EUPHEM



EUPHEM REPORT

Summary of work activities Maximilian Riess European Public Health Microbiology Training Programme (EUPHEM), 2018 cohort

Background

According to the European Centre for Disease Prevention and Control (ECDC) Advisory Group on Public Health Microbiology ('national microbiology focal points'), public health microbiology is a cross-cutting area that spans the fields of human, animal, food, water, and environmental microbiology, with a focus on human population health and disease. Its primary function is to improve health in collaboration with other public health disciplines, in particular epidemiology. Public health microbiology laboratories play a central role in detection, monitoring, outbreak response and the provision of scientific evidence to prevent and control infectious diseases.

European preparedness for responding to new infectious disease threats requires a sustainable infrastructure capable of detecting, diagnosing, and controlling infectious disease problems, including the design of control strategies for the prevention and treatment of infections. A broad range of expertise, particularly in the fields of epidemiology and public health microbiology, is necessary to fulfil these requirements. Public health microbiology is required to provide access to experts in all relevant communicable diseases at the regional, national and international level in order to mount rapid responses to emerging health threats, plan appropriate prevention strategies, assess existing prevention disciplines, develop microbiological guidelines, evaluate/produce new diagnostic tools, arbitrate on risks from microbes or their products and provide pertinent information to policy makers from a microbiological perspective.

According to Articles 5 and 9 of ECDC's founding regulation (EC No 851/2004) 'the Centre shall, encourage cooperation between expert and reference laboratories, foster the development of sufficient capacity within the community for the diagnosis, detection, identification and characterisation of infectious agents which may threaten public health' and 'as appropriate, support and coordinate training programmes in order to assist Member States and the Commission to have sufficient numbers of trained specialists, in particular in epidemiological surveillance and field investigations, and to have a capability to define health measures to control disease outbreaks'.

Moreover, Article 47 of the Lisbon Treaty states that 'Member States shall, within the framework of a joint programme, encourage the exchange of young workers. 'Therefore, ECDC initiated the two-year EUPHEM training programme in 2008. EUPHEM is closely linked to the European Programme for Intervention Epidemiology Training (EPIET). Both EUPHEM and EPIET are considered 'specialist pathways' of the two-year ECDC fellowship programme for applied disease prevention and control.

Stockholm, September 2020

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This report summarises the work activities undertaken by Maximilian Riess, cohort 2018 of the European Public Health Microbiology Training Programme (EUPHEM) at the Public Health Agency of Sweden (PHAS, Folkhälsomyndigheten)

All EUPHEM activities aim to address different aspects of public health microbiology and underline the various roles of public health laboratory scientists within public health systems.

Pre-fellowship short biography

Maximilian Riess holds a Diploma in Biochemistry with specialisation in immunology and virology from the Goethe University in Frankfurt am Main, Germany. He then successfully pursued a PhD in Biochemistry on the mechanisms of innate restrictions to HIV-1 from the Goethe University placed at the German Federal Institute for Vaccines and Biomedicines (Paul-Ehrlich-Institute). His research involved work under BSL-3 conditions on the sensing of HIV by innate immunity cells. He aims at combining his focus on immunology and virology with a translational perspective in public health. Therefore, his personal objectives to begin the EUPHEM fellowship were to broaden his knowledge in Public Health Microbiology as well as epidemiology and enter the field of public health.

Methods

This report accompanies a portfolio that demonstrates the competencies acquired during the EUPHEM fellowship by working on various projects, activities and theoretical training modules.

Projects included epidemiological investigations (outbreaks and surveillance); applied public health research; applied public health microbiology and laboratory investigation; biorisk management; quality management; teaching and public health microbiology management; summarising and communicating scientific evidence and activities with a specific microbiological focus.

The outcomes include publications, presentations, posters, reports and teaching materials prepared by the fellow. The portfolio presents a summary of all work activities conducted by the fellow, unless prohibited due to confidentiality regulations.

Results

The objectives of these core competency domains were achieved partly through project or activity work and partly through participation in the training modules. Results are presented in accordance with the EUPHEM core competencies, as set out in the EUPHEM scientific guide¹.

1. Epidemiological investigations

1.1. Outbreak investigations

Supervisors: Moa Rehn, Marika Hjertqvist

Outbreak of Salmonella enteritidis MLVA 2-10-7-3-2 in Sweden, 2018

From 9 October to 3 November 2018 an outbreak of *Salmonella enteritidis* with a Multiple Locus Variable Number Tandem Repeat Analysis (MLVA) profile 2-10-7-3-2 occurred in Sweden. An outbreak investigation was conducted by PHAS in collaboration with the regional County Council Departments of Communicable Disease Control and Prevention (CDC-department) of the affected counties and the national food agency (Livsmedelverket, SLV). A case-control study was undertaken to investigate the source of the outbreak. A total of 33 cases were identified, symptoms were mild to severe, and no death was reported. Cases were mostly adults and resided in 15/21 of the Swedish counties. Results of the case-control study suggest that being a case was associated with having eaten at a restaurant, and bacon and lettuce were the main suspected sources. No food item was available for source tracking and the environmental investigations were inconclusive. PHAS timely informed the public of the outbreak via its official website. Further public health measures such as counselling patients on food handling were of the responsibility of the regional centre for disease prevention and control departments and SLV.

The fellow wrote an analysis plan and participated in the questionnaire design, outbreak investigation team meetings, data analysis and interpretation and writing the report.

¹ European Centre for Disease Prevention and Control. European public health training programme. Stockholm: ECDC; 2013. Available from: http://ecdc.europa.eu/en/publications/Publications/microbiology-public-health-training-programme.pdf

Cross-border outbreak of Yersinia enterocolitica serotype 03 (ST-18) Outbreak in Sweden, 2019

Supervisors: Marie Jansson Mörk, Sharon Kuhlmann-Berenzon

Between 7 March and 11 April 2019, an unusually high number of Yersiniosis cases was reported to PHAS through the national electronic notification system for notifiable infectious diseases (SmiNet) and this signal became apparent on 25 March. Demographics were obtained through SmiNet. Routine trawling questionnaires were administered to the cases where possible in order to gather information about symptoms and food consumption. On 1 April, a request was sent out to all clinical microbiological laboratories in Sweden to send in *Y. enterocolitica* isolates to FOHM, primarily type O3 if local typing was done, or all *Y. enterocolitica* from domestic cases if local typing was not done. Isolates were analysed using whole genome sequencing (WGS), assessing both specific virulence genes, sequence type (ST) and a clustering analysis. After identification of clustering isolates by WGS an outbreak of *Y. enterocolitica* O3 (ST-18) was declared on 11 April 2019. Sharing of the outbreak sequence with Nordic countries triggered Danish authorities Statens Serum Institute (SSI) to start analysing their increased numbers of *Y. enterocolitica* O3 isolates by WGS. This analysis clearly revealed that Swedish and Danish cases shared the same infecting strain and authorities were facing a cross-border outbreak. The two countries' national public health agencies FOHM and SSI collaborated closely from thereon in the outbreak investigation but conducted separate analytical studies.

The outbreak was suspected to be foodborne, and the source of infection was thought to be nationally distributed. *Y. enterocolitica* infection usually follows consumption of raw or undercooked pork, of contaminated vegetables or unpasteurized milk, or exposure to contaminated water. Combined investigations with Danish authorities in this cross-border outbreak suggest that the likely source of this outbreak was fresh spinach sold at major retail chains in both countries. No other European countries reported having cases connected to the outbreak. Early sharing of signals of the outbreak obtained through epidemiological surveillance proved important in this international collaboration. The WGS based connection of Swedish and Danish cases as being part of the same outbreak allowed the Swedish authorities to acknowledge and endorse the Danish case control study results and accept spinach as a potential source of this outbreak also for Swedish cases. Trace back investigations by the food safety authorities of the two countries identified common batches of spinach sold to both countries from one producer. The findings in this investigation support that other sources of *Y. enterocolitica* than pork products like fresh products (vegetables/fruits) have to be considered and investigators should be aware of these. The Danish Food and Veterinary Agency posted a Rapid Alert System for Food and Feed (RASFF 2019.2145) notification on 12 June to inform the exporting country in order for them to follow up with the producer.

The fellow wrote an analysis plan and took the lead of the case-control study including writing the study protocol, questionnaire design, reporting to the outbreak investigation team meetings, data collection, analysis and interpretation and writing the report. The fellow also wrote and published a scientific article as shared first author in a peer reviewed journal. The outbreak investigation was presented at an international conference (ESCAIDE 2019) by the Danish shared first author of this investigation.

Training modules

Five training modules covered aspects of outbreak investigation and the fellow delivered own teaching activities on outbreak investigations (see 6. Teaching and pedagogy).

The three weeks **'Introductory Course'** of the fellowship covered a broad range of topics including basics of outbreak investigations (ten steps of outbreak investigations) and in depth exercises on descriptive and analytical analyses and the fellow got introduced to the range of analytical study designs. Content was provided by lectures, interactive sessions, case studies and group exercises.

During the one week **'Outbreak Investigation'** module the fellow learned in depth details important for different scenarios of outbreak investigations. The course was interactive and mainly included independent work in small groups leading the fellow through the ten steps of outbreak investigations, from questionnaire design, data entry and data management to data analysis including stratified analysis with the help of different software tools. This also included the use of STATA for data management and descriptive and analytical univariable analyses in cohort studies and case-control studies during outbreak investigations.

The one-week module **'Multivariable Analysis Module'** was an interactive statistics course covering multivariable analysis, stratification, interactions of variables, how to build logistic regression and binominal regression models in STATA. It provided the fellow with thorough understanding of analytical analyses and types of regression models.

The one-week module on **'Rapid Assessment and Survey Methods'** was an interactive course on surveys and sampling strategies and how to adapt to the targeted population, selection of an appropriate sample and the sampling strategy. Moreover, the module covered rapid risk assessments and practise thereof as well as rapid health assessment in complex emergency situations (CES), use of geo positioning systems in CES and setting up a surveillance system, interpret surveillance data, set an alert and response system in CES.

The one-week module on **'Management, Leadership and Communication in Public Health'** included interactive sessions on communication and presentation strategies and techniques and importance of public relations. The fellow gained important experience in communication with higher authorities and communication in emergency

situations to experts and the public. Furthermore, the course covered different management styles, team roles and evolution of team, the delegation of tasks, personality types and learning and motivating styles. Interactive sessions also taught on the provision of structured feedback and tools for effective time as well as stress management.

Educational outcome: Application of microbiological and epidemiological knowledge in outbreak situations; application of bacteriology concepts to the public health discipline; understanding the use and limitations of typing methods and their interpretation; participation in a multidisciplinary outbreak team and involvement in an outbreak investigation including case definition, case-finding, data collection, data analysis, laboratory typing methods, and communication; dataset management; conduct multivariable analysis: calculate and interpret point estimates and confidence intervals of association; select the multivariable analysis that is adapted to the study objective /design; identify the relevant variables needed to build an optimal regression model; control for confounding and effect modification at the analytical level; interpret the results of a regression model: meaning of parameters and the corresponding inferences; writing of outbreak report and scientific publication.

1.2. Surveillance

Surveillance activities during the COVID-19 crisis management and response, Sweden, 2020

Supervisor: Maria Axelsson, Mia Brytting

In late 2019 SARS-CoV-2 emerged as a new virus and spread worldwide in short time from the epicentre in Wuhan, China. SARS-CoV-2 causes the respiratory disease COVID-19. The outbreak was declared a Public Health Emergency of International Concern on 30 January 2020 and a pandemic on 11 March 2020. The first confirmed case was reported in Sweden on 31 January 2020. Since then multiple independent introductions have led to the establishment of community spread in every region of the country. The fellow got proactively involved in different aspects of the Swedish response regarding surveillance activities and public health management activities.

These included (i) epidemic intelligence, (ii) production of daily situation reports updates on the global and national outbreak situation, (iii) reviewing and summarising scientific evidence from recent literature in an analysis group with daily meeting and internal newsletter to PHAS (iv) production of knowledge base documents and contribution to national guidelines on period of infectiousness for different case situations and review response to a WHO report, (iv) hands on laboratory diagnostic in the sentinel surveillance program, (v) contribution to planning and design of a seroprevalence study and following a bi-weekly joint ECDC and WHO/Europe online meeting on COVID-19 sero-epidemiological studies. The fellow was offered an international deployment through GOARN to Timor Leste in the role of an epidemiologist to support the COVID-19 response but due to COVID-19 growing into a global pandemic and affecting the fellows host country, the deployment could not be realised due to global travel restrictions.

High impact of molecular surveillance in hepatitis A outbreak case detection in Sweden - a retrospective study 2009 – 2018

Supervisors: Josefine Lundberg Ederth, Theresa Enkirch, Lena Sundqvist

The Swedish hepatitis A surveillance includes sequence-based typing but its contribution to outbreak detection in relation to epidemiological investigations has not been fully evaluated. This project aimed to evaluate the role of sequence-based typing in hepatitis A outbreak detection and to describe the hepatitis A epidemiology in Sweden to improve surveillance. We retrospectively investigated hepatitis A virus sequences of 447 cases notified in Sweden 2009-2018 in a phylogenetic analysis of evolutionary distances to identify cases with similar virus sequences (≥459/460 identical nucleotides in the VP1/P2A junction). Unique sequences, dyads and sequence-based clusters (SBCs) were identified. Additionally, non-sequenced cases were attributed by epidemiological data and potential outbreaks were identified. We described those and assessed retrospectively if typing was instrumental for their detection. Samples of 55% (n=542/990) of the notified hepatitis A cases were referred to PHAS for typing and 447 (45%) were sequenced successfully. Sub-genotypes included IA (42.5%, n=190), IB (42.7%, n=191) and IIIA (14.8%, n=66). Phylogenetic analysis identified 154 unique sequences, 33 dyads (66 cases) and 34 SBCs (227 cases). The combination of molecular and epidemiological data revealed 23 potential outbreaks (201 cases). Cases were linked to those exclusively by sequence (59%, n=118), epidemiological data (11%, n=23)) or both types of information (30%, n=60). Sequencing was needed to identify 15/23 potential outbreak signals (65%). In summary, sequence-based typing contributed significantly to detect clustering cases and identify outbreak signals in Sweden. The results advocate for use of routine sequence-based typing to detect outbreak signals and thereby promote timely outbreak investigations and facilitate international collaborations.

The fellow wrote a study proposal and performed all steps of the project from data cleaning, data analysis and data interpretation. The fellow also presented this work at an international conference (ESCAIDE2019) and published a scientific article as first author in a peer reviewed journal.

Estimation of the number of suspected but discarded cases of acute rubella in Sweden, 2018

Supervisors: Hélène Englund

The rubella surveillance in Sweden faces two challenges in the context of elimination (i) there are usually no confirmed and notified rubella cases and (ii) suspected cases are not routinely reported. Due to the passive design of the surveillance system and the lack of cases as well as the lack of reporting of suspected cases, many of the standard performance indicators cannot be addressed accordingly for Sweden.

To aid the process of verification of successful rubella elimination in Sweden, we aimed to estimate the number of discarded suspected acute rubella cases in Sweden in 2018. For this, we gathered information on the anti-rubella IgM tests performed in 2018 by the five Swedish laboratories performing rubella IgM testing, and developed a decision tree to identify tests that had likely been performed due to a clinical suspicion of acute rubella infection, excluding congenital rubella syndrome (CRS). Additionally, we gathered information on the rubella diagnostics used in these laboratories to assess the quality of the diagnostic testing.

We estimated a rate of clinically suspected and discarded acute rubella cases of 0.25/100,000 inhabitants. This rate does not meet the WHO target of 2 discarded cases/100.000 inhabitants. It is however likely that additional clinically suspected and discarded cases of acute rubella occur each year, but could not be identified in this study due to the limited clinical information available. In addition, a high number of anti-rubella IgM tests are performed yearly in Sweden by proficient laboratories and we believe that if there were to be a case of acute rubella, it would be detected.

This project was a collaboration with the EPIET fellow Soledad Colombe of cohort 2018 and both fellows wrote a study proposal and performed all steps of the project from data collection, data cleaning and verification, data analysis and interpretation and writing the final report. The report is published as Annex to the annual report on measles and rubella surveillance to WHO.

National surveillance systems for vibriosis and Shewanella spp. infections in EU/EEA countries, September-October 2019

Supervisors: Johanna Takkinen, Aftab Jasir

In order to achieve an overview of countries in the European Union and the EEA who have or are planning to implement surveillance systems for vibriosis or for *Shewanella* infections, an online survey was conducted. It was disseminated to the National Focal Points for Food- and Waterborne Diseases and Zoonoses of the EU/EEA countries through the EPIS FWD. The main objective of the survey was to collect information about national surveillance systems on vibriosis (including all *Vibrio* other than toxin producing *Vibrio cholerae* O1 and O139 as causative agents) and *Shewanella* spp. infections.

Twenty four out of 31 EU/EEA countries replied to the survey leading to a response rate of 77%. All participating countries replied to both parts of the survey, relating to the surveillance systems for vibriosis and *Shewanella* spp. infections. Ten EU/EEA countries stated they had a surveillance for vibriosis in place. Surveillance activities varied from comprehensive mandatory notification of any type of vibriosis infection to more focused syndromic surveillance of food-poisoning and gastro-enterocolitis. The other 14 countries did not plan to introduce a surveillance system for vibriosis in the next two years. Two EU/EEA countries had a surveillance system for *Shewanella* spp. infections in place. One EU/EEA country intended to introduce such a surveillance system within one year. None of the 21 remaining countries had plans to establish such a surveillance system in the near future.

Responses also indicated ongoing national and international research projects underlining the public health interest in vibriosis and *Shewanella* spp. infections. The collected data will be useful to ECDC and EU/EEA countries where an assessment for the future introduction of a surveillance system for these pathogens is planned.

This project was a collaboration of four EUPHEM fellows (Maximilian Riess, Ettore Amato, Marius Linkevicius, and Daniel Thomas-Lopez). The fellows collected and analysed the data and wrote a technical report on Vibriosis and *Shewanella* infection surveillance systems in EU/EEA for ECDC.

Molecular epidemiology of cryptosporidiosis in Sweden data of the past years in Sweden

Supervisors: Jessica Beser, Ioana Bujila, Anette Hansen

This project could not be taken up due to time investments in the COVID-19 response. A project proposal was formulated including literature research and the project itself will be pursued by the next EUPHEM fellow. The aim of this project was to describe the molecular epidemiological data of cryptosporidiosis cases in Sweden from 2018-2019 in order to demonstrate the value of the molecular surveillance program for cryptosporidiosis surveillance in

Sweden. The data is to be described and compared among the typed cryptosporidiosis cases and the overall epidemiology in terms of age, sex and region of infection. The species and subtype distribution of all typed samples will be summarised and analysed and detected as well as previously undetected cluster of subtypes will be compiled. Lastly, the C. hominis subtype IbA10G2 represents a globally prevalent subtype with increased virulence and proven potential to cause large scale waterborne outbreaks in Sweden. The collected isolates of this subtype will be analysed in terms of relatedness in more detail by an in-house developed protocol for higher resolution typing.

The fellow researched literature and wrote the study proposal.

Training modules

The three weeks **'Introductory Course'** of the fellowship introduced the basic concepts of surveillance systems, including the principles of surveillance, and how to develop, validate, evaluate and operate a surveillance system. As a part of this course, the fellow also participated in the development of the study protocol for analysing the contribution of using mobile dating applications to spread of sexually transmitted infections among sexually active heterosexuals in Wales, UK. Content was provided by lectures, interactive sessions, case studies and group exercises. Moreover, the modules **'Multivariable Analysis Module'**, **'Rapid Assessment and Survey Methods'** and **'Management, Leadership and Communication in Public Health'** covered relevant content as outlined above (1.1)

Educational outcome: Analyses of epidemiological and microbiological surveillance data, interpretation of such data to generate information for action and write a surveillance report; Evaluation of an existing surveillance system; Provide microbiological (EUPHEM) advice on improvement or maintenance of surveillance systems; questionnaire design to national microbiological laboratories and to the EU/EEA EPIS-FWD network; summarise, analyse and interpret survey results to assess surveillance practices; understanding the challenges and limitations of surveillance systems; understanding the authorities and responsibilities of those involved in surveillance activities; participation in disease-specific networks at the European level; review literature; formulation of specific public health recommendations; communication with different partners; presentation for public health specialists; writing of scientific articles.

2. Applied public health microbiology research

Multi-country occurrence of non-toxigenic cholera and non-cholera Vibrio infections in Nordic countries and countries bordering the Baltic Sea in 2018

Supervisors: Cecilia Jernberg, Anette Hansen, Marika Hjertqvist

In the recent years, countries in northern Europe have witnessed an increase in *Vibrio* infections during heatwaves, including 2018. *Vibrio* bacteria are ubiquitous in aquatic and marine habitats. Non-cholera *Vibrio* species cause self-limiting vibriosis, but can rarely lead to invasive clinical presentation. We aimed to describe the epidemiology of vibriosis and map the genetic diversity of the isolates collected from seven countries (Norway, Sweden, Finland, Denmark, Poland, Estonia and Latvia) in 2018 in order to propose recommendations for control measures.

A retrospective cross-sectional study was conducted using laboratory-based or passive surveillance data, analysing demographics, geographical distribution, seasonality and severity of vibriosis cases. Travel-related cases were not included. Relatedness of isolates was investigated by phylogenetic single-nucleotide-polymorphism (SNP) analysis of whole genome sequencing data. In total, we identified 445 vibriosis cases with median age of 52 years (1-101) and male-to-female ratio of 1.6. Exposure was known for 116 cases of which 109 (94%) reported exposure to seawater. Infections by species showed a geographical disparity and were unevenly distributed across age groups. The odds of developing severe infection was associated with (i) being 65-79 (OR=3.6; 95%CI:1.6-8.2) and >80 years old (OR=15.0; 95%CI:4.2-53.2), (ii) *V. vulnificus* (OR=20.4; 95%CI:3.7-112.8) and *V. parahaemolyticus* (OR=2.6; 95%CI:1.1-6.2) and (iii) summer season (OR=6.0; 95%CI:2.8-13.1). Although phylogenetic analysis showed diversity between Vibrio isolates, two *V. vulnificus* clusters (<10 SNPs) were identified in Norway and in Sweden. In summary, severe infections with *V. vulnificus* and *V. parahaemolyticus* represent a public health threat during summer seasons for the population at risk in the Nordic region and countries bordering the Baltic Sea. These countries may consider introducing or harmonising vibriosis surveillance based on their own public health priorities in order to advise the public and authorities on control measures.

The fellow was principal investigator of the project in Sweden and wrote an independent national report on this matter as well. This project was a collaboration of four EUPHEM fellows (Ettore Amato, Marius Linkevicius, Daniel Thomas-Lopez and Maximilian Riess). The fellows equally contributed to writing a study protocol and all steps of the project from data collection, data cleaning, data analysis, and data interpretation and wrote an abstract and a scientific publication. Each fellow independently worked with their country-related dataset and while a multi-country analyses was carried out jointly. The fellow created automatized STATA scripts for epidemiological data analysis and

produced a national epidemiological report. The four principle investigators together wrote a scientific article as shared first authors and aimed to submit to a peer reviewed journal, the work was also submitted for presentation at an international conference (ESCAIDE2020) by Ettore Amato.

Comparison of WGS based ABR prediction with AST data of VRE and CRE isolates from recent years in Sweden

Supervisors: Petra Edquist, Kristina Rizzardi

PHAS conducts national microbial surveillance programmes including phenotypic antimicrobial resistance (AMR) surveillance of vancomycin resistant Enterococci (VRE) and carbapenem resistant Enterobacteriaceae (CRE). We evaluated the diagnostic performance of a genotypic AMR predictions pipeline versus the gold standard of phenotypic antimicrobial susceptibility testing (AST) to improve testing algorithms. Phenotypic AST data (gradient and disc diffusion test) and genotypic predictions (using the ResFinder database on whole genome sequencing (WGS) data) were available. Isolates included vancomycin resistant Enterococcus faecium (n=560) and CRE producing Escherichia coli (n=357) and Klebsiella spp. (n=304; including 259 K. pneumoniae). We calculated sensitivity, specificity, positive and negative predictive value and accuracy of the genotypic predictions versus phenotypic AST. Predicted genes were compared for associated levels of resistance in terms of median minimum inhibitory concentrations or inhibitory zone values for some classes of antibiotics. Sequence types (based on WGS data) were investigated for frequencies of occurring resistance determinants. Genotypic AMR predictions were accurate for several drug species combinations: teicoplanin, vancomycin, tigecycline and linezolid resistance in *E. faecium* (97.5%, 98.0%, 99.1% and 99.5% respectively) and for gentamicin, amikacin and trimetoprim in E. coli (90.9%, 94.0 and 97.5%, respectively). Concordance of phenotypic testing by genotypic prediction was less accurate in Klebsiella spp. with best performances reaching accuracies of 87.6% (gentamycin), 85.1% (amikacin), and 85.3% (Ciprofloxacin). Within classes of antibiotics, some genes conferred higher phenotypic resistance than others. Regarding standard-of-care antibiotics, we detected very few linezolid resistant VREs (6/560) and few amikacin resistant CRE E.coli (40/357) and Klebsiella spp. (63/304). Genotypic AMR predictions can replace work intensive phenotypic AST for some drug species combinations but for Klebsiella spp. the bioinformatics analysis pipeline needs optimization. Including additional reference databases and refining relevant list of genes for specific antibiotics will increase the accuracy of genotypic predictions to be able to substitute further phenotypic testing. The genotypic prediction does not have a clinical utility.

The fellow wrote a study proposal and performed all steps of the project from data cleaning, data analysis, and data interpretation and wrote an abstract for an international scientific conference and a report.

Training modules

The three weeks **'Introductory Course'** of the fellowship covered a broad range of topics including development and presentations of study protocols, including study objectives, aims, methods and expected outcomes. Fellows developed study protocols in group exercises and familiarised themselves with the topic of antimicrobial resistance in a problem-based learning exercise.

During the one week **'Outbreak Investigation'** module a session on whole genome sequencing and phylogeny was taught. Moreover, the modules **'Multivariable Analysis Module'** and **'Management, Leadership and Communication in Public Health'** covered relevant content as outlined above (1.1)

Educational outcome: identification of a public health problem; conduct all stages of a public health microbiology research project from planning to writing a scientific paper; design study protocol; managing a team of scientists; identify limitations; disseminate and communicate the information; apply both microbiological and epidemiological knowledge in surveillance; collecting, collating, cleaning and analysing data; apply and develop knowledge of typing methods used for Vibrio species; conduct multivariable analysis; assessment of laboratory methods to improve diagnostic procedures; review literature; formulation of specific public health recommendations; communication with different partners; presentation for public health specialists; writing of scientific articles.

3. Applied public health microbiology and laboratory investigations

Generation of whole genome sequences of 200 *B. pertussis* isolates from 2008-2019, Sweden

Supervisors: Thomas Åkerlund

A selection of 200 isolates of *Bordetella pertussis* was done based on the age of the cases. Those were cultured and WGS sequences were generated from the prepared genomic material. The sequences will be further analysed as a

pilot study to support initiation of the national implementation of the pertussis molecular surveillance programme at PHAS. Moreover, they will be used to assess the diversity of circulating *B. pertussis* strains in Sweden and whether antigen-drift was present 2009-2019. Isolates were sequenced by next generation sequencing using Illumina technology. The sequencing data underwent quality control and the in-house bioinformatics pipeline will be utilized for analysis of the whole genome sequences to search for vaccine component genes (pertussis toxin (PTX), filamentous hemagglutinin (FHA), pertactin (PRN) and fimbriae genes (FIM2,3)) and other virulence genes.

The fellow wrote a study proposal and performed the laboratory procedures including selection of and growing of the isolates, DNA extraction and preparing samples for sequencing by an external contractor. The fellow participated in the quality control of the sequences.

Collection and laboratory investigation of non-toxigenic cholera and non-cholera Vibrio isolates, Sweden, 2018

Supervisors: Cecilia Jernberg, Anette Hansen, Marika Hjertqvist

The Public Health Microbiology Research project "Multi-country occurrence of non-toxigenic cholera and non-cholera *Vibrio* infections in Nordic countries and countries bordering the Baltic Sea in 2018" included a microbiological investigation of the genetic diversity of *Vibrio* isolates. We aimed to generate whole genome sequences of all isolates and analyse those phylogenetically but also investigate occurrence and distribution of specifically antimicrobial resistance determinants, virulence genes and biofilm genes. For this, a laboratory investigation was required in which isolates were collected, DNA samples obtained and sequenced by whole genome sequencing (WGS). This investigation included the nationwide collection of isolates from 24 laboratories that serve the 21 regions of Sweden.

The fellow requested and collected isolates from the Swedish microbiological laboratories, cultured all isolates and determined their species by MALDI-TOF, he extracted DNA of all isolates and selected 76 of those for sequencing by Illumina next generation sequencing through an external contractor and wrote a final report.

Laboratory diagnostics in the sentinel surveillance of COVID-19, Sweden, 2020

One of the surveillance systems employed during the global COVID-19 in Sweden was the sentinel surveillance amongst others in order to keep an overview about the extent of disease spread in the population. The fellow was trained in the laboratory workflow of sentinel sample diagnostics and qualified to carry out the sample registration and handling, extraction of viral RNA and RTqPCR assay for the detection of SARS-CoV-2 RNA. In the initial phase of the expansion of the Swedish sentinel surveillance system for influenza to COVID-19, the fellow was also responsible for weekly reporting aggregated numbers of tests performed and positive tests to the European surveillance platform TESSy.

The fellow carried out the aforementioned steps in the laboratory work flow and worked closely together with the other team members.

Training modules

Content relevant to this core competency was acquired through the three weeks **'Introductory Course'** (outlined under 2) and the modules **'Multivariable Analysis Module'** and **'Management, Leadership and Communication in Public Health'** (outlined under 1.1).

Educational outcome: Identification of a public health problem; apply concepts of bacteriology to public health disciplines; determine the use and recognise the limitations of diagnostic and typing methods and interpret their results in light of surveillance and epidemiological studies; recognise specific issues related to the use of laboratory methods in investigations of rare and emerging diseases; design study proposal; managing a team of scientists; identify limitations; disseminate and communicate the information; apply both microbiological and epidemiological knowledge in surveillance; collecting, collating, cleaning and analysing data; review literature; formulation of specific public health recommendations; communication with different partners; presentation for public health specialists; writing of scientific articles.

4. Biorisk management Biosafety round in PHAS BSL-2 laboratory

Supervisor: Katherina Zakikhany

The biosafety round is a regular routine at PHAS and consists of a pre-activity survey and activities during the day of inspection. Target audience were the heads of the units in the department and they were to cascade the findings to the units' members. During the process knowledge of and the practical implementation of the biosafety and biosecurity routines were controlled. During the tour of inspection, the strengths and deficiencies in following the routines were reviewed aiming to raise awareness for biosafety as well as biosecurity aspects and the standard routines in the laboratories of the department.

The fellow participated as an observer, in the formal inspection of the agencies' own laboratories and was involved in the activities and discussions during the day of inspection.

WHO EURO Regional conference: Polio laboratory network and poliovirus containment, 2019

Supervisor: Katherina Zakikhany

In this conference, the poliovirus laboratory network and the containment specialists (NAC, national authority for containment of poliovirus) of each country convened together. More than 100 participants from 46 nations of the WHO/Europe region attended the meeting. During the three-day meeting the participants received an update on the current situation of poliovirus spread and outbreaks worldwide, update and guidance on the laboratory network performance and progress of containment implementation. Additionally, workshops were conducted to address questions from the national representatives and to further explain details of guidelines and methodical approaches.

The Fellow participated as an observer and accompanied the country delegates during the conference. It was an excellent opportunity to learn how such an international network collaborates, interacts in different roles and works towards a common goal. Moreover, it deepened the fellow's knowledge on the range of work being done in both the laboratory work with poliovirus and the biosafety aspects related to the eradication and endgame strategy.

Pre-fellowship experience

The fellow practised extensive work in a BSL-3 laboratory before entering the fellowship, therefore an additional BSL-3 training was not required. Likewise, a further project focusing on sexually transmitted diseases was deemed not obligatory due to his work experience with HIV.

Training modules

The Biosafety and Quality management module was cancelled.

Educational outcome: Understanding and experience of principles and practices applied for biorisk management; use of appropriate decontamination strategies/ personal protection and their applicability in field situations; determine the need for quality management, biosecurity management, and crisis response as core elements of management of a public health microbiological laboratory; assessment and mitigation.

5. Quality management

External quality assessment for the molecular diagnostics of Influenza virus A and B

Supervisor: Mia Brytting, Eva Hansson-Pihlainen

An EQA for molecular detection and characterization of circulating influenza viruses is yearly performed by the diagnostic laboratories in Sweden. By monitoring the standard of diagnostic performance, this EQA plays a key role in strengthening national diagnostic capacity for influenza virus. Participating laboratories receive a panel of 10 representative influenza specimens (influenza A and B), which they identify and subtype using their RTqPCR assay of choice.

A total of 19 laboratories participated in the EQA. The result of the EQA showed that all laboratories identified the correct influenza clade in at least one assay. Subtyping of influenza linages is not obligatory but was performed successfully by all laboratories that attempted to do so except one laboratory one sample that was not correctly identified in one laboratory. No false positive results were reported.

In conclusion, the overall result of this panel indicated that the laboratories in Sweden were well prepared for the coming influenza season.

The fellow evaluated and summarized the results, made improvements to the reporting format, and wrote parts of the report of the 2018 influenza EQA.

Information on the proficiency of Swedish laboratories for detection of anti-rubella IgM antibodies, 2018

Supervisors: Hélène Englund

The elimination of rubella in the WHO European Region is a target formulated by the WHO Regional Office for Europe. To aid the process of verification of successful rubella elimination in Sweden, the fellow gathered the evidence showing proficiency of Swedish laboratories in the testing for anti-rubella IgM and IgG antibodies.

The national reference laboratory for rubella diagnostics in Sweden is run at PHAS and is also accredited by WHO. However, all primary diagnostics for anti-rubella IgM, indicating acute infections, is performed by five of the regional laboratories in the country. Anti-rubella IgG analyses, indicating past infections or successful vaccination, are performed at other laboratories in the country as well. All five laboratories perform both IgG and IgM analyses using commercially available methods, but on different platforms. Some laboratories use more than one platform. The antirubella IgG tests in all five laboratories are accredited by Sweden's national accreditation body (the Swedish Board for Accreditation and Conformity Assessment, SWEDAC), and the anti-rubella IgM tests are accredited by SWEDAC in three of the five laboratories. All laboratories undergo regular external quality assessments for at least one of the two tests (EQA). Demonstrating proficiency of laboratory anti-rubella IgM testing for diagnostic purposes corroborates proficiency and suggests little performance bias between laboratories. It also indicates that quality indicators for surveillance are met. Use of standard operating procedures, attending EQA panels and accreditation of tests at the laboratory strongly support proficiency.

This project was a collaboration with the EPIET fellow Soledad Colombe of cohort 2018 and both fellows wrote a study proposal and performed all steps of the project including survey design, data collection, data cleaning and verification, data analysis and interpretation and writing the final report. The report is published as Annex to the annual report on measles and rubella surveillance.

Increasing the knowledge of diagnostic algorithms for vibriosis in Sweden, 2018

Supervisors: Cecilia Jernberg, Anette Hansen, Marika Hjertqvist

Sweden employs a passive vibriosis surveillance system. In preparation of a multi-country collaborative project on vibriosis in 2018 in the Nordic countries and countries bordering the Baltic Sea, a survey on vibriosis diagnostics was conducted in Sweden. This survey assessed the sample types analysed for vibrio bacteria and the methods used in the laboratories to identify and subtype vibrio in these samples and was sent by the fellow in parallel to the call for isolates for that project.

Thirteen laboratories replied to the questionnaire (13/24, 54%). Sample types from which the agent can be isolated in the respective laboratories included wound secret (12/13), blood/serum (11/13), ear secret (12/13), likvor (10/13), urine (9/13), other secrete (12/13), faeces (11/13) and other (7/13). All laboratories subtyped the species using at least MALDI-TOF. Isolates were saved after isolation for different periods: not at all (4/13, 31%), up to one year (3/13, 23%) or more than one year (6/13, 46%). One laboratory that does not save samples at all would save it still if it was an invasive isolate PCR based panels including probes for *Vibrio* spp. were used for species identification in 2/13 (15%) of the laboratories. Of not, as of now, only isolation of the agent but not a positive PCR test is included in the case definition for a confirmed case in Sweden, this case definition is being updated. A third laboratory would use a PCR panel during outbreak investigations if necessary.

The fellow created the methodological questionnaire of laboratory testing algorithms regarding vibrio infections and analysed the data.

Training modules

The Biosafety and Quality management module was cancelled.

Educational outcome: Understand the principles and practices of quality assurance; apply the concepts of external quality assurance (EQA); evaluate results of an EQA; assessment of laboratory methods to improve surveillance and diagnostics procedures; Understand importance of quality control and quality management programmes to ensure day-to-day laboratory consistency and to be able to produce accurate and reliable results for use in diagnostics, surveillance and research; application of bacteriology concepts to the public health discipline; understanding the use and limitations of typing methods and their interpretation.

6. Teaching and pedagogy

Importance of AMR as PH threat: The example of carbapenemase resistant Enterobacteriaceae

A four-hour lecture on AMR of Enterobacteriaceae was prepared and delivered by all EUPHEM fellows. This teaching assignment was carried out during the introductory course on Spetses. Target audience were the fellows themselves, the tutor and facilitators. Topics included a general introduction on AMR and Enterobacteriaceae and PH importance of the subject, followed by carbapenem resistance, mechanisms of action and spread of resistance. Furthermore, phenotypical, PCR and sequencing assays for detection and molecular epidemiology were introduced. The knowledge of participating fellows was assessed before and after the activity to evaluate the activity.

Polio eradication and endgame strategy and polio surveillance at PHAS

The fellow prepared and conducted a 1h lecture on poliovirus and poliomyelitis for PH specialists from Mozambique during their 2-week site visit to PHAS. The lecture was an introduction on poliovirus, poliomyelitis, the Global Polio Eradication Initiative and the Eradication and Endgame Strategy as well as the laboratory surveillance of poliovirus infections as part of the enterovirus surveillance in Sweden.

Teaching activity "Introduction to surveillance and outbreak investigation" for Södertörn University master students

This teaching activity was planned and carried out by Soledad Colombe and Maximilian Riess, the EU-track EUPHEM and EPIET fellows at PHAS. Participants were master students of the course "Infectious Disease Control" from Södertrön University. The director of the course contacted the fellows with specific requirements on what needed to be taught. Material from previous years existed (power point slides and a case study) which the fellows amended and updated. Additionally, activities included pre-course preparations, conducting the lectures and case study and collecting feedback via the course evaluation. Moreover, a timeline was prepared and additional handouts were created.

The program started off with a short presentation of PHAS followed by two hours of teaching in the morning and one hour in the afternoon: one lecture for surveillance, one for outbreak investigation and one for microbiological investigations. The first two were taught by Soledad Colombe while the third lecture was taught by the fellow. Each lecture was building on the previous one, to remind the students of the previously seen concepts. The teaching sessions were very interactive and encouraged the students to participate, which they did very well.

A summary sheet about the ten steps of an outbreak investigation and how to calculate ORs and IRs was prepared as extra material and handed out to them at the end of the lectures so that they could re-use it during the casestudy. In the afternoon, the class was divided into two groups and each of the fellows facilitated the case study (an outbreak investigation of cryptosporidiosis). The teaching activity was evaluated afterwards and received very good feedback.

Facilitation of an outbreak investigation case-study for 5th year veterinary students

A case-study on 'An outbreak of Trichinosis in France' was facilitated two times for 5th year veterinary students as part of their course 'Veterinary public health with applied epidemiology and epizootiology'. This included pre-course preparations, conducting the case study and collecting feedback via the course evaluation. Group sizes were about 10 students in each group and one session was conducted in the morning and one in the afternoon.

The case study was provided and extra material on how to construct a 2x2 table and the formulas for relative risk and odds-ratio, the ten steps of an outbreak investigation and exemplary epidemic curves for different types of sources was prepared by the fellow. During the case-study, students calculated ORs and drew an epidemic curve in smaller groups of 2-3 and shared with the whole group on a white board. The case study was split in four parts, which were handed out to the students in four injections one after the other. A thorough evaluation was done at the end of the complete course and a quick feedback of the participants indicated that they found the case-study very interesting and felt they have benefited from participating.

Facilitation of an outbreak investigation case study for EPIET/EUPHEM fellows

During the outbreak investigation module in Berlin, in December 2018, the fellow facilitated together with EUPHEM fellows Carina Brehony and Daniel Thomas López and Erik Alm as ECDC expert a case study on 'An outbreak of hepatitis A in Europe'. This included pre-course preparations, conducting the case study and collecting feedback via the course evaluation.

The three facilitators were invited to this task by Silvia Herrera Leon in advance to the outbreak investigation module in Berlin. A first planning session took place during ESCAIDE2018 in Malta with, who is one of the original authors of the case study.

The teaching activity was carried out together with Erik Alm, an ECDC expert on WGS, who lead the plenary parts. The facilitators engaged in the working phases with the fellows to give advice and clarify the current objectives or tasks.

Training modules

The three weeks **'Introductory Course'** of the fellowship included an introduction on different learning styles and ways of learning and pedagogical styles in education for adults. The one-week module on **'Management, Leadership and Communication in Public Health'** included interactive sessions on communication and presentation strategies and techniques how to lead, communicate with and motivate effectively different personality and learning styles.

Educational outcome: Identify training needs in a particular target group; defining learning objectives; plan and organize training events; give lectures applying didactic/pedagogical techniques; moderate case studies; preparing lecture material; delivering lectures to university students and public health professionals; facilitating group work around case studies; use diverse pedagogical techniques to stimulate learning; plan and conduct evaluation of training.

7. Public health microbiology management

Public health microbiology management during projects and activities

General public health microbiology management was central component of all projects and activities during the fellowship. For all projects, the fellow described the benefit to PH and was engaged in scientific communication to peers and stakeholders. All projects required careful ethical and integrity considerations, in particular the outbreak investigations, and projects on HAV, rubella, and vibriosis during which the fellow handled and analysed case data. The fellow acquired team building and negotiation skills by working as a team member during the outbreak investigations and COVID-19 pandemic response and the importance of communication between teams and maintaining a consensus- and results-oriented attitude has been emphasised throughout the fellow's work. National and international collaborations during the fellowship such as the outbreak investigations, COVID-19 response work, the vibriosis project and the EU/EEA survey demanded effective and skilled communication with experts from various disciplines from regional laboratories, national agencies, and within the ECDC project also with the EU/EEA member states. The project-based nature of the fellow's work demanded a high flexibility, and trained time management and organisational skills and the abilities to prioritise, to produce high quality deliverables and collaborate with disciplines across PHAS and internationally. Interdisciplinary work was required in different aspects during all national projects the fellow was working alongside epidemiologist and microbiologist from different departments. Especially during outbreak investigations, the fellow was part of multidisciplinary teams consisting of epidemiologists, laboratory technicians, local health authorities, physicians, statisticians, food safety specialists, and/or bioinformaticians.

Training modules

The fellow acquired valuable knowledge and experience in this core competency in the **'Management, Leadership** and **Communication in Public Health'** module. The covered content is outlined above (1.1). Moreover, the oneweek module on **'Rapid Assessment and Survey Methods'** was a very relevant interactive course including sessions on rapid risk assessments and practise thereof as well as rapid health assessment in complex emergency situations (CES).

Educational outcomes: Apply the rules of local, national and international organisations involved in infectious disease control; coordinate response through use of communication mechanisms and other tools; understand team management; understand time management; working in a multidisciplinary public health team; recognising the role of different agencies; plan, schedule and organise research projects; organise and participate in meetings; give and accept feedback; communicate through scientific writing and oral presentations.

8. Communication

Publications

*shared first authorship

- Espenhain L*, Riess M*, et al. Cross-border outbreak of Yersinia enterocolitica O3 associated with imported fresh spinach, Sweden and Denmark, March 2019. Eurosurveillance [Internet]. 2019 Jun 13 [cited 2020 Jun 9];24(24). Available from: https://www.eurosurveillance.org/content/10.2807/1560-7917.ES.2019.24.24.1900368Text
- 2. **Riess M**, Enkirch T, Sundqvist L, Lundberg Ederth J. High impact of molecular surveillance in hepatitis A outbreak case detection in Sweden a retrospective study 2009 2018. Eurosurveillance. Accepted
- 3. Amato E*, **Riess M***, Thomas-Lopez D*, Linkevicius M*, et al. Vibriosis in Northern Europe: an emerging public health threat? *In preparation*
- 4. Amato E*, **Riess M***, Thomas-Lopez D*, Linkevicius M*. Technical report: National surveillance systems for vibriosis and Shewanella spp. infections in EU/EEA countries. ECDC. *Under clearance*

Reports

- 1. National outbreak of *Salmonella enteritidis* MLVA 2-10-7-3-2 in Sweden, 2018. Colombe S., Riess M.
- 2. Swedish investigation of the cross-border outbreak of *Yersinia enterocolitica* O3 associated with imported fresh spinach, Sweden and Denmark, March 2019. Riess M., Colombe S
- 3. Estimation of the number of suspected but discarded cases of acute rubella in Sweden, 2018. Colombe S, Riess M, Englund H
- 4. Collection and whole genome sequencing of *Vibrio* spp. isolates causing vibriosis, Sweden, 2018. Laboratory investigation report. Riess M
- 5. Rise of vibriosis in a heatwave year, Sweden, 2018. National epidemiological report. Riess M
- 6. Report: Biosafety round in BSL-2 laboratory, PHAS, Sweden, 2019. Riess M
- 7. Conference report: Regional conference of the polio laboratory network and poliovirus containment. Riess M
- 8. External quality assessment scheme EQUALIS for influenza A and B typing, Sweden, 2019. Robertsson KD, Brytting M, Riess M
- 9. COVID-19:
 - a. COVID-2019 omvärldsbevakning (Daily situation report; 3 March 16 April 2020)
 - b. Scientific evidence summary: Asymptomatic transmission of COVID-19 (Mid-April 2020)
 - c. Scientific evidence summary: Summary ongoing seroprevalence studies (until 8 June 2020)
 - d. Scientific evidence summary: Literature compilation on PCR positivity (13 May 2020)
 - e. Guidance document: Period of infectiousness of COVID-19 cases (15 May 2020)
 - f. Review for Sweden of the WHO/EURO document on: "Social and Physical Distance Measures Implemented in Europe to Slow the Spread of COVID-19"
- 10. Validation of the whole genome sequence based antibiotic resistance analysis pipeline for vancomycin resistant enterococci, Riess M
- 11. Generation of whole genome sequences of 200 B. pertussis isolates from 2008-2019, Sweden, Riess M

Conference presentations

Presenting author underlined.

- 1. <u>Riess M</u>, Enkirch T, Sundqvist L, Lundberg Ederth J. 'The role of molecular surveillance in HAV outbreak detection in Sweden a retrospective study 2009 2018' ESCAIDE2019, Stockholm, Sweden. November 2019
- 2. <u>Espenhain L</u>*, Riess M*, et al. Cross-border outbreak of *Yersinia enterocolitica* O3 associated with imported fresh spinach, Sweden and Denmark, March 2019. ESCAIDE, Stockholm, Sweden. November 2019
- 3. <u>Riess M</u>, Rizzardi K, Edquist P. Comparison of phenotypic and genotypic antimicrobial susceptibility testing of VRE and CRE isolates in Sweden, 2016-2018. ESCAIDE, online. November 2020
- 4. <u>Amato E</u>*, Riess M*, Thomas-Lopez D*, Linkevicius M*, et al. Vibriosis in Northern Europe: an emerging public health threat? ESCAIDE, online. November 2020
- 5. <u>Beser J</u>, Kuhlmann-Berenzon S, Galanis I, Riess M, Rehn M, et al. Seroprevalence for SARS-CoV-2 and associated factors in the Rinkeby-Kista district of Stockholm, Sweden, 22-24 June 2020 ESCAIDE, online. November 2020

Other

1. EUPHEM representative of cohort 2018: spokesperson and point of contact for fellows, the ECDC Fellowship programme heads, the training site forum, and the EPIET Alumni Network (EAN)

- Riess M., Linkevicius M., Angermeier H., Gonçalves P., Amato E., Thomas-Lopez D., Brehony C., Johansen T., 'Importance of AMR as PH threat: The example of carbapenemase resistanct Enterobacteriaceae' EUPHEM PBL (Introductory Course). 05 October 2018 lecture 2x1.5h min
- Riess M., 'Polio Eradication and Endgame Strategy and the Swedish laboratory surveillance of poliovirus' Public Health Agency of Sweden. 19 October 2018 – lecture 30 min
- 4. Riess M., 'Microbiology in Surveillance and Outbreak investigations' Lecture to master students of Södertörn University. 20 February 2019 lecture 45 min
- 5. Riess M., 'Introduction: what is the EUPHEM program?' Microbiology seminar at the Public Health Agency of Sweden. 20 September 2019 lecture 10 min
- Riess M., 'The role of molecular surveillance in HAV outbreak detection in Sweden a retrospective study 2009 – 2018' Microbiology seminar at the Public Health Agency of Sweden. 20 September 2019 – oral presentation 30 min
- Riess M., 'The role of molecular surveillance in HAV outbreak detection in Sweden a retrospective study 2009 – 2018' The Nordic Mini Project Review Module, Copenhagen, Denmark. 12 March 2019 – oral presentation 15 min
- Riess M., Colombe S., 'Evaluation of a surveillance system in the context of national elimination: the case of Rubella' The Nordic Mini Project Review Module, Copenhagen, Denmark. 12 March 2019 – oral presentation 15 min
- 9. Riess M., 'The role of molecular surveillance in HAV outbreak detection in Sweden a retrospective study 2009 2018' Project Review Module, Prague, Czechia. 28 August 2019 poster presentation 10 min
- 10. Riess M., 'Country update Sweden: Multi-country occurrence of Vibrio infections other than cholera in Nordic countries in 2018' Project Workshop, Oslo, Norway, 9 September 2019 oral presentation 30 min
- Riess M., Beser, J., Fischer N., 'The future of EPIET/EUPHEM' Presentation to the Director of ECDC during the Management, Leadership, and Communication in Public Health Module, ECDC, Stockholm, Sweden. 14 February 2020 – oral presentation 15 min
- 12. Riess M., 'Comparison of WGS based ABR prediction with AST data of VRE and ESBL isolates from recent years in Sweden' The Nordic Mini Project Review Module, Copenhagen, Denmark. 6 March 2020 oral presentation 15 min
- 13. Revision of a manuscript.
- 14. Revision of the WHO EURO report "Social and Physical Distancing Measures Implemented in Europe to Slow the Spread of COVID-19" on behalf of PHAS, Department of Communicable Disease Control and Health Protection.

Training modules

The one-week module on **'Management, Leadership and Communication in Public Health'** included interactive sessions on communication and presentation strategies and techniques and importance of public relations. The fellow gained important experience in communication with higher authorities and communication in emergency situations to experts and the public. Furthermore, the course covered different management styles, team roles and evolution of team, the delegation of tasks, personality types and learning and motivating styles.

Interactive sessions also taught on the provision of structured feedback and tools for effective time as well as stress management.

Educational outcome: Communicate effectively with scientific experts from a multidisciplinary background, authorities, the public and the media in the form of publications, reports, interviews, and oral presentations; communicate through scientific writing and oral presentations.

9. EPIET/EUPHEM modules attended

- 1. EPIET/EUPHEM Introductory Course, Spetses, Greece, 24 September 12 October 2018
- 2. Outbreak Investigation Module, Robert Koch-Institut, Berlin, Germany, 3 7 December 2018
- 3. Multivariable Analysis Module, Instituto de Salud Carlos III, Madrid, Spain, 25 29 April 2019
- 4. Rapid Assessment and Survey Methods Module, School of Public Health, Zagreb, Croatia, 13 18 May 2019
- Project Review Module, Institut postgraduálnIho vzdělávánI ye zdravotnictv (IPVZ), Prague, Czechia, 26 30 August 2019
- Management, Leadership, and Communication in Public Health Module, ECDC, Stockholm, Sweden, 10 14 February 2020
- 7. Vaccinology, online, 4 May 24 June 2020, online.
 - a. Institute Pasteur, SPOC (Small Private Open Course), 4 May 12 June 2020, online
 - Rijksinstituut voor Volksgezondheid en Milieu (RIVM), facilitated sessions, 22-24 June 2020, webinar.

10. Other training

- 1. On-site visit to ECDC Emergency Operations Centre (EOC). Introduction to the EOC. 16 October 2018 1 hour
- 2. Swedish language classes up to level B1+.
- Qualifications for the use of PSS DNA/RNA extraction robots (PSS MagLEAD; Bruker) and pipetting robots (QIAgility; Brand), RTqPCR device (StepOnePlus)
- 4. Introduction to GDPR in 11 modules. In-house online course 11x15min
- 6. Nordic Project Review Module, Copenhagen, Denmark 11 12 March 2019. Module with feedback from Nordic expert on scientific projects in order to ensure meeting of EPIET / EUPHEM standards. 2 days
- 7. Nordic Public Health meeting, PHAS, Sweden, 23 September 2019, 0.5 days
- 8. Nordic Project Review Module, Helsinki, Finland 5 6 March 2020. Module with feedback from Nordic expert on scientific projects in order to ensure meeting of EPIET / EUPHEM standards. – 2 days
- 9. Introduction to Next-generation sequencing, Stockholm, Sweden, 21 April 2020 2.5 hour
- 10. The Global Outbreak Alert and Response Network (GOARN), online course, 10 May 2019 1.5 hour
- 11. Working with GOARN in the Field, online course, 11 May 2019 1.5 hour
- 12. Introduction to R course. EPIET Alumni Network and Recon. ECDC, Stockholm, 25-26 November 2019. 2 days
- 13. EPIET/EUPHEM meetings at PHAS. The weekly meetings on epidemiological and microbiological aspects of their projects were organized by fellows and supervisors.

Discussion

Coordinator's conclusions

One of the main goals of the EUPHEM programme is to expose the fellows to different public health experiences and activities, thus enabling them to work across various disciplines. This report summarises all activities and projects conducted by Maximilian Riess during his two-year EUPHEM fellowship (cohort 2018) as an EU track fellow at the Public Health Agency of Sweden. The portfolio includes laboratory and epidemiological projects covering viral, bacterial and parasitic pathogens across a variety of disease programmes, according to the matrix portfolio of EUPHEM. The projects here described are in line with the 'learning by doing' approach of the EUPHEM programme and fulfilled the core competency domains described for professionals in their mid-career and above. During the twoyear fellowship, the fellow, supervisors and training site have demonstrated the capability of addressing communicable disease threats in a structured joint approach between public health microbiology and epidemiology such as rubella project where Max together with EPIET fellow worked closely to address a public health problem. It is important to mention that Max has not only contributed to project at national dimension but also has been involved in cross border project, (Sweden and Denmark serotype O3 (ST-18) Outbreak) as well as European collaborative project on multi-country occurrence of non-toxigenic cholera and non-cholera Vibrio infections in Nordic countries and countries bordering the Baltic Sea in 2018. Max has been active in contributing to training of others during his fellowship with the development of new training materials as well as direct training and facilitation activities which highlights the contribution that fellows can make to capacity building beyond the programme. It is of huge importance to emphasise that Max contributed to COVID-19 pandemic response by production of knowledge base documents and contribution to national guidelines on period of infectiousness for different situations and review response to a WHO report, hands on laboratory diagnostic in the sentinel surveillance program, take part in the planning and design of a seroprevalence study and following a bi-weekly joint ECDC and WHO/Europe online meeting. Max has shown great ability in working in a multidisciplinary team handling complex tasks in addition to his planned projects of the fellowship. All projects had a clear outcome, with results communicated in scientific journals and at conferences and the activities were complimented by nine training modules providing theoretical knowledge. The contributions made by Max indicate the importance of developing and maintaining a critical mass of highly competent public health microbiologists within Member States to contribute towards national preparedness as well as being available for responses in the interest of the EU. The EUPHEM Coordinator Team concludes that the fellow has succeeded in performing all his tasks to a very high standard and has conducted himself in a highly professional and effective manner throughout. Without any doubt Max will be an excellent future leader in PHM that he already demonstrated during his fellowship. We wish the fellow every success in his future career.

Supervisor's conclusions

The EUPHEM programme was a great opportunity for Maximilian and has provided him with many tools to make his way in the field of public health microbiology and epidemiology. It has been a pleasure to mentor Maximilian for the past two years and it has been wonderful to see him develop within the programme and acquire many new skills. His projects covered all core domains within the EUPHEM programme and showed that he was able to work on all these projects independently. His scientific knowledge and goal-oriented personality, along with his open-mindedness, positivity, and excellent communication skills was very much appreciated by supervisors and colleagues.

Maximillian's work contributed in many ways to the agencies mission to strengthen and develop public health and his commitment was not only but definitely especially appreciated during the global Covid-19 pandemic.

It was a great pleasure to work with Maximilian at the Public Health Agency of Sweden and we highly appreciate his contribution and achievements within the fellowship programme and the host institute. We wish Maximilian every success for the future and his future career.

Personal conclusions of fellow

Two years in the EUPHEM program reached their end and I look back very satisfied both with my professional development and my achievements. I am grateful for this remarkable opportunity; this program cannot be compared with anything else for its character is unique. The combination of tailored opportunities to gain broad knowledge and expertise in a learning by doing fashion and structured learnings delivered in the form of modules was excellent and suited my personality and needs. This approach allows to cater to the fellows' needs individually allowing independence, freedom to develop and guidance in a well-balanced fashion. It allowed me to grow most in those core competencies which were of the highest interest to me. I could not deploy to the mission with GOARN that I was offered, which I certainly regret, because I believe these international missions are a very valuable part of the program and provide insights that one does only gather in the field.

I was extremely motivated to let EUPHEM be my transitioning from academic research to public health functions and I am convinced this is what I achieved. My training site, the Public Health Agency of Sweden, was very well organised, provided a broad variety of project opportunities and a very welcoming atmosphere across the whole agency which made it easy to get in touch with experts for each task and work closely together. The program does not produce specialists for specific pathogens but it rather creates generalists in the sense that we all deepened our knowledge in a broad range of disease groups and trained to quickly understand a new topic and successfully navigate it. Personally, this is how I understood my past two years of EUPHEM and how I feel I benefitted most of it.

Beyond strengthening the core competencies of public health microbiology and field epidemiology, this program creates a European network of professionals that speak the same language in terms of technical vocabulary. This harmonisation and the personal connections will prove highly valuable in my future career for public health.

Acknowledgements of fellow

During the past two years I had the opportunity to work together with remarkable mentors and friends. I would like to take this opportunity and express my gratitude towards them. First and foremost, I would like to thank ECDC for accepting me into this program and the Public Health Agency of Sweden for welcoming me as a EUPHEM fellow. My thanks go to my local training site supervisor Katherina Zakikhany, for her mentoring, kind engagement and support in all my activities. My warmest thanks also to my ECDC frontline coordinators Frantiska Hruba and Aftab Jasir, who have always been available with counsel, an outside perspective and invaluable advice. A special thank you to Mia Brytting for her constant support and guidance and to her whole unit for welcoming me so kindly and warmheartedly, it was always a pleasure to see everyone at work. I would like to extend my appreciation to all the experts that I had the opportunity to work with in my projects and to Moa Rehn, who was always available to support and give guidance on my professional development in public health epidemiology. It was a pleasure to work with you all and I am grateful for the time you spend with me, your patience and the knowledge you shared.

Thank you to the EPIET/EUPHEM family at the agency for sharing your impressions and advice. My heartfelt and special recognition to Soledad Colombe, my fellow EPIET companion in Stockholm. Not only did we begin this journey together but you were a great inspiration to me throughout the fellowship.

I am also thankful to all the other fellows of cohort 2018, I am honoured to have shared this remarkable two years with you. We learned together, we had fun together, we suffered together from the start through a medicane on Spetses and concluded our fellowship with the beginning of a global pandemic sharing our experiences in real time across Europe. I treasure the memories we share and hope there are many more to come. Ettore, Marius, Daniel, my fellow EUPHEMs in the Nordics, I am truly thankful we met and work together.

As a representative of the cohort 2018, a bit of extra work came my way but I would never have stood a chance without my fellow representatives, Sonia Boender and Ettore Amato, thank you for all your energy and dedication.

Lastly, I cannot forget to thank my dear family and partner who supported me in all my decision and held out the two years with and without me.