# EUPHEM



## **EUPHEM** REPORT

## Summary of work activities Marius Linkevicius 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.

This report summarises the work activities undertaken by Marius Linkevicius, cohort 2018 of the European Public Health Microbiology Training Programme (EUPHEM) at the Finnish Institute for Health and Welfare (THL), Helsinki, Finland. 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.

The views expressed in this publication do not necessarily reflect the views of the European Centre for Disease Prevention and Control (ECDC).

## **Pre-fellowship short biography**

Prior to joining the EUPHEM programme, Marius worked as a researcher in the antibiotic resistance development field at Uppsala University, Sweden, where he had obtained his PhD degree in Medical Sciences. A wish to broaden the horizon beyond academia and to contribute to solutions of health problems brought Marius to the public health sector and EUPHEM. He was particularly interested in gaining experience in public health microbiology and intervention epidemiology with practical skills in outbreak investigation, infectious disease surveillance, laboratory quality and biorisk management, as well as leadership and communication in 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 guide<sup>1</sup>.

### 1. Epidemiological investigations

#### 1.1. Outbreak investigations

Supervisors: Lotta Siira, Jussi Sane

#### *Outbreak of invasive pneumococcal disease among shipyard workers, Turku, Finland, May to November 2019*

On 3 October, Turku University Hospital alerted THL about seven *Streptococcus pneumoniae* (pneumococcus)positive blood cultures among pneumonia patients with a link to a shipyard in Turku. After confirming an increase in invasive pneumococcal disease (IPD) cases in the region, we declared an ongoing IPD outbreak at the shipyard and formed an outbreak control team to investigate and contain it.

A confirmed outbreak case was defined as an individual who had worked at the shipyard after 1 February 2019 and presented with a clinical diagnosis consistent with IPD or pneumococcal pneumonia and had pneumococcus isolated from blood or cerebrospinal fluid (CSF) or pneumococcal antigen detected in urine. If there was no laboratory confirmation, the case was defined as probable.

We identified 31 confirmed and six probable cases between 3 May and 28 November 2019. We interviewed 25 of the 37 cases and the majority of them were current smokers, mostly without underlying conditions, working on the final stages of ship outfitting with no common activities outside work. Thirty confirmed cases had been hospitalised and treated for septic pneumococcal pneumonia and one case died from pneumococcal meningitis. Additionally, six probable cases were treated at a hospital within the same period. Pneumococcal isolates were available for 25 confirmed cases. We identified serotypes 12F (n=13), 4 (n=11) and 8 (n=1) and analysed 17 isolates by whole genome sequencing (WGS) to determine the multilocus sequence typing (MLST), core and accessory genome MLST profiles. Three sequence types (STs) were observed: ST6202 (serotype 12F, n=9), ST801 (serotype 4, n=7) and ST1480 (serotype 8, n=1). Genomes of isolates of the same serotype were similar with  $\leq$ 4 allelic differences within serotype 4.

On 16 October, we decided to implement vaccination and promote hygiene measures to control the outbreak. Additionally, we encouraged the use of respiratory protective equipment for those exposed to metal fumes and inorganic dust. Since 17 October, vaccination with pneumococcal polysaccharide vaccine (PPV23), covering all

<sup>&</sup>lt;sup>1</sup> 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

three detected serotypes, and seasonal influenza vaccine were offered at the shipyard by the shipyard management and the local health authorities. The target group of over 4,000 employees who worked on the final stage of ship outfitting were vaccinated and the outbreak was controlled.

We hypothesized that the risk of IPD at the shipyard was affected by the combination of working conditions (e.g. parallel tasks in close proximity with exposure to metal fumes and inorganic dust without personal protective equipment in poorly ventilated or draughty conditions) and personal habits (e.g. heavy smoking). Therefore, we recommended the shipyards to assess the risk of tasks and working conditions to identify effective preventive strategies and to implement the necessary hygiene measures to ensure protection of the employees from occupational infectious disease hazards.

The fellow participated in all stages of the outbreak investigation, from contributing to designing questionnaires, conducting interviews, collating and analysing the data, providing situation updates, to writing and publishing the final outbreak report as a first-author article.

#### **Training modules**

The fellows received training during the *ECDC Fellowship Introductory Course* on topics such as proposal of public health recommendations during outbreaks, application of basic statistics on epidemiological/laboratory data analysis, examination of associations between exposures and outcomes, controlling for biases, confounders and effect modifiers as well as communication of results to different stakeholders.

The ten steps of outbreak investigation were presented during the *Outbreak Investigation Module* and the fellows learned about questionnaire design, data collection and management, descriptive and univariate analyses, statistical tests and their interpretation, analytical study designs including cohort and case-control studies with stratified analysis. Additionally, molecular typing methods and phylogeny as well as mapping of cases were presented. Epidemiological and microbiological software, such as EpiData Manager and Entry Client, Stata, QGIS, SSE and MEGA, were applied during computer exercises and case studies.

The principles of multivariate analysis and its different types (linear, logistic, Poisson, Cox, multilevel) were introduced during *Multivariable Analysis Module*. Computer exercises and case studies using Stata and R helped the fellows to identify relevant variables for optimal regression model building as well as to control for confounding and effect modification at the analytical level.

The *Management, Leadership and Communication in Public Health Module* provided practical skills for team building and effective communication during crisis as well as task prioritisation and time management under pressure.

The fellows were introduced to effective control strategies during the vaccine preventable disease outbreaks during the *Vaccinology Module*.

**Educational outcome:** the fellow was actively involved in all outbreak investigation steps undertaken by the multidisciplinary outbreak control team, gained deeper knowledge about ten steps of outbreak investigation and applied epidemiology and microbiology skills trained during the above-mentioned modules. Fellow's contributions included case definitions, questionnaire design, case interviews by phone, data collection and management of a dynamic line list, descriptive statistical data analysis, situation reports to the stakeholders, internal roundtable updates during weekly outbreak meetings, participation in the field trip of the outbreak grounds, the interpretation of microbiological typing and WGS data, writing outbreak report and coordinating the publication of the report in a peer-reviewed journal as a first author.

#### 1.2. Surveillance

Supervisors: Carita Savolainen-Kopra, Soile Blomqvist, Outi Lyytikäinen, Johanna Takkinen, Aftab Jasir

#### Non-polio enterovirus surveillance in Finland, 1995-2019

Viral meningitis has become a leading cause of central nervous system infections in children, with up to 47% accounted for by enteroviruses (2007-2011). THL was interested in improving the existing non-polio enterovirus (NPEV) surveillance in order to ensure effective and timely detection of emerging NPEVs in Finland to be able to implement control measures. The aim of this project was to describe the NPEV surveillance using the notification data from the Finnish National Infectious Disease Register (NIDR) in order to determine, if severity of NPEV infections can be inferred from the current surveillance, and to recommend surveillance improvements, if severity cannot be predicted.

Enterovirus surveillance in Finland is based on monitoring poliovirus. Healthcare services (general practitioners and hospitals) send samples to clinical microbiology laboratories for diagnostics. The laboratories are obliged to report all enterovirus findings to the NIDR. However, the deposition of typing results is not mandatory. If the positive enterovirus finding is registered for the stool sample, the laboratory must send the sample to Enterovirus Reference Laboratory at THL for typing under the Communicable Diseases Act and Decree. Currently, clinical information about enterovirus infections is not collected in NIDR. We used NIDR for a retrospective descriptive analysis of 5,074 NPEV (excluding rhinoviruses) laboratory notifications reported during 1995-2019.

During the past 25 years, infants below the age of 2 years were the most NPEV-affected age group in Finland. Laboratory positive findings were mainly reported from three healthcare districts (Southwest Finland, 30%; Helsinki and Uusimaa, 15%; North Ostrobothnia, 14%) during epidemic seasons occurring during July-December and peaking in September/October. Irregular waves of increased epidemic activity of NPEVs were observed during specific years, with the largest national outbreak caused by E30 registered in 2010. Only CSF was identified as a good proxy for severe NPEV infections. However, over 80% of NPEV-positive findings were diagnosed from samples other than CSF, which by themselves do not indicate a severe outcome. While specific NPEV types are not exclusively associated with severe disease, sometimes they can cause particular symptoms and severe infection. However, barely 1% of analysed notifications contained NPEV type information with only one typing result reported in the past ten years. Additionally, the absence of clinical information in the register further complicated any overall conclusions about severity of NPEV infections in Finland.

Due to current NIDR limitations mentioned above, severe NPEV cases could not be identified or estimated. Therefore, in order to better capture and monitor emerging and re-emerging NPEV threats to public health in Finland, we recommended supplementing laboratory notifications with standardised symptom details from attending physicians and improving the collection of typing information to NIDR by providing guidance to the reporting laboratories on how typing information should be deposited to the register.

The fellow was involved in all stages of this project, from planning, reviewing literature, analysing the data using R, to writing a final report, communicating the findings to the stakeholders and submitting a conference abstract.

## *Surveillance systems for vibriosis and Shewanella spp. infections in the EU/EEA countries, 2019*

In order to achieve an overview of countries in the European Union (EU) and the European Economic Area (EEA) who have or are planning to implement surveillance systems for vibriosis or for *Shewanella* infections, we conducted an online survey and disseminated it to the National Focal Points for Food- and Waterborne Diseases and Zoonoses (FWD) of the EU/EEA countries through the EPIS (Epidemic Intelligence Information System) FWD platform during September-October 2019. The main objective of the survey was to collect information about national surveillance systems on vibriosis (including all vibrios other than cholera toxin-producing *Vibrio cholerae* O1 and O139 as causative agents) and *Shewanella* spp. infections.

Twenty-four of 31 EU/EEA countries replied to the survey, response rate 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 had surveillance for vibriosis in place. The extent of surveillance activities varied from comprehensive mandatory notification of any type of vibriosis infection to more focused syndromic surveillance of food poisoning and gastro-enterocolitis. None of the other countries planned 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 with one additional EU/EEA country intending to introduce such a surveillance system within one year. The remaining EU/EEA countries had no plans to establish surveillance 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-López). The fellows collected and analysed the data and wrote a technical report on vibriosis and *Shewanella* spp. infection surveillance systems in EU/EEA for ECDC.

#### **Training modules**

During the *ECDC Fellowship Introductory Course* the fellows were introduced to surveillance definition and its types, ways of setting up surveillance systems and how to analyse and interpret surveillance data. Additionally, evaluation of surveillance systems using different attributes were discussed and practically applied during module activities.

Fellows were taught the basics of data cleaning and dataset management as well as data analysis using Stata and R during the *Outbreak Investigation Module*.

During the *Rapid Assessment and Survey Methods Module*, fellows were trained on how to plan and conduct a survey to address public health questions, how to analyse the results of surveys and use them to drive public health decisions. The fellows were also introduced to mapping software QGIS and KoBoCollect for mobile phones, which they used during practical exercises.

The *Management, Leadership and Communication in Public Health Module* provided a deeper understanding of indicator- and event-based surveillance during the Epidemic Intelligence Tutorial. Furthermore, the fellows were trained on communicating the information for action in an effective way to different stakeholders.

**Educational outcome:** the fellow developed understanding and experience on how to conduct the analysis and interpretation of existing laboratory surveillance data trends and formulate corresponding recommendations for the internal and external stakeholders. The fellow got acquainted to public health registers and acquired valuable skills

in QGIS and R during register data management and analysis. Furthermore, the fellow identified surveillance system gaps and learned how to provide constructive feedback on surveillance system improvements as well as write reports summarizing the findings of the analysed surveillance data.

### 2. Applied public health microbiology research

Supervisors: Saara Salmenlinna, Tarja Pitkänen

#### *Multi-country occurrence of vibriosis in the Nordic countries and countries bordering the Baltic Sea, 2018*

*Vibrio* bacteria are ubiquitous in aquatic and marine habitats. Non-toxigenic *V. cholerae* and non-*V. cholerae* vibrios cause self-limiting vibriosis, which can rarely lead to severe clinical presentation. In the last years, countries in northern Europe have witnessed an increase in *Vibrio* infections during heat waves, especially in 2018. We aimed to describe the epidemiology and 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.

We conducted a retrospective cross-sectional study using laboratory-based or passive surveillance data, analysing demographics, geographical distribution, seasonality and severity of vibriosis cases. Travel-related cases were excluded. Additionally, we investigated the relatedness of isolates by phylogenetic single nucleotide polymorphism (SNP) analysis of WGS data, which was also used to discover antimicrobial resistance, virulence and biofilm determinants present in the studied isolates.

We identified 445 vibriosis cases with median age of 52 years (range 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) age groups 65-79 (OR=3.7; 95% CI: 1.6-8.6) and 80+ years old (OR=14.6; 95% CI: 4.1-52.2), (ii) *Vibrio vulnificus* (OR=25.2; 95% CI: 4.3-147.5) and *Vibrio parahaemolyticus* (OR=3.4; 95% CI: 1.3-8.7) and (iii) summer season (OR=6.2; 95% CI: 2.8-13.6). Although phylogenetic analysis showed diversity between *Vibrio* isolates, two *V. vulnificus* clusters (<10 SNPs), one in Norway and one in Sweden, were identified.

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.

This project was a collaboration of four EUPHEM fellows (Maximilian Riess, Ettore Amato, Marius Linkevicius and Daniel Thomas-López). The fellow was a principal investigator of the project in Finland with contribution in equal terms to the design of the project, the drafting of research protocol, a conference abstract and the final manuscript. In addition, the fellow liaised between national stakeholders and international collaborators and facilitated interactions during collaboration as well as data processing agreement negotiations. Moreover, the fellow gathered the epidemiological information from the NIDR and coordinated the acquisition of WGS data of Finnish isolates with particular involvement in antimicrobial resistance analysis.

#### **Training modules**

The *ECDC Fellowship Introductory Course* provided training from designing, preparing and conducting applied research projects by combining field epidemiology and public health microbiology techniques to interpreting and communicating findings as well as formulating recommendations for public health action. Additionally, the fellows learned to formulate research questions and produce a research study proposal.

During the *Outbreak Investigation Module*, the fellows were introduced to the next generation sequencing technologies, basics of molecular phylogeny and bioinformatics analysis as well as WGS workflows and pipelines in public health. Additionally, the fellows were provided hands-on experience in analysing, visualising and interpreting WGS data using MEGA software during case studies.

The *Management, Leadership and Communication in Public Health Module* trained fellows in many aspects of management and collaboration including presentation of effective project proposals, time management, team building and collaboration, delivery of constructive feedback and presentations according to target audiences.

**Educational outcome:** the fellow actively participated in all aspects of operational research project, which included identifying knowledge gaps in public health, formulating a research question, performing a literature review, outlining a project proposal and writing a study protocol, identifying necessary laboratory methods and data analysis tools, collecting and analysing data using R, drawing conclusions as well as proposing recommendations and communicating them to the stakeholders. Furthermore, the fellow developed project management and administration skills as a principal investigator and project coordinator at the training site in Finland. Additionally, the fellow applied efficient communication and teamwork abilities during collaboration with other investigators of the study.

### **3. Applied public health microbiology and laboratory investi**gations

Supervisors: Niina Ikonen, Anu Haveri, Mia Kontio, Jussi Sane, Pamela Österlund

#### Human respiratory syncytial virus types A and B in Finland, 2010-2018

Human respiratory syncytial virus (RSV) causes acute lower respiratory tract infections in infants and elderly. The global burden of RSV caused acute lower respiratory tract infections is estimated to be around 33 million annual occurrences with 3 million hospitalisations and 59,600 in-hospital deaths in children younger than 5 years old. THL is preparing for the eventual introduction of RSV vaccine in Finnish population, therefore the aim of this project was to implement an RSV typing assay in order to describe the distribution of RSV types in Finland and provide information for RSV surveillance.

Quantitative reverse transcription polymerase chain reaction (qRT-PCR) is considered to be a sensitive and rapid method for RSV detection and typing in all age groups. We chose the variable RSV nucleoprotein gene for RSVA and RSVB type differentiation in a qRT-PCR-based assay using primers and probes courtesy of Statens Serum Institut, Denmark. We validated the implemented assay using five commercial RSV external quality assurance (EQA) panels from 2014-2018 (n=44). After validation, we typed all available RSV positive specimens (n=301) from 2010-2018. The collection consisted of influenza and other respiratory viruses sentinel (outpatients) and non-sentinel (hospitalized and intensive care unit (ICU) patients) surveillance specimens.

Assay sensitivity for detecting RSVA was 82% (14/17 positive specimens), and for detecting RSVB, 100% (21/21). Assay specificity was 100% for both types (6/6 negative specimens). In the typed collection, 187 specimens (62%) contained RSVB, 99 (33%) – RSVA and 3 (1%) – both viruses. Twelve specimens (4%) were negative. RSVB was the main type during 3/4 investigated RSV epidemic seasons (2011-2012, 2015-2016 and 2017-2018). Overall, RSVB dominated in males (96/155, 62%) and females (68/98, 69%) as well as in children, especially in the risk group of under 2-year-olds (76/105, 72%) and age group 10-19-year-olds (40/55, 73%). RSVB was also a leading type in outpatients (156/238, 66%), hospitalized (26/39, 67%) and ICU (8/15, 53%) patients.

The newly introduced RSV typing assay detected both RSV types. The typing results provided a first glance at baseline information for RSV surveillance in Finland between 2010-2018 with RSVB dominating in the screened collection. We recommended continuing the ongoing typing of RSV positive specimens to provide information on RSV type distribution for surveillance and a possible future vaccination programme. Additionally, to improve representativeness, we suggested increasing the number of collected RSV specimens, in order to enable population wide conclusions about RSV type circulation in Finland in the future.

As a principal investigator, the fellow participated in all steps of the project from planning, literature review, drafting of a project proposal, implementing and validating the assay in a laboratory, to using the assay as a tool to determine virus type variability, analysing the collected data, summarizing the findings and communicating the results in poster format in a conference as well as proposing recommendations.

#### Measles in twice MMR-vaccinated individuals in Finland, 2017-2019

Finland is facing the challenge of waning measles-mumps-rubella (MMR) vaccine-induced antibodies in the population, whose protection is dependent only on vaccination, as the exposure to wild-type measles virus (MV) is rare. Additionally, twice MMR-vaccinated individuals with insufficient protection can contract a mild form of measles with atypical symptoms, which may be overlooked by clinicians, or undiagnosed in the laboratory due to late, nonoptimal or insufficient samples. Lastly, geographical variation in vaccination coverage can present difficulties in the outbreak situation.

We performed a retrospective descriptive analysis of clinical and laboratory data from twice MMR-vaccinated measles cases to inform measles contact tracing guidelines in Finland. We extracted data on laboratory confirmed measles cases notified between 2017-2019 from the laboratory information management system (LIMS) and combined them with clinical information. We analysed available clinical symptoms, complications and laboratory (immunoglobulin (Ig) M and IgG levels, qRT-PCR cycle threshold (Ct) values, genotyping) data as well as we performed MV isolation in Vero/hSLAM cell cultures in order to predict possible MV transmissibility.

We grouped measles cases (n=31) into 15 unvaccinated, 8 vaccinated ( $\leq 2$  doses of measles containing non-MMR vaccines) and 8 twice MMR-vaccinated (both doses received in Finland). Unvaccinated and vaccinated groups were IgM positive, while twice MMR-vaccinated individuals were IgM negative. Additionally, vaccinated and twice MMR-vaccinated individuals were IgM negative. Additionally, vaccinated and twice MMR-vaccinated individuals were IgM negative. Median qRT-PCR Ct values showed an increasing trend at 26 (unvaccinated), 28 (vaccinated) and 32 (twice MMR-vaccinated) cycles, respectively. MV was successfully isolated only for the unvaccinated group (5/15). Clinical information systematically collected from five twice MMR-vaccinated cases showed that fever and rash were the only common symptoms, while conjunctivitis, coryza, Koplik's spots and cough were not consistently observed. None of these cases developed serious complications or required hospitalization and no secondary cases were reported among contacts of twice MMR-vaccinated cases during the study period in Finland.

Lack of documented secondary cases combined with negative MV isolations and indications of lower viral load observed in our small study population suggested that further measles transmission from twice MMR-vaccinated cases was unlikely. Therefore, we recommended limiting the resource-intensive contact tracing only to risk groups and close contacts in a country with high vaccine coverage for both MMR doses.

The fellow was involved in planning stages of the project, performing a literature review, becoming familiar with the laboratory methods and applying them in the laboratory, analysing, interpreting, and presenting the data as well as proposing recommendations and submitting an abstract to a conference.

#### The setup of a West Nile virus detection assay in the expert laboratory at THL, Finland

The peak circulation of West Nile virus (WNV) in EU was observed in 2018 with 1,605 annual cases. Additionally, WNV was detected as north as Berlin and both Slovakia and Germany detected their first autochthonous mosquitoborne WNV infections during the 2019 transmission season. Even though Finland has no past evidence of WNV circulation, anti-WNV antibodies were detected in mallards in 2006. Moreover, *Culex pipiens* is an established mosquito vector in Finland. The above-mentioned facts demonstrate the potential of WNV spread northwards. The aim of this project was to introduce a WNV detection assay into the routine procedures of THL in order to increase the diagnostic preparedness for the emerging pathogens in Finland.

qRT-PCR is considered to be a sensitive, specific and rapid method for WNV detection. We tested primers and probes from two previously published assays using routine PCR protocols of respiratory virus sentinel surveillance at THL. One of the primer/probe sets proved to perform well during the modified sentinel surveillance qRT-PCR protocol with higher annealing temperature. We chose this setup for further validation of the assay with the EQA panel from Quality Control for Molecular Diagnostics in the future.

This WNV detection assay complements the WNV diagnostics currently in place at a clinical microbiology laboratory at THL and allows confirming future importations of the virus into the Finnish population as well as detection of future autochthonous transmissions. Furthermore, it further strengthens molecular diagnostic capacity building for emerging vector-borne pathogens nationally and EU-wide and is an important contribution to the laboratory pre-paredness activities at THL.

The fellow planned the study, performed the literature review, drafted the project proposal, received training and independently applied the laboratory methods, produced a final report and communicated the findings at the training site on the implemented assay.

#### **Training modules**

During the *ECDC Fellowship Introductory Course* the fellows were introduced to microbial characterization methods and their relevance in public health laboratories. Additionally, the fellows learned how to identify key laboratory investigations and choose appropriate laboratory methods for suspected pathogen characterization.

The *Project Review Module* provided fellows with strategies of clear and targeted delivery of oral and poster presentations to the peers.

Communication techniques to different target audiences as well as time management while working on multiple projects were presented during the *Management, Leadership and Communication in Public Health Module*.

During the *Vaccinology Module*, the fellows were taught how to apply and evaluate appropriate control strategies in response to vaccine preventable disease outbreaks.

Even though the *Biorisk and Quality Management Module* was cancelled, the provided materials from previous years emphasised the importance of biorisk management and quality control during any laboratory investigation.

**Educational outcome:** the fellow gained valuable work experience in accredited laboratories, became familiar with workflows and standard operating procedures (SOPs) in pathogen diagnostics as well as learned to identify, implement, validate and apply suitable methods for public health microbiology and laboratory investigations. Furthermore, the fellow continued acquiring experience in project planning, managing timeline and multiple projects by setting priorities, reviewing relevant literature, summarizing findings, proposing recommendations and communicating the results to the experts from multidisciplinary fields.

### 4. Biorisk management

Supervisors: Susanna Sissonen, Hanna Valtonen, Pamela Österlund

#### Laboratory preparedness training and risk assessment of work with West Nile and Usutu viruses at biosafety level 3 laboratory at THL, Finland

Both WNV and Usutu virus (USUV) are members of the genus *Flavivirus*, and *Flaviviridae* family. These pathogens can cause serious human or animal disease, but they do not ordinarily spread from one infected individual to an-

other. As effective treatment and preventive measures, such as vaccines, are not available, the viruses can pose high risk to the individual, but low risk to the community. The above-mentioned criteria are used to classify WNV and USUV as microbial risk level 3 pathogens in Finland.

In order to be able to implement the WNV diagnostic assay at THL, isolation experiments of WNV and USUV at biosafety level 3 (BSL-3) laboratory were necessary to obtain viral genetic material for positive and negative controls. The aim of this project was to perform a literature review and evaluate the risks associated with laboratory handling of these pathogens and control measures necessary to ensure safety of personnel during work at BSL-3 laboratory.

We started the project after successful completion of *Biosafety and Biosecurity Training Course* at THL, which covered theoretical topics on laboratory biosafety levels and microbial risk group classification, biosafety and biosecurity legislation and standards, biosecurity and dual use of infectious materials, laboratory acquired infections, risk assessments, laboratory physical barriers, personal protective equipment (PPE), safe working practices, design of BSL-3 laboratories. The training also included a visit to the BSL-3 facility, practical exercise on putting on and wearing PPE.

During the risk assessment, we summarized the current knowledge of WNV and USUV and described the decontamination methods, inactivation techniques, safe transport and storage of infectious material, waste management as well as risks of release of the pathogens outside BSL-3 facility. After the approval of the risk assessment, we performed WNV and USUV RNA extraction experiments and followed all the predefined steps for safely transport of infectious material to BSL-2 laboratory to continue work for the diagnostic assay setup.

The produced risk assessment document was integrated into the SOPs of BSL-3 facility at THL providing guidance and safety information for personnel engaging into WNV and USUV microbiology and laboratory investigations. Additionally, it enabled the subsequent development and implementation of diagnostic protocol for WNV, an emerging viral pathogen, at THL.

The fellow assessed risks associated with microbial risk group 3 pathogens, wrote the SOP, used BSL-3 appropriate PPE, performed work at BSL-3 laboratory following all the safety steps, decontaminated and transported material from BSL-3 to BSL-2 laboratory.

#### **Training modules**

The *Biorisk and Quality Management Module* was cancelled, but the materials from the previous year provided insights into biorisk management and quality control, identification and mitigation of biorisk as well as shipment practices and protocols for infectious substances.

**Educational outcome:** the fellow gained knowledge of the importance of biorisk management, and the requirements needed to control risks associated with the handling, storage and disposal of toxic biological agents in laboratories. Moreover, the fellow developed understanding of the processes associated with BSL-3 laboratories as well as biosafety, risk assessment and mitigation procedures.

### 5. Quality management

Supervisors: Saara Salmenlinna, Lotta Siira

#### *Vibrio spp. diagnostics in Finland: from phenotypic detection to whole genome sequencing*

Considering the current situation of global warming and its impact on increasing temperature of the Baltic Sea and more frequently occurring heat waves, Northern European countries, including Finland, need to be prepared for the increase of *Vibrio* spp. infections by monitoring the situation of *Vibrio* spp. infections, raising clinical awareness and implementing effective diagnostic detection of these emerging pathogens.

Due to varying number of *Vibrio* isolates submitted to THL throughout the year, it is difficult to maintain constantly available supply of the needed materials for phenotypic diagnostic tests. Furthermore, WGS is an established procedure for the characterisation of other pathogens at THL and skilled personnel is available to perform the analysis. In order to use resources in an optimal way and perform rapid strain comparison, genomic surveillance and sharing of data between EU member states, a WGS pipeline for *Vibrio* identification was a desired addition to the routines of THL. The aim of this project was to evaluate the pipeline by comparing the WGS results with the traditional biochemical and serological detection methods using *Vibrio* spp. isolated from clinical and environmental samples as well as WGS results from the literature.

We evaluated THL WGS pipeline for *V. cholerae* serotyping, biotyping and cholera toxin detection (ReMatCh module) as well as *Vibrio* spp. species identification (Kraken module) to provide initial data supporting the planned transitioning from the phenotypic to WGS-based *Vibrio* spp. identification tools. We compared the two pipeline modules to the phenotypic tests by analysing the results of two sets of *Vibrio* isolates (THL and Public Health England collections). The ReMatCh module was able to correctly identify *V. cholerae* species, O1 serogroup, El Tor biotype and cholera toxin with sensitivity (Se) and specificity (Sp) values >95%, but was lacking sensitivity in identifying O139 serogroup (Se: 28.6%; Sp: 100%) and classical biotype (Se: 66.7%, Sp: 99.6%). Kraken module was able to correctly identify with 100% concordance (Cc) the most important pathogenic vibrios: *V. cholerae, V. parahaemolyticus* and *V. vulnificus*, as well as other vibrios, *Vibrio fluvialis* and *Vibrio mimicus*, but did not correctly assign *Vibrio alginolyticus* (Cc: 50.0%), *Vibrio metschnikovii* (Cc: 0%) and *Vibrio ordalii* (Cc: 0%) species.

As the further validation of these methods will be performed in the future at THL, we recommended evaluating a larger number of positive controls that include all the targets in the ReMatCh module, which would give a more accurate sensitivity estimate. Additionally, to improve species identification by the Kraken module, more isolates of *Vibrio* species other than *V. cholerae* or *V. parahaemolyticus* should be screened and the expanded Kraken reference database containing all the genomes of *Vibrio* species to be detected should be used.

The fellow performed the literature review, became familiar with the phenotypic as well as genotypic diagnostic methods, performed the analysis of WGS data and compared it to the phenotypic results, contributed to interpretation of the results and wrote the report.

#### Streptococcus pneumoniae external quality assurance

Serotyping is important to monitor the effectiveness of pneumococcus vaccination programmes and serotype distribution in the population. EQA schemes of pneumococci allow expert laboratories document performance in identifying the capsule of the pathogen, improve and maintain high quality of pneumococcal typing. Thus, it is essential to organize pneumococcal EQA rounds in expert and reference laboratories. This self-organised interlaboratory pneumococcal EQA exchange is performed bi-annually by the participating laboratories according to a rotation established in the valid EQA agreement. The aim of EQA activity was to ensure a high quality of pneumococcus serotyping at participating expert laboratories by organizing the 2019B round.

We distributed a selected blinded panel of seven invasive pneumococcal isolates of seven different serotypes collected during routine surveillance in Finland in 2019 to eight expert laboratories from eight countries. The panel was shipped in compliance with international packaging and transportation requirements for infectious substances according to International Air Transportation Association (IATA) Dangerous Goods Regulations UN3373 Category B. The report form was distributed by email and as a paper copy along with the specimens to the participating laboratories.

Overall, the agreement both between laboratories and methods was high. Only one isolate proved difficult to serotype by a WGS based methods. All reporting laboratories concluded it being the serotype 23B and were in agreement. WGS based PneumoCaT/SeroBA analysis failed to provide an unambiguous serotyping result, although the top hit reported by all laboratories using this method was 23B1.

The above-mentioned case highlights the benefit of access to phenotypic methods to resolve isolates with aberrant results by WGS as well as discriminate outbreaks of emerging serotypes, where no genotyping data exists. As participation in pneumococcal EQA helps laboratories ensure their high quality of typing procedures and comparability with the results of other countries as well as it helps to validate new methods, e.g. WGS based serotyping, we recommended to continue organising the EQA rounds in the future.

The fellow reviewed the literature, became familiar with phenotypic and genotypic methods in the laboratory, contributed to the practical aspects of the EQA round organization including serotype confirmation using phenotypic method, isolate preparation, packing and shipping according to IATA regulations, data analysis and interpretation as well as final report writing.

#### HIV drug resistance surveillance laboratory internal audit

Audit is an essential part of the quality assurance programme of a laboratory and is a means of assessing whether one is achieving one's stated objectives. A quality assurance programme covers all aspects of the service provided including laboratory processes and operating procedures, policies on the induction and training of new staff, staff development, laboratory manuals, equipment maintenance, documentation of test methods used, safety policies, sample handling, quality control verification activities, recording and reporting practices. The aim of this activity was to perform an internal audit of the human immunodeficiency virus (HIV) drug resistance surveillance function in the National HIV Drug Resistance Surveillance Laboratory at THL.

The fellow interviewed the head of the laboratory Kirsi Liitsola to evaluate the process management and quality control as well as documentation indicators. The laboratory has a quality management system including external quality controls. Overall, the laboratory maintains high quality (general indicator 98%) with appropriate and well-documented routines in place. No significant deviations that would negatively impact the laboratory functions were identified during the audit. The laboratory collects the needed information for the analysis and provides result summaries for the annual report of infectious diseases. The clear online instructions specifying the necessary details for sample submission and transport are available online for the customers. The staff and laboratory managers utilise electronic LIMS, which can be used to easily access the collected test results and their accompanying metadata for analysis. This information is accessible only to the authorised personnel to ensure personal data security and confidentiality.

Following well-functioning procedures of the laboratory, the fellow identified a few minor things for improvements. Provided the availability of time and resources, the result delivery time could be shortened by implementing a secure electronic solution instead of currently available letter format. Additionally, an automated link between LIMS and NIDR should be created to deposit HIV subtype information and sequences to provide more complete information for HIV surveillance in one place. Furthermore, the laboratory might benefit from preparation of monthly summary reports of the technical records instead of the currently chosen yearly format and it could perform the interpretation of the test results against the population-based reference intervals.

The fellow was actively involved in all steps of the audit from interviews to writing of the report.

#### **Training modules**

The *Biorisk and Quality Management Module* materials from previous years introduced all aspects of internal and external quality assurance.

**Educational outcome:** the fellow developed understanding and learned to apply concepts of quality management, got acquainted with laboratory ISO (International Organization for Standardization) standards and certification procedures of expert laboratories. Additionally, the fellow gained practical quality management experience by contributing to method validation procedures, EQA round organization as well as internal audit of an expert laboratory.

### 6. Teaching and pedagogy

Supervisors: Aftab Jasir, Ralf Reintjes

#### Importance of antimicrobial resistance as a public health threat with the emphasis on carbapenem resistance in Enterobacteriaceae

During the ECDC Fellowship Introductory Course, EUPHEM fellows participated in the problem-based learning (PBL) exercise, during which they were presented with the scenario describing the carbapenem resistant *Enterobacteriaceae* isolates in Greece. The fellows discussed the scenario, identified the problem and went through the seven steps of PBL to find the solution to the problem. The fellows devised a plan to tackle the problem of antimicrobial resistance (AMR) by conducting an interactive seminar covering different topics including AMR as a public health threat with specific example of carbapenem resistance mechanisms in *Enterobacteriaceae*, laboratory methods for AMR detection and their role in molecular epidemiology. The moderated seminar was presented to the audience of scientific experts and their learning was assessed using an AMR quiz delivered through smartphone application Kahoot. The preparation and delivery of the seminar increased the knowledge on AMR issue of both the scientific experts as well as EUPHEM fellows.

#### Developing and delivering a lecture on coronaviruses and facilitating case studies during the Essentials of Infectious Disease Epidemiology Course

The fellow participated in the one-week training for healthcare professionals during the *Essentials of Infectious Disease Epidemiology Course*, which was organized by the School of Health Sciences at Tampere University. The aim of the training assignment was to develop and deploy learning tools according to pedagogical techniques suitable for adult learners.

The fellow developed a lecture "*Coronaviruses – what we should know*", which was aimed at the postgraduate and master students. Additionally, the fellow delivered four case studies: *Salmonellosis in the Caribbean, Trichinosis in Paris (France), Haemolytic-uremic syndrome in Hamburg (Germany)* and *Gastroenteritis in Kalundborg (Denmark)*.

We evaluated the training activity by surveying the participants at the end of the course (100% response rate). Most respondents (94%) found the content of the course adequate and the ratio of theoretical lectures and practical exercises/case studies was considered to be balanced by all respondents. The difficulty of the content of "*Coronaviruses – what we should know*" was found as balanced by the majority of the respondents (94%). One person considered it as too advanced. The majority of the respondents thought that the content of the practical exercises/case studies was also well balanced in terms of difficulty. Most of the participants (89%) found the revision sessions useful for their learning. Most of the respondents (83%) stated that the course has increased their knowledge in infectious disease epidemiology with 56% of the respondents *definitely* and 44% *likely* to apply the acquired knowledge in the future.

The activity expanded fellow's knowledge on the topic of coronaviruses, through a short literature and online material review to prepare for the lecture. Additionally, the activity allowed to further train and develop the teaching skills and apply the knowledge of learning styles and 3 Vs (visual, vocal, verbal) of communication to make the presentation visually appealing and balanced with regards of theoretical and practical content. Finally, the activity contributed to mindfulness and understanding the importance of cultural differences and how they affect the same public health issues in the various parts of the world.

### **Training modules**

During the *ECDC Fellowship Introductory Course* the fellows were presented with practical aspects on preparing a training plan and training material for different target audiences. Additionally, the student-centred pedagogy technique of problem-based learning was practically demonstrated.

The fellows were exposed to theory behind the learning styles and 3 Vs during the *Management, Leadership and Communication in Public Health Module*.

The *Project Review Module* trained the fellows on chairing presentations, providing and receiving constructive criticism.

**Educational outcome:** the fellow learned and gained experience on organising a seminar, outlining training activity objectives, developing and delivering a lecture as well as facilitating case studies to multidisciplinary audience, evaluating the training activity outcomes for prospective improvements.

### 7. Public health microbiology management

#### Outbreak investigation and project management

Each project and outbreak investigation included various aspects of public health management from participation in project developmental meetings, collaborating with multidisciplinary teams, effective managing of timelines to maintaining the links between the epidemiologists and microbiologists as well as public health specialists and researchers. Through conducted projects and activities, the fellow contributed to the generation of evidence for control strategies and policies that support improvement of public health situation in Finland and beyond.

The fellow was actively engaged in a spectrum of coordination and communication activities as a principal investigator at THL especially during an outbreak investigation in a shipyard as well as multi-country collaboration on vibriosis occurrence in Northern Europe. The activities spanned from mediating between legal department of the training site and the international collaborators for *Vibrio* project and data agreement signing to situation updates and communication on planned response and control measures aimed to the internal and external stakeholders during outbreak investigation in a shipyard. During these activities the fellow has strengthened team building, negotiation and effective communication skills.

#### Nordic Mini Project Review Module, 2020

The EPIET/EUPHEM Nordic Mini Project Review Module (NMPRM) is an informal forum for public health professionals from the Nordic and Baltic countries taking part in either the EPIET or EUPHEM. The participants are invited to share ideas on the project presentations delivered by the EPIET/EUPHEM fellows with intention to provide constructive feedback. Additionally, the experts of different public health fields are selected to facilitate discussions. Overall, the module serves as a platform for strengthening the network of public health professionals in the region as well as it helps the fellows to prepare for the upcoming conferences and the Project Review Module organized by the ECDC.

The fellow was part of organizing committee of the module and contributed to the tasks that included information dissemination to the participants, development of the module programme and module guide, internal and external facilitator selection and engagement, event management, social programme development as well as event evaluation. Even though the global COVID-19 situation has affected the number of participants, the overall satisfaction of the module was high. Hence, we believe that the NMPRM should be organized in future years.

#### Epidemic intelligence gathering during COVID-19 pandemic, 2020

The first case of the coronavirus disease 2019 (COVID-19) in Finland was confirmed on 29 January 2020 and the first autochthonous COVID-19 case was reported a month later. The first restrictions on people's lives were applied in March leading to the state emergency announcement on 16 March. The first death from COVID-19 was reported on 21 March. Since then the epidemic in Finland has slowed down and the state emergency has been revoked on 15 June.

In the beginning of February, the fellow got involved in the preparation of a daily COVID-19 situation report, which included collation of information gathered on case counts, deaths and recoveries inside and outside of China, new recommendations and risk assessments by the World Health Organization, ECDC, the Centers for Disease Control and Prevention and other public health agencies, new findings emerging from research in form of peer-reviewed and pre-print articles, scanning of the Twitter feed and reviewing news reports from around the globe. The information was forwarded to the heads of the Department of Health Security at THL and the COVID-19 emergency response team members.

In the end of March, the fellow developed an R script and a daily R Markdown-based report providing information on COVID-19 situation in the Nordic countries and Estonia. The daily update contained information on each country's case distribution over time including the dates for introduction of COVID-19 testing strategies. Additionally, the report was supplemented with the information on cumulative incidence proportion as well as the proportion of

positive tests adjusted to population of the country and the community mobility trends. The gathered information was used to produce briefings for the national authorities and communicated to the public. The fellow also contributed to the editing of English version of THL website dedicated to COVID-19-related information.

#### **Training modules**

The *Management, Leadership and Communication in Public Health Module* provided the fellows with theoretical knowledge as well as practical simulation exercises on responsibilities of leaders and managers in public health, different management styles and their applications for people, team and situation management. The fellows learned about the time management strategies and task delegation to promote the development opportunities for others as well as team building, constructive feedback and effective communication during crises.

**Educational outcome:** throughout the fellowship the fellow was exposed to different aspects of public health management, which helped developing skills in identifying the communicable disease threats and applying strategies to prevent and control them. The fellow learned to recognise and describe the added value of the projects and activities, pinpoint and utilize the benefits of multidisciplinary team work as well as apply negotiation skills and deliver targeted public health messages to the stakeholders.

### 8. Communication

#### **Publications**

- Linkevicius M, Cristea V, Siira L, Mäkelä H, Toropainen M, Pitkäpaasi M, Dub T, Nohynek H, Puumalainen T, Rintala E, Laaksonen ME, Feuth T, Grönroos JO, Peltoniemi J, Frilander H, Lindström I, Sane J. Outbreak of invasive pneumococcal disease among shipyard workers, Turku, Finland, May to November 2019. Euro Surveill. 2019;24(49):1900681. doi: 10.2807/1560-7917.ES.2019.24.49.1900681.
- 2. Amato E<sup>\*</sup>, Riess M<sup>\*</sup>, Thomas López D<sup>\*</sup>, **Linkevicius M**<sup>\*</sup> et al. Vibriosis in Northern Europe: an emerging public health threat? Manuscript. *In preparation*. 2020. <sup>\*</sup>Equal contribution.

#### **Reports**

- 1. Linkevicius M, Savolainen-Kopra C, Blomqvist S, Lyytikäinen O. Non-polio enterovirus surveillance in Finland, 1995-2019. Surveillance report. 2020.
- 2. Linkevicius M, Österlund P. The setup of a West Nile virus detection assay in the expert laboratory at THL, Finland. Laboratory report. 2020.
- 3. Amato E<sup>\*</sup>, Riess M<sup>\*</sup>, Thomas López D<sup>\*</sup>, Linkevicius M<sup>\*</sup>. Surveillance systems for vibriosis and *Shewanella* spp. infections in the EU/EEA countries. ECDC technical report. *Under clearance*. 2020. <sup>\*</sup>Equal contribution.
- 4. Linkevicius M, Salmenlinna S. *Vibrio* spp. diagnostics in Finland: from phenotypic detection to whole genome sequencing. Validation report. 2020.
- 5. Linkevicius M, Siira L. *Streptococcus pneumoniae* external quality assurance. EQA report. 2020.
- 6. Linkevicius M. HIV drug resistance surveillance laboratory internal audit. Audit report. 2020.
- 7. Linkevicius M. Training public health professionals: evaluation and reflection. Evaluation report. 2020.
- 8. Linkevicius M, Cristea V. EPIET/EUPHEM Nordic Mini Project Review Module 2020. Evaluation report. 2020.

#### **Conference presentations**

- 1. Linkevicius M, Ikonen N. Human respiratory syncytial virus types A and B in Finland, 2010-2018. Poster presented by Marius Linkevicius. European Scientific Conference on Applied Infectious Disease Epidemiology (ESCAIDE), 2019, Stockholm, Sweden.
- 2. Amato E<sup>\*</sup>, Riess M<sup>\*</sup>, Thomas-López D<sup>\*</sup>, Linkevicius M<sup>\*</sup>, Pitkänen T, Jernberg C, Hjertqvist M, MacDonald E, Anthony-Sami J, Wołkowicz T, Rjabinina J, Salmenlinna S, Fuursted K, Hansen A, Naseer U, the *Vibrio* investigation group. Multi-country occurrence of non-cholera *Vibrio* infections in the Nordic countries and countries bordering the Baltic Sea in 2018. Poster presented by Ettore Amato. ESCAIDE, 2020, online. <sup>\*</sup>Equal contribution.

#### **Selected other presentations**

- 1. Linkevicius M. *E. coli* with reduced susceptibility to tigecycline: experience with WGS. Oral presentation. Outbreak Investigation Module, 2018, Berlin, Germany.
- 2. Linkevicius M. Measles in twice MMR vaccinated individuals in Finland since 2017 risk of onward transmission. Oral presentation. Nordic Mini Project Review Module, 2019, Copenhagen, Denmark.
- 3. Linkevicius M. Antimicrobial resistance in *Vibrio* pathogens: literature overview in European studies. Oral presentation. *Vibrio* workshop, 2019, Oslo, Norway.
- 4. Linkevicius M. *Vibrio* infections in the Nordic countries and the countries bordering the Baltic Sea in 2018 FINLAND. Oral presentation. Environment and Health Research Seminar, 2019, Kuopio, Finland.

- 5. Linkevicius M. Measles in twice MMR-vaccinated individuals, Finland, 2017-2019. Oral presentation. Nordic Verification Committee for Measles and Rubella Elimination Meeting, 2019, Helsinki, Finland.
- 6. Linkevicius M. Enterovirus surveillance in Finland. Oral presentation. Nordic Mini Project Review Module, 2020, Helsinki, Finland.

#### Other

- 1. Measles virus isolation in Vero/hSLAM cell line video. 7 March 2019.
- 2. Frequently asked questions about pneumococcus and pneumococcal vaccination for the shipyard workers in Turku, THL website. 16 October 2019.
- 3. Colistin-resistant *Klebsiella pneumoniae* article appraisal for Eurosurveillance. 5 February 2020.
- 4. Frequently asked questions about COVID-19 to the public, THL website. March-May 2020.

#### **Training modules**

During the *ECDC Fellowship Introductory Course* the fellows were presented on how to deliver an oral communication efficiently to different target audiences as well as how to visualize the presentation slides by summarizing the findings in a meaningful way and choosing the key messages.

The *Project Review Module* provided further instructions both oral and poster presentations and allowed the fellows to apply their presenting skills in practice to their peers and scientific facilitators.

The *Management, Leadership and Communication in Public Health Module* further emphasised the importance of identifying and tailoring the single overriding communication objective, target audience and applying verbal, visual and vocal skills to deliver an effective presentation.

### 9. EPIET/EUPHEM modules attended

- 1. ECDC Fellowship Introductory Course, Spetses, Greece, 24 September-12 October 2018.
- 2. Outbreak Investigation Module, Berlin, Germany, 3-7 December 2018.
- 3. Multivariable Analysis Module, Madrid, Spain, 25-29 March 2019.
- 4. Rapid Assessment and Survey Methods Module, Zagreb, Croatia, 13-18 May 2019.
- 5. Project Review Module, Prague, Czechia, 26-30 August 2019.
- 6. Management, Leadership and Communication in Public Health Module, Stockholm, Sweden, 10-14 February 2020.
- 7. Vaccinology Module, Online, 4-24 June 2020.

### **10. Other training**

- 1. ESCAIDE, Saint Julian's, Malta, 21-23 November 2018.
- 2. Communicable Disease Surveillance in Finland, THL, Helsinki, Finland, 18 September 2018.
- 3. Quality Management at THL, THL, Helsinki, Finland, 29 October 2018.
- 4. Spoken professional Swedish at B1 level, Kieliavain, Helsinki, Finland, 30 January-27 February 2019.
- 5. Professional Swedish at THL, THL, Helsinki, Finland, 12 February-7 May 2019.
- 6. THL R packages, THL, Helsinki, Finland, 19 March 2019.
- 7. BSAFE, United Nations security awareness training, online, 18 April 2019.
- 8. Spoken professional Swedish at B2 level, Kieliavain, Helsinki, Finland, 1 July-7 August 2019.
- 9. EPIET Alumni Network (EAN) Mini Module 'Social media for public health professionals', National Institute of Public Health (SZÚ), Prague, Czechia, 31 August-1 September 2019.
- 10. RECON/EAN Workshop 'Introduction into R for outbreak analytics', ECDC, Stockholm, Sweden, 25-26 November 2019.

## Discussion

### **Coordinator's conclusions**

The work depicted in this portfolio attests for the dedication and talent of Marius Linkevicius. He was already an accomplished microbiologist with expertise in the area of antimicrobial resistance at the start of the programme and he undertook the EUPHEM fellowship with the objective of widening his knowledge in public health microbiology. Under this premise, he developed projects offered in wide, very interesting and useful topics at THL. Guided by his site supervisors, Marius was introduced to the importance of risk assessment and quality management systems, to which he took with gusto. The review of the surveillance system for emerging NPEV disease resulted in a sug-

gestion to fine-tune the national laboratory reporting system and his work on analysis of outbreak data led to advising vaccination as an effective intervention to control an outbreak of pneumococcal disease in shipyard workers in Turku (Finland). The COVID-19 and vibriosis project activities provided a golden opportunity to not only learn how to establish surveillance systems from baseline, but to refine his public health management and communication skills, and thus his work contributed to strengthening the network of collaborating Nordic and European Public Health Institutes. His hard work, organisational skills and rigorous approach to task development made it a pleasure to guide Marius through the fellowship. He leaves the programme ready to undertake the tasks of a laboratory lead in Public Health Microbiology.

### Supervisor's conclusions

When Marius joined THL, he already had a solid scientific background and was ready to embark on a journey of further discovery. Over the past two years, the EUPHEM programme has enabled him to grow a broad understanding of public health microbiology and epidemiology and has made him a versatile public health professional. He has implemented the skills learned through training modules and gained hands-on experience both in the laboratory and outside it. Through a variety of projects, Marius has added significantly to the core activities of THL for example by contributing to the expansion of WGS to *Vibrio*, initiating and implementing improvements to the surveillance of RSV and enterovirus, expanding national preparedness for WNV, investigating a pneumococcal outbreak, performing epidemic intelligence on COVID-19 and expanding the knowledge base for measles among the MMR vaccinated. He has participated in communicating with stakeholders, the public and colleagues both nationally and internationally. Marius has proven himself able to handle dynamic situations, such as demanding outbreak work, while being a productive and pleasant team member and keeping on top of overlapping activities with diligence. He has undertaken his tasks with great interest; his motivation can be exemplified by his learning R, capturing measles on camera, and taking an interest in the public health implications of global warming. As the fourth EU-track EUPHEM fellow at THL, Marius has been instrumental in furthering collaboration between the laboratory and epidemiological functions. It has been a true pleasure to be part of his journey in public health at THL.

### **Personal conclusions of fellow**

The EUPHEM fellowship has served as an opportunity to expand my academic microbiology experience with the skills and knowledge in the public health field. I have been fortunate to be stationed at THL with an experienced team of public health experts who have shared their expertise through supervision of the projects and activities I was engaged in. I developed competencies in outbreak investigation, infectious disease surveillance, laboratory quality and biorisk management as well as leadership and communication in public health by applying 'learning by doing' approach, which is in the core of the fellowship programme. The collaborations between the public health specialists including epidemiologists and microbiologists are key in successful prevention and control of the communicable disease threats nationally and internationally. Therefore, together EPIET and EUPHEM graduates dispersed around the EU/EAA Member States constitute a strong network of professionals improving the health of people in Europe and beyond.

### **Acknowledgements of fellow**

I would like to express my gratitude to my training site supervisors Carita Savolainen-Kopra and Lotta Siira for welcoming me at THL and encouraging me each step of EUPHEM experience. I am also very grateful to the EPIET site supervisors Jussi Sane and Outi Lyytikäinen for their support and sharing their insights in the field of epidemiology. I am thankful to all my project supervisors and other colleagues at THL for fruitful collaborations and memorable times inside and outside the office. I am grateful to the past and present EPIET fellows at THL, Timothée Dub and Charlotte Hammer, for a nice atmosphere at work. A special thanks goes to my EPIET counterpart Veronica Cristea for working and sharing the fellowship experience with me.

I would like to extend my sincere thanks to my scientific frontline coordinator Aura Andreasen for her dedication and positive attitude guiding me through the fellowship. I am also thankful for the support from Aftab Jasir, Loredana Ingrosso and Silvia Herrera Leon as well as all the EPIET and EUPHEM coordinators who created a stimulating learning environment during modules. Thank you to the Fellowship Faculty Office for ensuring smooth administration of the programme. It has been a pleasure to be a part of the cohort 2018 and meet every single one of my EPIET, EUPHEM, PAE, UK- and Norwegian-FETP fellows. A particular delight was working with Ettore Amato, Daniel Thomas-López and Maximilian Riess.