# **EUPHEM**



# **EUPHEM** REPORT

## Summary of work activities Ettore Amato 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 Ettore Amato, cohort 2018 of the European Public Health Microbiology Training Programme (EUPHEM) at the Norwegian Institute of Public Health (NIPH), Oslo, Norway. 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.

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# **Pre-fellowship short biography**

Prior to his EUPHEM fellowship, Ettore Amato worked at the European Commission, Directorate General for Health and Food Safety, Brussels (DG SANTE) as policy assistant in the Food Hygiene Unit and consultant for the Rapid Alert System for Food and Feed (RASFF) for two and a half years. His duty comprised follow-up and validation of the European Union Reference Laboratories (EURL) activities on *Campylobacter* and *Salmonella*, draft answers to oral and written questions and petitions of Members of the European Parliament and collaboration on the management of alerts and multi-country foodborne outbreaks. He obtained his Ph.D. in Public Health at University of Milan while working at the regional Enteric-Pathogen Reference Laboratory (Lombardy, Italy) with a research interest in molecular epidemiology and whole genome sequencing of foodborne bacterial pathogens.

**Fellowship assignment:** On 11<sup>th</sup> September 2018, Ettore started his EUPHEM fellowship at the Norwegian Institute of Public Health (NIPH) in Oslo – Norway, under the supervision of Dr Didrik Vestrheim. His ECDC EUPHEM frontline coordinators were Silvia Herrera-Leon (Instituto de Salud Carlos III, Madrid) and Aftab Jasir (ECDC EUPHEM Fellowship programme, Sweden). This report summarizes the work performed during his fellowship.

# **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

Supervisor: Emily MacDonald

### 1.1.1 Large waterborne Campylobacter outbreak in Askøy, Norway

On the evening of 6 June 2019, the Medical Officer in Askøy reported an outbreak of gastroenteritis to the NIPH. In a 24-hour period, 10 people had been hospitalized with fever, abdominal pain and diarrhoea, approximately 30 individuals had sought medical attention from out-of-hours primary health care services (OPHS). At least one person had tested positive for *Campylobacter*. Staff of the OPHS noted that many patients presenting with gastroenteritis had home addresses near each other, which led to a suspicion that drinking water could be the source of the outbreak.

We investigated the outbreak to confirm the source, extent of the outbreak and effect of control measures. A case was defined as a person in a household served by Water Supply System A (WSS-A) with gastroenteritis with duration >24 hours from 1-19 June 2019. Pilot interviews, telephone survey, and an SMS-based cohort study of residents served by WSS-A was conducted. System information of WSS-A was collected. Whole genome sequencing on human and environmental isolates was performed.

A large waterborne outbreak of *Campylobacter* causing an estimated 1,500 ill occurred in Askøy in Norway in June 2019. Residents served by the reservoir had a 4.6 higher risk of illness, compared to other. *Campylobacter jejuni* isolated from cases (n=24) and water samples (n=4) were identical. The source of contamination was most likely

<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

environmental contamination through cracks in a mountain reservoir, likely due to heavy rainfall after an extended dry period.

Water distribution systems, including reservoirs are susceptible to contamination, highlighting the importance of conducting water safety planning, update the infrastructure and perform risk-based surveillance a to mitigate risks, in particular since external risks such as climate factors are changing.

**Role:** Ettore participated as part of the outbreak investigation team deployed in Askøy island (Hordaland, Norway) in order to support local authorities. The main tasks were setting-up a reporting system of cases from hospitals, GPs and emergency room, monitoring of cases reported through the legevakt (emergency room) in Askøy and providing daily epi-curve updates. In addition, the fellow participated in the epidemiological SMS-based cohort study protocol.

### 1.1.2 Increased number of scabies cases in Norway, 2018

Between October and December 2018, several general practitioners (GPs) and dermatologists reported increasing numbers of patients with scabies to the NIPH. In addition, the Department for Pest Control at NIPH received many enquiries regarding scabies from members of the public, school nurses, kindergartens and long-term care facilities. On 11<sup>th</sup> January, a multidisciplinary meeting on scabies was hold at the NIPH in order to discuss these findings and define next steps. Data analysis of cases reported through the syndromic surveillance system under the International Classification of Primary Care (ICPC-2) code 'S72 – infestation mites' showed an increase of cases since 2014. However, these preliminary findings were considered inconclusive as the ICPC-2 code was used as proxy for scabies cases. Therefore, it was decided to investigate alternate data sources to confirm the increase in order to identify risk groups and target control measures.

**Role**: Ettore participated as co-investigator and part of the multi-disciplinary investigation team carrying out a scientific literature search on scabies's seasonality, treatments, resistance mechanisms and incidence per country.

### 1.1.3 Cluster of Yersinia enterocolitica cases in Norway, 2019

On 13<sup>th</sup> January 2020, the NIPH was notified by the National Reference Laboratory for Enteropathogenic Bacteria (NRL) about a cluster of five *Yersinia enterocolitica* O:3 cases. The outbreak was identified by whole-genome sequencing (WGS) and the isolates were identical to cgMLST. It was decided to initiate an investigation coordinated by the outbreak investigation team at the Norwegian Institute of Public Health in close collaboration with the relevant municipal consultants, the Veterinary Institute and the Norwegian Food Safety Authority. The aim of the outbreak investigation was to get an overview of the extent of the outbreak, describe the cases and identify a common source of infection in order to implement control measures. Preliminary results suggested a link with vegetable products, no additional new cases were detected.

**Role**: Participation as part of the outbreak investigation team contributing in the data collection and analysis of trawling questionnaires from cases.

### 1.1.4 COVID-19 Pandemic

The detection and spread of an emerging respiratory pathogen are accompanied by uncertainty over the key epidemiological, clinical and virological characteristics of the novel pathogen. This is the case for the novel coronavirus (SARS-CoV-2), first detected in Wuhan city, China in December 2019. On March 2020, World Health Organisation announced COVID-19 outbreak a pandemic.

**Role**: Ettore have contributed to the daily literature review of published manuscripts on COVID-19 and SARS-CoV-2 during the COVID-19 emergency supporting the epidemiological group.

### **Training modules**

The <u>EPIET/EUPHEM Introductory Course</u> provided participants with the basic concepts of logistical and analytical approach to outbreak investigations through three weeks of lectures, interactive sessions, case studies, group work, and writing of a research protocol as training in public health microbiology and intervention epidemiology. The course introduced fellows to the ten steps of an outbreak investigation.

The <u>Outbreak Investigation Module</u> was an interactive course methodologically going through the steps required in an outbreak investigation, form data entry and management, designing of questionnaires, descriptive and analytical data analyses, findings' communication and implementation of control measures. Participants were also given practical training in when and how to perform analytical studies for an outbreak investigation, including descriptive, cohort and case-control studies.

The <u>Multivariable Analysis Module</u> provided a more comprehensive understanding of the principles of statistical analyses, and how to build an optimal model using linear, logistic, Poisson and Cox regression.

The <u>Management, Leadership and Communication in Public Health Module</u> trained fellows in many aspects of management, collaboration and communication including time management and team collaboration.

### **Educational outcome:**

As a co-investigator and member of multidisciplinary outbreak investigation teams, Ettore has applied microbiological and epidemiological knowledge in outbreak situations, participated and gained a good understanding of all ten steps

of an outbreak investigation especially during emergency situations and high media attention. The performed activities include taking part in a field visit, designing and distributing questionnaires by e-mail/SMS, framing case definitions, performing descriptive and analytic statistical analyses, communicating with municipal health authorities and interpretation of epidemiological and microbiological typing data.

### **1.2. Surveillance**

Supervisors: Didrik Vestrheim, Umaer Naseer and Emily MacDonald

# 1.2.1 Epidemiology and molecular characterisation of invasive group A streptococcal infections in Norway during 2015-2018

*Streptococcus pyogenes* or group A streptococcus is an exclusively human pathogen that causes mild infections of the throat and skin, as well as severe infections and life-threatening complications. The project aimed to provide an insight into the epidemiological situation of invasive group A streptococcal infections (iGAS) in Norway in order to (i) evaluate any epidemiological change occurring during the three years (2015-2018) and (ii) assess the added value and limits of next generation sequencing (NGS) data for antimicrobial resistance surveillance.

Since 1993, all iGAS in Norway have been mandatory notifiable to the Norwegian Surveillance System for Communicable Diseases (MSIS) and the corresponding isolates are sent to the National Reference Laboratory (NRL) at NIPH. Surveillance data on antimicrobial susceptibility, multi-locus sequence type and emm-type is retrospectively analysed and linked with demographic and clinical manifestation data to calculate age and sex distributions, major emm- and sequence types and prevalence ratios (PR) on associations between emm-types and clinical manifestations.

**Role**: Ettore was involved in the literature search developing the surveillance protocol. According to the new General Data Protection Regulation, the fellow as principal investigator carried out all the management and administrative steps of ethical approval request to the Regional Committee for Medical and Health Research Ethics and impact assessment to the Data Protection Office.

### 1.2.2 Syndromic surveillance of Scabies in Norway, 2006-2018

Between October and December 2018, several clinicians in Norway reported an increase in scabies diagnoses. As scabies is not notifiable in Norway, we investigated alternate data sources to confirm the increase in order to identify risk groups and target control measures.

We extracted data on consultations from the Norwegian Syndromic Surveillance System (NorSySS) and reported outbreaks from the Norwegian disease outbreak notification system (Vesuv) from 2006 to 2018. Although there is not a specific diagnosis code for scabies in the NorSySS database, the International Classification of Primary Care (ICPC-2) code 'S72 – infestation mites' was considered the most appropriate proxy for scabies. We compared NorSySS data with the data on drug use from the Norwegian Drug Wholesales Statistics database and the Norwegian prescription database (NorPD).

Between 2006 and 2018, 39,796 consultations for mite infestations were registered in NorSySS. Of these, 26,681 (67%) were reported from 2013 to 2018. The number of consultations for mite infestations during the study period was highest in 2018 at 6,080 consultations, which was almost threefold increase compared with 2012. The distribution in the age of patients was significantly different (Pearson chi-squared p value <0.001) during 2006–12 in comparison with the period 2013–18 with a higher proportion of patients in age group 15–19 years (14% vs 21%) and 20–29 years (31% vs 34%) between 2013 and 2018. Data from the Wholesales Statistics showed increasing sales of permethrin starting in 2014, with the largest amount of cream sold in 2018 (1,300 kg).

Although we cannot yet conclude on the reasons for the demonstrated increase, clinicians should be vigilant to ensure scabies is being appropriately diagnosed and treated. As scabies is largely diagnosed on clinical grounds since there are no standardised laboratory tests available, treatment failure may occur due to wrong diagnosis, incorrect use of cream, or improper intake of oral treatments. Therefore, early diagnosis confirmations and proper treatment are critical for avoiding the spread of infestation and outbreaks.

**Role**: Ettore was involved as principal investigator and part of the multi-disciplinary investigation team in the study design. The main tasks included collection, analysis and interpretation of data from the Norwegian Syndromic Surveillance System. In addition, the fellow was responsible for the manuscript drafting and publication in peer-reviewed journal as first and corresponding author.

### 1.2.3 Surveillance of antimicrobial susceptibility among Viridans Group Streptococci and Pneumococci in Norway during 2017-2018

Viridans group streptococci (VGS) represent a diverse group of potentially pathogenic gram-positive cocci that form a part of the normal flora in the oropharynx, urogenital tract, and gastrointestinal tract. Clinical laboratories must be able to accurately differentiate *S. pneumoniae* from other VGS commonly found in clinical samples to facilitate appropriate antimicrobial therapy. The emergence and spread of antimicrobial resistance (e.g. penicillin and macrolide antibiotics) have made the selection of the optimal antimicrobial therapy difficult for *S. pneumoniae*. Parallel increases in the rates of resistance to those antibiotics have also been observed among the VGS, which are commensal organisms of the oropharyngeal tracts of healthy individuals but which are also a major cause of endocarditis and bacteraemia in neutropenic patients.

This project aimed to shed light on the antimicrobial resistance of VGS and their role in the transmission of resistance genes among the non-susceptible pneumococci. Results from this study, may contribute to evaluate the need for a laboratory-based surveillance on antimicrobial resistance for VGS in Norway in order to control and limit the selection pressure that promotes development and transmission of resistance.

Role: Ettore was involved in the literature search and developing the surveillance project proposal.

# 1.2.4 Survey on national surveillance systems for vibriosis and Shewanella spp. infections in EU/EEA countries

In September 2019, an online survey regarding the surveillance of *Vibrio* spp. and *Shewanella* spp. infections was sent to the National Focal Points for Food- and Waterborne Diseases and Zoonoses of the EU/EEA countries due to lack of a complete overview of such surveillance systems in Europe from scientific literature. The collected data will be also useful to ECDC and EU/EEA countries where an assessment for the future introduction of a surveillance system for these pathogens is planned.

**Role**: Ettore, in collaboration with ECDC and EUPHEM fellows placed in Nordic countries, have participated in the survey drafting, data collection, analysis and interpretation and drafting of the surveillance survey report on *Vibrio* and *Shewanella* infections in EU/EEA countries.

### 1.2.5 Surveillance for COVID-19 human infections in Norway

COVID-19 has spread rapidly around the world, affecting every community directly or indirectly. Stringent public health and social measures have been put in place by all countries to slow the spread of COVID-19. As public health authorities, it is critical that robust surveillance is in place or put in place to control the spread of COVID-19 and guide ongoing implementation of control measures.

**Role**: Participation as part of the team working with surveillance and preparedness activities, specifically in implementing the questionnaire for the first COVID-19 cases of the Outbreak Registry.

### **Training modules**

The <u>EPIET/EUPHEM introductory course</u> familiarised fellows with the development, evaluation and analysis of surveillance systems.

The <u>Rapid Assessment and Survey Methods module</u> familiarised fellows with the use of sampling methods adapted to study populations and on how to contribute to the multidisciplinary and international response to complex emergencies situations and apply their skills to serve public health interventions such as surveillances.

### **Educational outcome:**

Ettore learned the complexities involved in preparing to set up a surveillance system. The fellow developed understanding and experience on how to analyse existing laboratory and syndromic surveillance data and select appropriate methods, interpret, formulate recommendations and write reports using the data.

## 2. Applied public health microbiology research

Supervisors: Umaer Naseer, Emily MacDonald and Hans Blystad

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

*Vibrio* bacteria are ubiquitous in aquatic and marine habitats. Non-cholera *Vibrio* species cause self-limiting vibriosis but can rarely lead to severe clinical presentation. In the last years, countries in northern Europe have witnessed an increase in *Vibrio* infections during heatwaves, including 2018. 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.

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. Relatedness of isolates was investigated by phylogenetic single-nucleotide-polymorphism (SNP) analysis of whole genome sequencing (WGS) data.

We identified 441 vibriosis cases with median age of 52 years (1-101) and male-to-female ratio of 1.6. Exposure was known for 112 cases of which 106 (95%) 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 group >65 years old (OR=14.2; 95% CI:4.0-50.8), (ii) *V. vulnificus* (OR=23.7; 95% CI:4.1-139.2) and *V. parahaemolyticus* (OR=3.2; 95% CI:1.2-8.3) and (iii) summer season (OR=6.2; 95% CI:2.8-

13.7). Although phylogenetic analysis showed diversity between *Vibrio* isolates, two *V. vulnificus* clusters (<10 SNPs) were identified in Norway and Sweden.

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.

**Role**: Ettore as project coordinator of the multi-country project between 7 EU/EEA countries (Norway, Sweden, Denmark, Finland, Poland, Estonia and Latvia) was involved in the development and coordination of the project design and the joint scientific research protocol. The main tasks included joint collection, analysis and interpretation of epidemiological and molecular data in close collaboration with principal investigators placed in the Nordic countries. Epidemiological analysis included descriptive and multi-variable analysis of reported cases. Molecular analysis included phylogenetic single-nucleotide-polymorphism (SNP) analysis and AMR, virulence, biofilm determinants analysis using WGS data, contributing in setting up a WGS pipeline in Norway using different databases and thresholds specific for *Vibrio* spp.. In addition, the fellow was participating in the manuscript drafting for peer-reviewed journal as first-shared and corresponding author.

### 2.2 Awareness, knowledge and willingness to be tested for HIV among men who have sex with men in Norway: community survey 2019-20

In 2017, it was estimated that nearly 37 million people were still living with HIV and nearly 2 million new infections occurred. HIV has reached every corner of the globe, but some regions or populations groups are more affected than others. Tremendous progress has been made in the fight against HIV over the last two decades such as the introduction of antiretroviral therapy, lifelong treatment and pre-exposure prophylaxis. Despite this progress, the number of people living with HIV is still increasing. This can be explained by two phenomena: i) infected individuals live longer thanks to effective treatment and ii) new infections still occur since current use of prevention methods is not high enough and infected individuals are diagnosed too late. In other words, there is too much time between the occurrence of infection and its diagnosis.

This project aimed to assess awareness, knowledge and willingness to be tested for HIV infections among the MSM community in order to identify possible barriers to testing and propose plans for HIV prevention interventions tailored to the MSM community in Norway.

**Role**: Ettore was involved in the literature search developing the research protocol. According to the new General Data Protection Regulation, the fellow as project leader carried out the ethical and impact assessment evaluation for project feasibility.

### 2.3 Research for COVID-19 human infections in Norway

COVID-19 has spread rapidly around the world, affecting every community directly or indirectly. As with many novel respiratory pathogens, key epidemiological, clinical and virological parameters of the virus and the outbreak dynamics are unknown at the beginning, particularly its ability to spread in the human population and its virulence (case-severity).

**Role**: Participation as part of the research team working in the implementation of the protocol 'first few cases and contact investigation for 2019-novel coronavirus (2019-nCoV) infection' published by WHO. Drafting Ethical approval and evaluating project feasibility based on capacity and needs in Norway.

### **Training modules**

The <u>EPIET/EUPHEM Introductory Course</u> familiarised fellows with developing and presenting study protocols.

The <u>Outbreak Investigation Module</u> introduced methods of whole genome sequencing and next generation sequencing.

The <u>Management, Leadership and Communication in Public Health Module</u> trained fellows in many aspects of management, collaboration and communication including time management, team collaboration, and efficient presentation deliveries according to target audiences.

The <u>Multivariable Analysis Module</u> provided a more comprehensive understanding of the principles of statistical analyses, and how to build an optimal model using linear, logistic, Poisson and Cox regression.

### **Educational outcome:**

Ettore was familiarised with all stages of conducting a public health research project, from identification of the public health problem, reviewing literature, writing study protocols, understanding laboratory methods, analysing data, and writing scientific manuscripts.

# **3. Applied public health microbiology and laboratory investigations**

Supervisors: Umaer Naseer, Emily MacDonald and Hans Blystad

### *3.1 Laboratory-based surveillance of Vibriosis and Shewanella infections in Norway, 2014-2018*

Gram-negative bacilli *Vibrio* spp. and *Shewanella* spp. are a major cause of severe waterborne infection. This project aimed to describe the epidemiology of invasive and mild non-cholera *Vibrio* and *Shewanella* spp. infections in Norway during the 5-years period 2014-2018 and to explore possible relatedness of Norwegian isolates in order to evaluate additional preventive and control measures.

The data were provided to NIPH by the medical microbiological laboratories in Norway. Information was collected on non-cholera *Vibrio* and *Shewanella* cases. *Vibrio* isolates were sent from the local reference laboratories, where the primary isolation and identification is performed, to the national laboratory at NIPH.

Between 2014 and 2018, 267 and 82 non-cholera Vibrio and Shewanella cases were detected and reported by Norwegian medical laboratories, respectively. Twenty out of 21 Norwegian laboratories replied to the NIPH's survey on total number of cases during the study period reaching a response rate of 95.2%. Following an average of 41.3 non-cholera *Vibrio* and 12 *Shewanella* cases reported annually from 2014 to 2017, we observed an increased number of cases in 2018, when 102 and 34 cases were registered respectively. The number of *Vibrio* and *Shewanella* cases in 2018 was almost threefold increase (2.5-2.8) compared with the average of previous years. Reporting of cases followed a season distribution with mostly of non-cholera *Vibrio* (53.6%) and *Shewanella* (48.8%) infections during summer months. The majority of non-cholera *Vibrio* and *Shewanella* cases were males (57.3% and 67.1%) with a male to female ratio of 1.3 and 2.0 respectively. The median age of the cases was 36 for non-cholera *Vibrio* and 48 years old for *Shewanella* infections. The highest incidence was reported in the age groups >65 years old (24.5%). Non-cholera *Vibrio* and *Shewanella* infections showed a similar geographical distribution with the highest number of cases reported in the South-East region, followed by South, West, Center and North region. Phylogenetic Single-Nucleotide-Polymorphisms (SNP) analysis of *Vibrio* isolates detected two small clusters of non-toxigenic *Vibrio cholerae* with <30 SNPs difference and a major cluster of 8 *V. vulnificus* isolates with <5 SNPs difference during the study period.

Overall the study further investigated the epidemiology of *Vibrio* and *Shewanella* spp. infections in Norway. An increasing number of cases was reported during the period under study (2014-2018), especially during the last warmest summer in 2018. Descriptive epidemiological analyses gave an insight into age and sex distribution, as well as seasonal variation of *Vibrio* and *Shewanella* infections. Molecular analysis using WGS provided useful information on the relatedness of Norwegian isolates and the similarity with strains isolated at national level. This study provided valuable scientific information in order to update current public health advices and prevent infections especially during heatwaves in summer.

**Role**: Ettore was involved in the literature search developing the project design and the scientific protocol. According to the new General Data Protection Regulation, the fellow as principal investigator carried out all the management and administrative steps of ethical approval request to the Regional Committee for Medical and Health Research Ethics and impact assessment to the Data Protection Office. The fellow was also involved in the sequencing analysis at the national laboratory performing bacterial isolation and DNA extraction of the Vibrio isolates. The main scientific tasks included collection, analysis and interpretation of epidemiological and molecular data. In addition, the fellow was in charge of the report drafting for the Norwegian laboratories and updating public health advices published on NIPH webpage.

### **Training modules**

The EPIET/EUPHEM Introductory Course familiarised fellows with developing and presenting study protocols.

The <u>Outbreak Investigation Module</u> introduced methods of whole genome sequencing and next generation sequencing.

The <u>Time Series Analysis Module</u> trained fellows in find associations between independent data such as climatic factors and increase of the number of cases.

The <u>Management, Leadership and Communication in Public Health Module</u> trained fellows in many aspects of management, collaboration and communication including time management, team collaboration, and efficient presentation deliveries according to target audiences.

### Educational outcome:

The fellow deepened his public health microbiology knowledge in terms of laboratory investigations gaining experience preparing the scientific protocol, working with the Norwegian laboratories network, managing time and collaborating with experts.

## 4. Biorisk management

Supervisors: Siri Feruglio, Tone Bjørndal Johansen and Didrik Vestrheim

### 4.1 BSL-3 Biosafety and Biosecurity training

Training for BSL-3 preparedness laboratory staff at NIPH included a general theoretical and a general practical part given by Siri Feruglio and Tone Bjørndal Johansen. Topics covered were laboratory biosafety levels and microbial risk group classification, biosafety and biosecurity legislation and standards, risk assessments, physical barriers in the laboratory, personal protective equipment, safe working practices and operating procedures including following spills, illness, fires etc. The fellow learnt how to put on and wear PPE, work in the laboratory, and manage laboratory waste. In addition, the fellow participated in training on virus RNA-extraction and handling suspicious letters potentially contaminated with *Bacillus anthracis* (anthrax) in the BSL-3 laboratory glove box; this part of the training was given by Veronica Klausmark and Margrete Solheim. The fellow received a BSL-3 training certificate issued by NIPH.

### **Training modules**

The fellow was trained by the Norwegian Institute of Public Health. Theoretical material was also provided by ECDC.

### **Educational outcome:**

Ettore developed an understanding of the importance of biorisk management, and the requirements necessary to control risks associated with handling, storage and disposal of biological agents and toxins in laboratories, understanding the processes associated with BSL-3 and BSL-4 laboratories as well as biosafety risk assessment and mitigation.

## 5. Quality management

Supervisor: Didrik Vestrheim and Umaer Naseer

### 5.1 Survey on Pertussis for laboratories in Norway

The ECDC Annual Epidemiological Report on pertussis surveillance (published in 2019) reported 42,242 cases of pertussis in EU/EEA countries in 2017. Individuals  $\geq$  15 years of age accounted for 62% of all cases reported. Infants below the age of one year, too young to be vaccinated, were the most affected age group, with the highest rate of 53.9 per 100 000 population and three deaths reported. Five EU countries (Germany, The Netherlands, Poland, Spain and United Kingdom) accounted for 76% of all reported cases. The Notification rate in EU/EEA countries is 9.4 cases per 100 000 population. Norway reported the highest notification rate with 46.1 per 100 000 population, followed by The Netherlands, Germany and Denmark. Following this background, the Norwegian Institute of Public Health (NIPH) planned to send a national survey on pertussis diagnostic capability and practices in the diagnostic laboratories in Norway in order to evaluate the testing activity and the methods used by the Norwegian laboratories for possible future harmonisation.

**Role**: Ettore was involved in the survey design, the internal piloting process and the update of the email address list of Norwegian laboratories.

# 5.2 External Quality Assessment (EQA) for typing of Shiga toxin-producing Escherichia coli (STEC)

On February 2020, the NIPH was invited to participate to the `Tenth External Quality Assessment (EQA) scheme for typing of Shiga toxin-producing *Escherichia coli* (STEC) in 2019-2020 organised by the Statens Serum Institut on behalf of the European Food- and Waterborne Diseases and Zoonoses Programme, ECDC (ECDC-FWD). The aim of the EQA was harmonization of the typing methods used by the European laboratory network, in order to produce comparable typing data for STEC isolates between laboratories and to ascertain high quality data submissions to the European Surveillance System (TESSy).

The STEC EQA included three parts: O and H Serotyping, virulence gene determination (*stx1*, *stx2*, *eae*, *aaiC*, *aggR* and subtyping) and molecular typing-based cluster analyses (PFGE and/or WGS). For this purpose, NIPH received 10-blinded STEC isolates for serotyping/virulence profile determination and 10-blinded STEC isolates for cluster identification.

**Role**: Ettore was involved in the EQA's procedures and the submission of the report through the official online platform.

### Training modules

The fellow was trained by the Norwegian Institute of Public Health. Theoretical material was also provided by ECDC.

#### **Educational outcome:**

Ettore familiarised with and applied the concepts of quality assessment and harmonisation of laboratory methods as an essential aspect of quality management systems.

## 6. Teaching and pedagogy

# 6.1 Delivering lecture through Problem-Based Learning (PBL) on Importance of AMR as Public Health treat

Problem-Based Learning (PBL) as part of a one-day exercise during the ECDC EPIET/EUPHEM Introductory course in Spetses (Greece). Ettore, in close collaboration with EUPHEM fellows cohort 2018, delivered a training lecture on the importance of Antimicrobial Resistance (AMR) as public health treat, hospital acquired infections and carbapenemases resistance.

### 6.2 Developing teaching materials and delivering lecture on Travel Vaccinations

Teaching given as part of a one-day course on vaccines organised by the NIPH in collaboration with the University of Oslo, School of Pharmacy, for university students. Ettore developed and delivered lecture covering the role of vaccines in preventing disease during or after travel was covered and participants were familiarised with the factors that should be considered when giving travel advice related to vaccination.

### 6.3 Developing teaching materials and delivering presentation on multi-country outbreak of Salmonella Agona infections linked to infant formula

Teaching given as part of a one-day course during the ECDC EPIET/EUPHEM Outbreak Investigations module in Berlin (Germany). Ettore delivered a training lecture to EUPHEM fellows on the multi-country outbreak of *Salmonella* Agona infections linked to infant formula highlighting the importance of risk assessment, management and communication in multi-country outbreaks.

### 6.4 Developing teaching materials and delivering presentation on Vibrio infections during a Nordic countries workshop organised by NIPH

On September 2019, a Vibrio Workshop was organised by NIPH. EUPHEM fellows involved in the multi-country *Vibrio* project jointly discussed the preliminary findings in each country. In addition, teaching lectures were delivered by NIPH experts to fellows. Ettore was involved as presenter for the Norwegian data, organiser and chair of the workshop on behalf of NIPH.

# 6.5 Developing teaching materials and delivering presentation on outbreak investigations

Teaching given as part of an academic course at the University of Milan for university master students. Ettore developed and delivered a teaching lecture including a case-study describing an outbreak of gastrointestinal disease caused by *Campylobacter* in drinking water in Norway. In addition a reflective teaching report and an evaluation of the teaching assignment was written following the training.

# 6.6 Collaboration in developing a case study on implementation of surveillance systems

Ettore collaborated in developing a case-study on the new *Vibrio* surveillance system in place in Norway. The case study was carried at Göteborgs universitet (Sweden) by the EPIET fellow placed in Norway in March 2020.

### **Educational outcome:**

Ettore learned and gained experience on all stages of teaching, from outlining course objectives, developing the curriculum and lectures, giving lectures and facilitating case studies to different audiences.

## 7. Public health microbiology management

### 7.1 Management during outbreak investigations

All outbreak investigations undertaken throughout the fellowship involved public health management, including time management, communicating between epidemiologists and the microbiology laboratory, team building and coordination, research collaboration and management of cultural differences in international contexts. For all projects, the fellow described the benefit to public health microbiology and was engaged in scientific communication to peers and stakeholders. During the outbreak investigations, Ettore was engaged in scientific communication to peers/stakeholders and involved in planning response and control measures. Some of the acquired skills included team building and negotiation skills by working as a team member during the projects working alongside

epidemiologists and microbiologists from different departments at NIPH. The fellows' communication output in terms of manuscripts, reports, and presentations are listed in *section 8*.

### 7.2 Management of ethical approval and data protection processes

According to the new General Data Protection Regulation, Ettore as principal investigator and project leader processed and followed-up all the management and administrative steps of ethical approval request to the Regional Committee for Medical and Health Research Ethics and impact assessment to the Data Protection Office. These extensive procedures were carried out both for the surveillance project on group A streptococcal infections and the research project on *Vibrio* and *Shewanella* infections in Norway.

### 7.3 Management and Coordination of the Multi-Country Vibrio project

In line with the General Data Protection Regulation and national legislations, Ettore as project coordinator was in charge of the multilateral country collaboration agreements writing the final agreements in collaboration with third parties involved and their legal departments. The fellow was also organising and chairing Teleconference meeting between Nordic countries and countries bordering the Baltic Sea during the project. Ettore also organised and participated in this two-day Nordic Vibrio Workshop which was held at NIPH in September 2019. The main tasks included the practical arrangements, including inviting principal investigators, drafting the agenda for the workshop and identifying and inviting local experts to facilitate sessions.

### 7.4 Management of Peer-Review processes in collaboration with Journal Editors

During his fellowship, Ettore was invited and accepted to be a peer reviewer for three scientific manuscripts sent to Lancet Infectious Diseases, Parasite Epidemiology and Control and BMC Infectious Diseases journal.

### 7.5 Management of team working activities

Ettore was involved in the team working activity between the EPIET/EUPHEM fellow in view of the presentation for the Management, Leadership and Communication in Public Health module.

### **Training modules**

The <u>Management, Leadership and Communication in Public Health Module</u> familiarised participants with understanding roles and responsibilities in public health management settings. Topics covered included the identification and application of different management styles, team roles and team evolution, the delegation of tasks and the provision of structured, clear and efficient feedback.

### **Educational outcome:**

Ettore experienced general public health management throughout his projects, such as applying principles of scientific communication to peers, stakeholders and the public, recognising the role of different agencies, identifying interdisciplinary needs between public health professionals.

## 8. Communication

### 8.1 Scientific Publications related to the EUPHEM fellowship

- Amato E., Dansie L.S., Grøneng G.M, Blix H.S., Bentele H., Veneti L., Stefanoff P., MacDonald E., Blystad H.H., Soleng A. Increase of Scabies Infestations, Norway, 2006 to 2018. Euro Surveill. 2019 Jun;24(23):190020. doi: 10.2807/1560-7917.ES.2019.24.23.190020.

- Hyllestad S., Iversen A., MacDonald E., **Amato E.**, Sørby Borge B.A., Bøe A., Sandvin A., Brandal L.T., Lyngstad L.M., Naseer U., Nygård K., Veneti L., Vold L. Large waterborne Campylobacter outbreak in Norway: use of multiple approaches to investigate contamination of the drinking water supply system. Euro Surveill. 2020 Sep; 25(35):2000011. doi: 10.2807/1560-7917.ES.2020.25.35.2000011.

- **Amato E.**, Riess M., Thomas-Lopez D., Linkevicius M. and *the Vibrio investigation team*. Vibriosis in Northern Europe in 2018: an emerging public health threat? - Manuscript in preparation.

### 8.2 Conference presentations

- Oral communication as invited speaker (25 minutes presentation) on *Vibrio* infections in 2018 at the Nordic Society of Clinical Microbiology and Infectious Diseases Conference (NSCMID 2019, September 12-15, Trondheim – Norway.

- Oral communication as invited speaker (10 minutes research report presentation) at the 8<sup>th</sup> meeting of the Nordic/Baltic Network for Water and Health. December 2019, Riga – Latvia

- **Amato E.**, Riess M., Thomas-Lopez D., Linkevicius M. and *the Vibrio investigation team*. Multi-country occurrence of non-toxigenic cholera and non-cholera *Vibrio* infections in Nordic countries and countries bordering the Baltic Sea in 2018. (Poster presentation, ESCAIDE 2020)

### 8.3 Reports and other communications

- Translation of informative material from Norwegian to Italian related to an outbreak of pneumococcal disease occurred on an International shipyard in Norway.

- Presentation of ecological study on scabies infestations in Norway 2006-2018 during the Project Review Module held in Prague, August 2019.

- Presentation of Norwegian data on scabies during a meeting with the Norwegian Medical Agency.

- Report on national surveillance systems for vibriosis and *Shewanella* spp. infections in EU/EEA countries (*submitted to ECDC*)

- Presentation of the teamwork results to the highest authorities at ECDC during the MLCPH module, February 2020.

- Replying to questions from Health Security officer during a simulation exercise of the MLCPH Module, February 2020.

### 8.4 Media - Press release

- Following media attention on scabies infestations, contribution to answers briefs for the spokesperson and media written questions from newspaper.

- Interviewed as principal investigator on the *Vibrio* project by NRK which is the Norwegian government-owned radio and television public broadcasting company, and the largest media organisation in Norway.

### Training modules

The <u>Introductory Course and the Project Review Module</u> familiarised participants with concepts relating to communicating efficiently and writing scientific articles, including how to present data in the form of tables and figures.

The <u>Management, Leadership and Communication in Public Health Module</u> familiarised participants with communication to different audiences including the public and higher authorities, and tailoring the main message depending on the audience.

### Educational outcome:

Ettore experienced and applied the principles of scientific communication to peers, stakeholders and the public, recognising the role of different agencies and the importance of clear communication targeted to different audiences.

## 9. EPIET/EUPHEM modules attended

- Introductory Course (IC), Spetses, Greece, Sep-Oct 2018 (3 weeks)
- Outbreak Investigation Module Robert Koch Institut, Germany, Dec 2018 (1 week)
- Multivariable Analysis Module Istituto de Salud Carlos III, Spain, Mar 2019 (1 week)
- Rapid Assessment & Survey Methods, Andrija Štampar School of Public Health, Croatia, May 2019 (1 week)
- Project Review Module, National Institute of Public Health, Czech Republic, Aug 2019 (1 week)
- Time Series Analysis Module National Institute for Public Health and Environment, Netherlands, Nov 2019 (1 week)
- Management, Leadership and Communication in Public Health Module ECDC, Sweden, Feb 2020 (1 week)
- Vaccinology Module provided by Institute Pasteur and ECDC through online platform (1 week)

## 10. Other training

- The European Scientific Conference on Applied Infectious Disease Epidemiology (ESCAIDE), Malta 2018;
- Training course on vaccinology provided by NIPH experts, Norway 2018
- EpiData exercise as part of the Copenhagen case study during the Outbreak Investigation Module (OIM) in Berlin;
- HIV Science MOOC provided by Institute Pasteur, 2019;
- R course provided by Norwegian Institute of Public Health, 2019;
- Nordic Mini Project Review Module, Copenhagen, Denmark, March 2019;

- Webinar course on Fundamentals of manuscript preparation (reference management, structure and abstract), Ethics (plagiarism, authorship, ownership, demystifying permissions), and Communication (writing lay summary, social impact) provided by Elsevier, 2019;
- Rapid Risk Assessment e-learning course provided by ECDC through EVA platform, 2019;
- United Nations Security in the field courses and GOARN eModules, 2019;
- Cross-border sharing of Public Health Data e-learning course provided by ECDC through EVA platform, 2019;
- Piloting outbreak simulation exercise at FHI, Oslo 2019;
- Basic R course organised by RECON, Stockholm, 2019;
- The European Scientific Conference on Applied Infectious Disease Epidemiology (ESCAIDE), Sweden 2019;
- WHO online course on Emerging respiratory viruses, including nCoV: methods for detection, prevention, response and control, 2020;
- Panel discussion with cross section of China's most leading experts on COVID-19, 2020;
- Italy's COVID-19 Experience: IANPHI Webinar by President of Italy's Istituto Superiore di Sanità, 2020;
- Fighting COVID-19 with Epidemiology: A Johns Hopkins Teach-Out, 2020;
- ECDC Video Conference: experience exchange on COVID-19 between ECDC and EPIET/EUPHEM fellows, 2020;
- One Health EJP Annual Scientific Meeting 2020 (OHEJP ASM 2020) 27-29 May 2020;
- Virtual Summer School on One Health organized by EFSA, June 2020;

# **Discussion**

## **Coordinator's conclusions**

One of the main goals of the EUPHEM programme is to expose fellows to diverse and multidisciplinary public health experiences and activities, thus enabling them to work across different disciplines. This report summarises all activities and projects conducted by Ettore Amato during his two-year EUPHEM fellowship (cohort 2018) as an EU track fellow at the Norwegian Institute of Public Health (NIPH) in Oslo, Norway. Ettore is the third appointed EU track EUPHEM fellow in Norway. The projects described in this portfolio demonstrate a diversity of public health microbiology projects. The epidemiological studies consisted from outbreak investigations (at regional and national level) to surveillance activities including invasive group A streptococcal or scabies infections in Norway or a survey on national surveillance systems for vibriosis and Shewanella spp. infections in EU/EEA countries. The laboratory and epidemiologically based projects covered all diverse range of disease programmes involving multidisciplinary working and teamwork on all levels such as physicians, laboratory technicians, epidemiologists, statisticians, government officials and public health officers, showing strength of the fellow and ability to work within such an extended environment(s). Ettore has shown a high capacity of public health management by working with an active role in interdisciplinary groups and bringing different professionals together. Activities were in line with the 'learning by doing' of the EUPHEM programme and fulfilled the core competency domains described for professionals in their mid-career and beyond. Activities were complimented by nine training modules providing theoretical knowledge. Projects had a clear outcome, with results communicated in scientific journals and at conferences. The contributions made by Ettore to NIPH work indicates importance of developing a future critical mass of highly skilled field 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 with a professional and critical attitude. We wish the fellow every success in his future career.

## **Supervisor's conclusions**

Ettore started the EUPHEM fellowship as an experienced microbiologist. Already from the start he was taking on tasks and projects with a very good sense for the public health need. He took a strong lead on the projects that was assigned to him, and also participated very actively in with suggestions and planning of projects. Ettore has also been building networks with colleagues in other countries, and among other things he initiated a project collaboration on Vibrio in seven countries. The numerous outputs of his projects have added to both national and international public health activities. Ettore has balanced very well between pragmatic problem solving and scientific work according to what has been the need in different situations. In all his activities, he has established good and strong relationships with project supervisors and co-workers from several departments in the institute.

## **Personal conclusions of fellow**

The EUPHEM fellowship has provided me with the unique and rewarding opportunity, both on a professional and personal level, to work on interesting national and international projects, collaborate with very experienced public health professionals at NIPH and attend high-quality training modules in the field of public health. Through my projects and activities, I have acquired key technical skills in public health microbiology and epidemiology. I have also further developed my interpersonal skills such as project management and coordination of multi-country project, cross-sector collaborations and risk communication through national media. I have especially appreciated the integrated approach between public health microbiology and epidemiology by bridging the gap and developing understanding between different disciplines, as well as establishing and expanding Europe-wide networks of highly skilled colleagues in public health. Overall, I think that the ECDC Training Programme has been a relevant step in my career as public health expert.

## **Acknowledgements of fellow**

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