The EPIET Alumni Network (EAN) mini-module, designed for participants with a professional background in public health, aimed to familiarise them with the basic concepts of infodemic management and to provide hands-on skills for communicating with media and the public on health-related topics. Henrieke was part of the organising committee that started preparations for this module in February 2022. They drafted a programme that consisted of an introduction to infodemic management (Day 1), and media management and communication (Day 2). Together with colleagues from the committee, Henrieke adjusted a case study that derived form the Media Manipulation Casebook to match the concepts introduced in the lectures. She facilitated the module and the case study.

Henrieke created an evaluation that received responses from 23/25 participants. Respondents highly appreciated the combination of practice and theory, and the case study, and indicated the need for further training in the future.

4.2 An introduction to applied epidemiology, ZIBI lecture series on infection biology, 6 July 2023, Berlin, Germany

Supervisor: Sofie Gillesberg Raiser

The Postgraduate Training for Applied Epidemiology (PAE) team invited Henrieke and another EPIET-EU track fellow, Mario Martin Sanchez, to prepare a one-hour lecture on applied epidemiology. The aim of the lecture was to convey the basic concepts of applied epidemiology including surveillance (covered by Mario) and the ten steps of an outbreak investigation (covered by Henrieke). The audience consisted of international doctoral researchers at the Centre for Infection Biology and Immunity (ZIBI Graduate School, Berlin) with backgrounds in bacteriology, virology and immunology. The lecture addressed surveillance and the steps of an outbreak investigation using diphtheria, which both Henrieke and Mario worked on, as a real-life example. It consisted of a PowerPoint presentation including interactive questions to help the audience to understand the purpose and uses of surveillance and know the ten steps of an outbreak investigation by the end of the session.

Educational outcome

By organising the above teaching activities, Henrieke learned how different course materials can be developed and delivered to different audiences. Moreover, she learned how to adapt her teaching methods depending on the professional background of the audience. By facilitating the case study, Henrieke was able to share her own experiences and consolidate her own knowledge on the topics addressed. In her opinion, these activities were enjoyable and rewarding experiences that helped her improve her competence as a teacher. Reflecting on the experience, Henrieke understood the importance of any future teaching to be primarily participant-driven. This implies stimulating participants to cover pre-course activities in order to familiarise themselves with the content, and to encourage them to ask questions. A further learning goal is to ‘know’ the audience in order to be able to adjust the teaching interactively, depending on the participants and their backgrounds, and to get participants to contribute from their expertise and prior knowledge.
5. Science communication

5.1 Publications related to the EPIET fellowship

5.1.1 Manuscripts published in peer-reviewed journals


5.1.2 Manuscripts (to be) submitted to peer-reviewed journals


5.1.3 Other reports

- Infektionsepidemiologisches Jahrbuch meldepflichtiger Krankheiten für 2021, Robert Koch Institute.

- Infektionsepidemiologisches Jahrbuch meldepflichtiger Krankheiten für 2022, Robert Koch Institute.


- ECDC technical report on mpox contact tracing data collection in EU/EEA Member States. [In preparation].

5.1.4 Study protocols


5.2 Conference presentations

- ECCMID, 18 April 2023, Copenhagen. Sudden increase of diphtheria with Corynebacterium diphtheriae among migrants arriving in Germany, 2022: statistical outlier – or detection of an outbreak? Due to the presenter being unable to attend in person, we organised the possibility to answer questions online during the ePoster session.


5.3 Other presentations


5.4 Other communications

- One-hour podcast on HIV cure research, 9 November 2021. Available at https://amboss.podigee.io/74-hiv
- Presentation on Infodemic Management during Outbreak Investigation Module, 7 December 2021
- Curation of the EPIET/EUPHEM Alumni Network Twitter account (@EANBoard) in the week of World AIDS Day, 28 November 2022–2 December 2022
- Presentation about the EPIET fellowship at the department of Infectious Diseases and Medical Microbiology of the Erasmus Medical Centre, Rotterdam, 26 May 2023.

6. EPIET/EUPHEM modules attended

1. Pre-Introductory Course E-learning modules, 13/09/2021-17/09/2021, online
2. Introductory Course, 20/09/2021-08/10/2021, online
3. Outbreak Investigation module, 06/12/2021-10/12/2021, online
4. Multivariable Analysis Module, 14/03/2022-18/03/2022, online
5. Introductory Course Part II, 19/04/2022-29/04/2022, Spetses, Greece
6. Rapid Risk Assessment methodology for public health events, 06/06/2022-10/06/2022, Stockholm, Sweden
7. Project Review Module, 29/08/2022-02/09/2022, Lisbon, Portugal
8. Time Series Analysis module, 07/11/2022-11/11/2022, Bilthoven, the Netherlands
9. Vaccinology module, 13/02/2023-17/02/2023, online
10. Management, Leadership and Communication in Public Health, 08/05/2023-12/05/2023

7. Other training

- Master of Science in Applied Epidemiology, Berlin School of Public Health, 01/09/2021-30/09/2023, Berlin, Germany
- Causal Inference with 'directed acyclic graphs', RKI, 13/10/2021-15/12/2021, Berlin, Germany
- Introduction course to R, RKI, 21/10/2021, Berlin, Germany
- Operational Research Inject Day, ECDC, 27/10/2021-28/10/2021, online
- Data Entry Inject Day, ECDC, 10/11/2021-11/11/2021, online
- Jour Fixe including SurvNet Introduction, RKI, 25/11/2021-26/11/2021, Berlin Germany
- Data Protection Training, RKI, 23/03/2022, Berlin, Germany, online
- Multivariable Analysis Inject Day, ECDC, 30/03/2022, online
- Information Technology Security Training, RKI, 17/05/2022, online
- Mpx training, Akademie für Öffentliches Gesundheitswesen, 22/06/2022, online
- Laboratory Module (Lab4Epi), RKI, 27/06/2022-29/06/2022, Berlin, Germany
- Introduction to Git and Github, EPIET fellow, 23/06/2022, online
- Jour Fixe, RKI, 30/06/2022-01/07/2022, Berlin, Germany
- Advanced Epidemiologic Methods: Mastering R for Epidemiologic Research, Charité Public School of Health, 22/08/2022-02/09/2022, online
- Public Health internship, Gesundheitsamt Friedrichshain-Kreuzberg, 26/06/2023-30/06/2023, Berlin, Germany.

8. Other activities

- German language lessons, twice weekly, 1 September 2021 – 10 September 2023
- Peer-to-peer weekly training on the use of R, 18 January 2022 – 1 April 2022
- Mentoring of EPIET-EU track fellow from Cohort 2022 via EPIET buddy programme, 21 March 2023 – 10 September 2023
- Participation in the RKI team in the Berliner Firmenlauf (institute-facilitated sporting activity), 16 May 2023.
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