EUPHEM



EUPHEM REPORT

Summary of work activities Heli Harvala Simmonds European Public Health Microbiology Training Programme (EUPHEM), 2014 cohort

Background

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'.

The ECDC Fellowship Training Programme therefore includes two distinct curricular pathways: Intervention Epidemiology Training (EPIET) and Public Health Microbiology Training (EUPHEM). After the two-year training EPIET and EUPHEM graduates are considered experts in applying epidemiological or microbiological methods to provide evidence to guide public health interventions for communicable disease prevention and control. Both paths that provide competency based training and practical experience using the 'learning by doing' approach in acknowledged training sites across European Union (EU) and European Economic Area (EEA) Member States.

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 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.

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This report summarises the work activities undertaken by Heli Harvala Simmonds, cohort 2014 of the European Public Health Microbiology Training Programme (EUPHEM) at the Public Health Agency, Stockholm, Sweden.

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

Pre-fellowship short biography

The fellow has both a scientific and a medical background; she obtained a Master of Sciences degree in Organic Chemistry and a PhD in Virology at the University of Turku, Finland in 2003. After that she moved to the UK, where she completed her medical registration before commencing specialist training in Medical Virology at the Edinburgh Royal Infirmary. She is a Fellow of the Royal College for Pathologists, and had done active research in the field of clinical and public health virology and epidemiology alongside her clinical work. She is interested in combining her Clinical Virology career with the public health, and especially keen to explore the significance of emerging virus infections.

Fellowship assignment: Public health Microbiology (EUPHEM) path

Methods

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

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

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

Results

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

1. Epidemiological investigations

1.1. Outbreak investigations

A. Hepatitis A outbreak in Uppsala, Sweden

Laboratory supervisor: Josefine Ederth

A total of 14 cases of acute hepatitis A virus (HAV) infections were notified from Uppsala during November 2014. All cases were shown to be infected with an identical strain of HAV genotype 1A, but despite the extensive investigations including trawling questionnaire no common source could be identified. Most of the cases were young school children aged between 4 and 10 years. Active case finding was conducted in one school involved, whereas one nursery decided to vaccinate everybody instead of testing. The fellow's role in this outbreak investigation was to perform HAV genotyping and sequence analysis of samples received in order to define an outbreak, and also communicate these findings to the outbreak investigation team.

B. Increased number of Campylobacter bacteremia cases in Sweden, 2014

Supervisors: Anders Wallensten and Cecilia Jernberg

A detailed retrospective investigation on *Campylobacter* infections in Sweden was performed; an increased numbers of *Campylobacter* detections in blood samples had been first noted in July 2014. It was thought that this could have been a result of a general increase in incidence of *Campylobacter* infections likely due to an outbreak, or the observed increase could have resulted from increased testing or from a change in laboratory methods. Data

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

on all notified laboratory-confirmed cases showed that the number of *Campylobacter* detections in stool samples had remained steady between 2010 and 2014, whereas the number of *Campylobacter* detections in blood samples had increased from 5 in 2010, 2 in 2011 and 10 in 2012 to 32 in 2013 and 83 in 2014. The annual testing numbers of blood and stool cultures in Sweden were also reviewed, but no significant changes were observed between 2010 and 2014. To investigate the possible change in laboratory methods, an on-line questionnaire regarding the methods used for blood culturing and detection of *Campylobacter* in blood was submitted to all 24 clinical microbiology. It was noted that new blood culture media bottles (BacT/Alert Plus) were introduced in Sweden towards the end of 2013. In 2014, a total of 76 campylobacteremia detections were done in laboratories which used these BacT/Alert Plus bottles (incidence 1.0 per 100.000 inhabitants), and only seven detections were done with the other blood culture bottles (incidence 0.2 per 100.000 inhabitants). The change in blood culture media bottles coincided with the increased detection of *Campylobacter* in blood in Sweden. These findings indicate the incidence of campylobacteremia has been underestimated, not only in Sweden but also elsewhere. The Fellow conducted all stages of this study; she planned the on-line questionnaire, explored the sources for the denominator data, analysed the results, and wrote as well as communicated the manuscript for publication (see 8.A2).

C. Cryptosporidium outbreak

Outbreak supervisor: Marika Hjertqvist

A total of 9 laboratory confirmed cases of *Cryptosporidium* were reported to the Public Health Agency of Sweden at the end of November, 2015. It was noted that all these cases had visited the dental fair in Göteborg between 12 and 14 November, which prompted further outbreak investigations including a case-control study. We informed 5000 participants of these initial findings, and advised to seek medical care if symptoms keeping with *Cryptosporidium* infection. A questionnaire exploring the potential risk factors was also submitted to them; 81 participants from 1560 respondents had experienced gastrointestinal symptoms between 14 and 24 November. However, infection in only 16 individuals had been laboratory confirmed. Based on molecular typing, all isolates received were closely related or identical to each other; no food samples were left for typing to confirm the link. As most dental fair participants had been exposed to the same food, the case-control study did not result any significant or conclusive findings. The fellow participated in outbreak meetings including the formation of the case definition and questionnaire, as well as the data analysis. She also gained familiarity with the molecular typing method currently used for *Cryptosporidium* in the Agency.

D. EHEC 0130 outbreak

Outbreak supervisor: Emma Löf

Whole genome sequencing (WGS) was introduced for the routine characterisation of all enteroheamorrhagic *Escherichia coli* (EHEC) cases in Sweden at the end of December 2015. Identification of an unusual high number of EHEC 0130 cases within a day-care center prompted initiation of outbreak investigations. A total of 64 cases were identified; 33 of them from the County of Västra Götaland whereas the remaining cases were spread over ten other counties. To identify the source of infection, a matched case-control study was carried out. Four healthy controls per case were randomly selected from a national population-based cohort group called 'Hälsorapport'. As a result, raisins (adjusted matched Odds Ratio [amOR]: 8.0; 95% Confidence Interval [CI]: 1.7-37.0) and sausages (amOR: 4.1; CI: 1.1-14.0) were identified as the most likely sources of infection. Random samples of raisins and sausages tested negative for EHEC and the biological plausibility of these findings remain unclear. Furthermore, all infections described have been mild and no cases of hemolytic uremic syndrome (HUS) were identified. This is consistent with the characteristics of this EHEC 0131 strain harboring the milder form of Shiga toxin-encoding gene (stx1a). The fellow participated to the outbreak meetings and was involved in the planning of trawling questionnaire as well as helping to finalise the study report together with an EPIET fellow.

E. Training modules

The EPIET/EUPHEM introductory course provided participants with the basic concepts of logistical and analytical approach to outbreak investigations, including the ten steps of an outbreak investigation. The module 'Outbreak investigations' taught fellows how to perform analytical epidemiological studies within outbreak investigations using various software packages. During the module fellows performed all steps involved in outbreak analysis from creation of a data entry file to the stratified analysis using EpiData, Stata and Microsoft Excel. They 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 'Multivariable analysis' module 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 in STATA.

Educational outcome: application of microbiological and epidemiological knowledge in outbreak situations; participation in a multidisciplinary outbreak team and involvement in outbreak investigations (case definition, case-finding, data collection, data analysis, laboratory typing methods, communication); dataset management; writing of report and scientific publication.

1.2. Surveillance

A. Cryptosporidium infections in Sweden, 2014 – understanding the regional differences in reported incidence

Supervisor: Cecilia Jernberg and Jessica Beser

This was a subproject of the collaborative project performed between the main three public health institutions in Sweden: Public Health Agency, National Veterinary Institute and National Food Agency. The main aim of the whole project was to map and analyse surveillance systems in place in Sweden for monitoring and early recognition of suspected outbreaks caused by the six most common zoonotic enteropathogens using a 'One Health' approach. In the first part of this project, data on primary human, animal and food diagnostics was collected. Here, the results from cryptosporidium human diagnostics are presented and the fellow was primarily involved in questionnaire design in human fields. She analysed the data obtained for Cryptosporidium, and proposed as well as wrote the manuscript which is summarised below (see 8.A5).

Cryptosporidium surveillance has revealed substantial differences in disease incidence throughout Sweden. The highest incidence of Cryptosporidium was noted in Halland, Jönköping and Uppsala counties in 2014 (33.44, 21.20 and 14.90 per 100.000 inhabitants, respectively), whereas the incidence varied between 0 and 3.94 in the remaining 18 counties. Microscopy with modified Ziehl-Neelsen staining (mZN) is the gold standard method for identification of *Cryptosporidium*, but PCR-based methods are also increasingly used. PCR-based methods are faster and easier to perform, and hence allow the screening of larger number of samples. The aim of this project was to evaluate how Cryptosporidium diagnostics is currently performed in Sweden in order to identify reasons for the observed differences between counties. An on-line guestionnaire regarding the screening strategies and laboratory methods used was submitted to all 26 clinical microbiology laboratories in Sweden. Twelve laboratories use mZN method, whereas four laboratories use PCR and four additional laboratories use both mZN and PCRmethod. Six laboratories do not provide any Cryptosporidium testing; they refer samples for testing elsewhere. Six of the eight laboratories using PCR-method have introduced PCR testing towards the end of 2014; two laboratories performing PCR testing from the beginning of 2014 are Halland and Uppsala. Laboratories in Halland, Uppsala and Jönköping screened the biggest number of stool samples (approximately 5000 samples each), whereas the remaining 18 counties either performed a small number of mZN staining annually (range: 20-1200 samples) or referred samples elsewhere for testing. In conclusion, Cryptosporidium infection is significantly underdiagnosed in Sweden, especially in counties where a selective testing criteria is used or when samples are referred elsewhere for testing. Introduction of PCR-based methods seem to improve the number of samples screened, and also the number of positives identified. We recommended requirement of further guidance for Cryptosporidium screening in Sweden.

B. European non-polio enterovirus surveillance and laboratory detection – are we prepared to detect a next enterovirus outbreak?

Supervisors: Eeva Broberg and Aftab Jasir

The aim of this study was to evaluate European preparedness for detection and characterisation of non-polio enteroviruses (EV) in order to improve our response for (re)-emerging enteroviruses linked to severe disease. Recent European outbreaks of EV-D68 and EV-A71 have both been associated with severe neurological infections, but the variety of non-polio enterovirus surveillance performed in Europe as well as the detection and typing methods used including their potential applicability for detection of specific enterovirus types is currently not known. An on-line survey exploring these factors was submitted to all EU/EEA countries; 29 out of 30 responded. Based on the survey, the laboratory-based non-polio enterovirus surveillance is performed in 27 countries but the activity measured as the number of enterovirus-positive samples typed in 2015 varied remarkably between the countries and the surveillance systems did not always include neurological or respiratory infections. Alarmingly, eleven countries reported that they had typed less than 50 specimens each. Guidance for systematic testing of individuals with neurological infections for enteroviruses is needed throughout Europe, not only in view of emerging enteroviruses but also for poliovirus. Furthermore, only eleven EU/EEA countries have introduced a specific surveillance for EV-D68, often utilising the existing sentinel surveillance systems. The survey also revealed issues relating to enterovirus typing/characterisation; seven countries are still relying on virus neutralisation which is known to be insensitive, labour-intensive and slow. It is important to consider what is required for introduction of sequencing based typing methods for enterovirus surveillance in those countries; is it the skills needed for sequencing, machinery and/or sequence management itself? Introduction of molecular surveillance throughout the EU/EEA region would be also hugely beneficial for poliovirus eradication, influenza surveillance and measles elimination programs.

This study was performed as an ECDC mission. The fellow has been responsible for all the steps from writing a study protocol for proposed project to survey design, data analysis and writing the manuscript (see 8.A6). As the project was closely related to the on-going work on environmental poliovirus surveillance in the EU/EEA region, the fellow has also been involved on survey design and analysis as well as manuscript writing for that project (see 8.A7).

C. Evaluation of Swedish RSV surveillance system

Supervisors: Mia Brytting and AnnaSara Carnahan

The Public Health Agency of Sweden provides comprehensive data on RSV (Respiratory Syncytial Virus) infections diagnosed in Sweden, and is based on voluntary reporting by microbiology laboratories and clinics performing the testing. These data are analysed and results published in the form of RSV report weekly. The RSV surveillance aims to guide clinicians through the RSV season, for example, to help them to optimize the timing of RSV immunoprophylaxis and prevent serious RSV infections among vulnerable infants in a costly manner. However, there was an increasing concern that the current system did not cover all RSV infections diagnosed in Sweden as the clinics and wards may have started to perform their own testing outside the main laboratories. Furthermore, there were concerns relating to the quality of methods used for the detection of RSV. The aim of this study was to evaluate how RSV testing is currently performed in Sweden and identify potential parties outside the current surveillance system, as well as evaluate the usefulness of RSV surveillance to clinicians. Two separate questionnaires were submitted; one to the microbiology laboratories performing the testing and one to the readers of RSV report. As a result, seven clinical chemistry laboratories and three paediatrics clinics not currently participating to Swedish RSV surveillance or quality control program were identified. Furthermore, insensitive testing method (chromatographic antigen detection test, often referred as near-patient test) was used by three laboratories and eight clinics. Reporting to the current surveillance system took 15 mins weekly, and nine laboratories found it time-consuming in the era of automation. The published data included in weekly RSV reports were used by most clinical readers (38/45); either to guide timing of RSV immunoprophylaxis, as for staff information or for hospital preparedness. In conclusion, RSV surveillance data was widely used but a need for a faster reporting platform was identified. The importance of confirming RSV results obtained by insensitive methods have been highlighted to the laboratories. Furthermore, clinical chemistry laboratories and clinics performing RSV testing have been encouraged to participate in RSV surveillance. These measures will instantly improve the Swedish RSV surveillance, and awareness of RSV in the pre-vaccination era. The fellow drafted all three on-line questionnaires, analysed the data and is currently writing the manuscript based on these findings (see 8.A8).

D. Training modules

The EPIET/EUPHEM introductory course introduced the basic concepts of surveillance systems, including the principles of surveillance, and how to develop, validate, evaluate and operate a surveillance system. As a part of this course, the fellow also participated in the development of the study protocol for introduction of RSV surveillance system in Germany. Furthermore, the specific approaches to the surveillance of vaccine-preventable diseases including calculation of vaccine coverage and vaccine effectiveness were presented at the 'Vaccinology module', and strategies utilised for the nutritional, morbidity and mortality surveys during the complex emergencies were covered in the 'Rapid assessment and survey methods module'.

Educational outcome: participation in disease-specific networks at the European level; analysis of national and European level surveillance systems; questionnaire design and computer tools; evaluation of laboratory-based surveillance system; understanding the challenges and limitations; authorities and responsibilities of those involved in surveillance; formulation of specific public health recommendations; writing of scientific articles.

2. Applied public health microbiology research

A. Epidemiology of Campylobacter jejuni infections in Sweden, November 2011 – October 2012: is the severity of infection associated with C. jejuni sequence type?

Supervisor: Anders Wallensten

Campylobacter ieiuni is the most common zoonotic bacterial cause of gastroenteritis in Europe, accounting for over 200,000 laboratory-confirmed cases every year. More than 8000 C. jejuni sequence types (STs) have been identified so far. Although very little is known about risk factors associated with the severity of infection, certain C. jejuni STs have been associated with the severe infections. A link between ST-22 and Guillain-Barré syndrome has been suggested, and ST-677 was recently linked to severe systemic infections. The aim of this project was to investigate risk factors associated with hospitalisation of C. jejuni-infected individuals. A total of 1,075 individuals with C. jejuni infection diagnosed between November 2011 and October 2012 in Sweden were included in this retrospective cohort study. Typing data for the isolates as well as clinical data including hospitalisation dates and diagnostic codes were obtained for C. jejuni -infected individuals. Factors associated with hospitalisation and length of hospitalisation were investigated by multivariable analysis. A total of 289 individuals were hospitalised due to C. jejuni infections, and those with co-morbidities were over 14-time more likely to become hospitalised than those without (Odds Ratio [OR] 14.39, 95% Confidence Interval [CI] 6.84-30.26). Furthermore, C. jejuni ST-257 (OR 2.38; CI 1.08-5.23), but not ST-22 or ST-677, was significantly associated with hospitalisation. In conclusion, ST-677 was not associated with increased hospitalisation or a longer hospital stay in our study whilst ST-257 was. Individuals with C. jejuni infection were generally more frequently hospitalised than previously demonstrated; the finding that requires further investigations especially when accurate hospitalisations rates are vital for the economic assessments. This project was done in close collaboration with National Veterinary Institute (SVA), which provided a fellow with a broader insight into the subject. The fellow wrote a research protocol for this study, performed all epidemiological analysis including multivariable analysis using STATA and wrote as well as communicated the paper for publication (see 8.A3).

B. Role of sequencing the measles virus heamagglutinin gene and hypervariable region in the measles virus investigations in Sweden during 2013-2014

Supervisors: Åsa Wiman and Mia Brytting

Molecular epidemiological investigations are vital not only in monitoring the progress of measles elimination but also establishing the source and transmission networks of specific measles virus strains. In the WHO European region, the genetic variability of circulating measles viruses has decreased and it has become increasingly difficult to determine the origin of a virus based on the currently obtained nucleoprotein (N) gene sequence alone. In this study, hemagglutinin (H) gene and hypervariable region were also amplified and sequenced from 53 out of 61 measles virus positive samples identified in Sweden between 2013 and 2014. 27 of these viruses were genotype B3, and the remaining 26 were genotype D8. Data on phylogenetic clustering of these viruses were compared to the epidemiological data. Both H gene and hypervariable region showed more variability than the N gene, and provided better differentiation of measles virus variants of the same genotype. In conclusion, the extension of the sequencing window to include the H gene and hypervariable region provided a more detailed picture of measles virus circulation in Sweden. Further identification and better molecular characterization of measles viruses also in an international context is essential for identifying transmission routes of measles within Europe and beyond, especially during the measles elimination end-game. This study highlights that the sequencing only the N gene region is not sufficient enough to reveal the transmission routes of measles virus, and the hypervariable region together with H gene should be used to complement these investigations. The fellow performed all the laboratory work for this study including phylogenetic analyses; she also wrote and communicated the manuscript for publication (see 8.A1).

C. Training modules

The EPIET/EUPHEM introductory module focused on the development and presentations of study protocols, including study objectives, aims, methods and expected outcomes, whereas the EUPHEM module 'Initial management in public health microbiology' concentrated on laboratory aspects, time management and team working during the research projects. The 'Outbreak investigations' and 'Multivariable analyses' modules provided further guidance and practical exercises for writing a scientific paper and abstract.

Educational outcome: conduct all stages of a public health microbiology research project from planning to writing a scientific paper; communicate all the stages of publication process including the critical revision of manuscript; review literature; design study protocol; identify limitations; disseminate and communicate the information; apply both microbiological and epidemiological knowledge in surveillance; apply and develop knowledge of typing methods used for Campylobacter species; conduct multivariable analysis.

3. Applied public health microbiology and laboratory investigations

A. The emergence and spread of moxifloxacin-resistant Clostridium difficile ribotype 231 in Sweden between 2006 and 2015

Supervisors: Kristina Rizzardi and Thomas Åkerlund

An aggregation of moxifloxacin-resistant *Clostridium difficile* ribotype 231 (RT231) was first identified in Stockholm county in 2008, whereas the spread of these RT231 isolates to 13 out of 21 Swedish counties became obvious by the end of 2015. The aim of this project was to investigate the epidemiology of *C. difficile* RT231 in Sweden between 2006 and 2015, and to evaluate whether this emergence could be associated with extended moxifloxacin usage. A total of 51 RT231 isolates were selected for the whole genome sequencing (WGS) and phylogenetic analysis. Based on the detailed SNP analysis, the circulation of three divergent sublineages of moxifloxacin-resistant *C. difficile* RT231 was demonstrated in Sweden during the 10-year study period. A set of closely related RT231 strains was identified in hospitals residing in the counties of Stockholm and Uppsala in 2008, whereas another set of RT231 isolates have continued to circulate in four different counties in the Uppsala-Örebro Health Care Region. A gradual drop in moxifloxacin use in the county of Stockholm coincided with a reduction of RT231 in the area, whereas the Uppsala County has the highest moxifloxacin prescription rate in Sweden. This study demonstrated the frequent transmission of *C. difficile* RT231 within and between counties indicating the importance of careful monitoring of hospitalised individuals infected with *C. difficile*. The study also identifies the need for a stricter moxifloxacin prescription policy. Furthermore, this study showed the usefulness and practicality

of WGS of *C. difficile* during the outbreak investigations. The fellow performed the cultivation of *C. difficile* strains for next generation sequencing, and was involved in the data analysis. She also wrote the manuscript, which has been submitted for publication (see 8.A4).

Educational outcome: identify the use and limitation of typing methods in outbreak investigations and surveillance; apply both microbiological and epidemiological knowledge in outbreak investigation and surveillance; apply knowledge of phylogenetics and existing measles database; understanding the roles and responsibilities of WHO accredited measles laboratory in the measles elimination process; interpret molecular laboratory data; understand the limitation of laboratory methods; analyse laboratory, drug resistance and national surveillance data; make scientific presentation at conferences; write scientific articles.

4. Biorisk management

A. Assessment of formaldehyde inactivation of emerging RNA viruses in terms of quality and biosafety of diagnostic electron microscopy

Supervisors: Kerstin Falk

The main aim of this project was to evaluate the efficiency of formaldehyde fixation using three different model viruses; one negative-sense RNA virus (Rift Valley Fever virus) and two positive-sense RNA viruses (Middle East respiratory syndrome coronavirus and Chikungunya virus). The formaldehyde fixation is expected to result effective inactivation of studied viruses and preserve the morphology of viruses better than the currently used glutaraldehyde. Published experimental data demonstrating virus inactivation by formaldehyde is largely lacking. Electron microscopy is in important component in the European Preparedness Plans for identification of emerging infectious diseases, and hence it is important to enhance both quality and biosafety of this method. This project provided to the fellow an opportunity to perform risk assessments required for the project, obtain practical experience on working with Chikungunya virus as well as use different decontamination strategies and personal protection at BSL3 laboratory. No scientific results have been obtained from this project yet.

B. Training modules

The EUPHEM module 'Biorisk management' provided training on techniques used for both biorisk and biosafety assessment as well as mitigation, including WHO recommendations on biorisk management in laboratories. Formal assessment and certificate was provided for international regulations on the transport of dangerous goods according to the International Civil Aviation Organization (ICAO). An overview of containment level 4 facilities was also provided and complemented with a visit to such laboratory at the Public Health Agency of Sweden, Stockholm. In addition, the fellow received formal introduction and assessment at her host site regarding safe working in BSL3 laboratory.

Educational outcome: understanding and experience of principles and practices applied for biorisk management; appropriate decontamination strategies and the use of personal protection in a BSL3 laboratory; knowledge of biosafety when working with infectious organisms; understanding the processes associated with BSL3 and BSL4 laboratories; biosafety risk assessment and mitigation; biosecurity risk assessment and mitigation.

5. Quality management

A. External quality assessment for influenza viruses

Supervisors: Helena Dahl and Mia Brytting

An external quality assessment (EQA) exercise for the molecular detection and characterization of currently circulating influenza viruses is organised annually for the Swedish microbiology laboratories. During the exercise, participating laboratories receive a panel of temporally representative influenza specimens, which they identify and subtype using methods of their choice. The selection process of influenza specimens included in the EQA panel was reviewed with the fellow, and she also participated to the evaluation and reporting of results obtained from the 2015 influenza panel. A total of 22 diagnostic laboratories participated to this EQA and 19 of them performed to high standard. As subtyping of influenza A(H1N1)pdm09 virus was only performed by 15 laboratories, all laboratories were reminded of their legal responsibility to notify all subtype A(H1N1)pdm09 infections in Sweden.

The EUPHEM module 'Quality Management' provided an overview of quality management systems used in diagnostic and public health laboratories according to the ISO15189 standards. Topics discussed included factors influencing quality in medical laboratories, internal and external quality control, accreditation, assessments and audits as well as importance of good documentation and record keeping.

Educational outcome: understand the principles and practices of quality assurance; prepare and analyse the results from an external quality assessment exercise; understand the local, national and European accreditation procedures.

6. Teaching and pedagogy

A. Training Session at the Meeting of the European Society for Clinical Virology

The fellow organised the first EUPHEM training session for the Annual Meeting of the European Society for Clinical Virology (ESCV) hold in Edinburgh, UK, September 2015. She contributed to the session from the initial idea to the practical performance, including identification of three additional facilitators and organising all the teaching materials. The idea arose from her previous experience; the clinical microbiology and scientist trainees often participate to the outbreak investigation at the local level but receive very little (if any) organised teaching on this topic. The session comprised a short introduction to the EUPHEM program followed by the introductory lecture to the outbreak investigations, and a case study on 'An outbreak of gastro-enteritis in Kalundborgh, Denmark'. A total of 32 participants from 11 different countries were divided into two groups during the case study, and both groups had two facilitators. The training session was highly appreciated by the participants, and will likely be repeated in another ESCV meeting.

B. Bioinformatics and Phylogeny Module for EUPHEM fellows

Supervisors: Aftab Jasir and Mia Brytting

The fellow led the organisation of the first Bioinformatics and Phylogeny Module, and contributed to the materials used during the module. A total of 17 EUPHEM fellows and five EUPHEM program co-coordinators including the Head of the EUPHEM program participated the module. The module provided fellows with basic definitions and concepts for the bioinformatics and basic phylogenetic analysis from a multiple sequence alignment to a constructing a phylogenetic tree in order them to be able to further develop their skills in next generation sequencing analysis. Three external experts and ten facilitators to support teaching were identified, and invited to the Module. The fellow drafted two case studies (one on 'The molecular investigations of the outbreaks of hepatitis A in Europe' and one on 'The molecular surveillance for influenza in Sweden) including raw sequence material based on her previous experience, and co-authored the third one ('Investigating a potential groups A streptococcus hospital transmission in the UK'). Other tasks undertaken by her included identifying prior knowledge and current learning needs of the co-fellows and developing the program based on the identified learning needs, coordinating the external experts and facilitators before and during the Module as well as writing the evaluation report based on the on-line questionnaire. Participants were very satisfied with the training activity and found the content very good; some fellows even thought this was the most relevant module for the EUPHEM fellows.

C. Phylogenetics Workshop for the ECDC Summer School

Supervisors: Aftab Jasir

The fellow participated in the planning and preparation of teaching materials for a two-day Phylogenetics Workshop hold at the 2016 ECDC Summer School in Stockholm. The workshop aimed to provide eleven participants with basic tools for phylogenetics in to order to allow them to deepen their knowledge and apply practical skills further in outbreak investigation and surveillance, either independently or together with microbiologists. It consisted of two lectures and three case studies. The fellow modified two previous case studies on Hepatitis A outbreak and Influenza surveillance according to the identified learning needs, and designed a new interactive case study around her project on *Clostridium difficile* investigations using next generation sequencing. The fellow facilitated independently all three interactive case studies, and had constructed detailed slides to guide each technical step from a multiple alignment to identification of antimicrobial resistance mutations and constructing ta phylogenetic tree. The workshop was targeted for both epidemiologists and microbiologists. The future need for expanding teaching in this field has been internationally recognised.

D. Facilitation of other case studies

The fellow acted as a facilitator for the case studies on 'Cryptosporidium in Östersund' and 'A epidemic Trichinosis in France'. The first case study was presented as a part of Introduction to Epidemiology course to the Medical Students from the University of Östersund, October, 2014, as well as to the Master of Infectious Disease Control course at Söderstorn Högskola, Stockholm, January 2014 and January 2015. The second case study was presented as a part of Epidemiological Investigations Course for the 5th Year Veterinary Students at the University of Uppsala, January 2014 and January 2015. Furthermore, fellow acted as a facilitator on the interactive case study on 'Ebola outbreak in Guinea' during the ECDC Module on Initial Management on Public Health Microbiology, February 2016.

E. Nordic Mini Project Review Module

The fellow co-organised together with EPIET fellow and participated to this two-day module, which is held annually in one of the Nordic countries to facilitate detailed presentation and discussion of current projects among EPIET and EUPHEM fellows in Finland, Sweden, Denmark and Norway. The tasks included the practical arrangements, drafting the program and inviting the local subject expert to each session. A total of 25 external experts (eight of them from ECDC) participated to the review of 15 projects, which were presented by 12 fellows.

Educational outcome: identify educational needs of target group; develop case studies and lectures based on educational needs; teach people with diverse background (MSc students, medical students, veterinary students, epidemiologists); plan, organise and deliver lectures, workshops and modules; teach laboratory, microbiology and epidemiological topics; organise meetings and workshops; guide case studies; evaluate teaching activities.

7. Public health microbiology management

A. Management during outbreak investigations and projects

Public health microbiology management was an important component of all projects and activities during the fellowship. During the campylobacteremia investigations and *Cryptosporidium* as well as RSV surveillance projects she communicated with Swedish microbiology laboratories, and during the enterovirus project, also with the European laboratories. The campylobacter, measles and RSV projects included intermediation between epidemiologist and microbiology laboratory, and *C. difficile* as well as measles project also acquired an efficient communication between the bioinformaticians and microbiologists. Organising the Bioinformatics and Phylogeny Modules for the EUPHEM fellows and for the ECDC summer school provided the fellow an opportunity to build and implement a vision as well as how to lead and motivate the team. In general, all her projects included ethical and integrity considerations, team building and coordination, research collaboration, time management and working in a multidisciplinary team with microbiologist, physicians, laboratory technicians, epidemiologists, statisticians and public health officers, from human, animal and food laboratories. For numerous projects in Sweden the fellow communicated with regional laboratories, national agencies, and within the ECDC project also with the EU/EEA member states.

B. Annual Meeting for the European Society for Clinical Virology

The fellow was involved in the organising committee for the annual meeting of European Society for Clinical Virology hold in Edinburgh UK, September 2014. It involved participation in teleconferences together with the organising committee, proposing the meeting program as well as suggesting and inviting the expert speakers to the meeting. The fellow was also involved in the review process of over 200 abstracts submitted to the meeting, and chaired a session on Enteroviruses during the meeting.

C. Training modules

The EUPHEM module 'Initial management in public health microbiology' focused on the understanding of roles and responsibilities in public health management. Topics included the introduction into different management styles, team roles and evolution of team, the delegation of tasks, the description of how to motivate teams to improve their performance, the provision of structured feedback, tools for effective time as well as stress management, communication with higher authorities and working under pressure in a complex emergency situation. **Educational outcome:** gain valuable experience of working in a different multidisciplinary public health teams; understand team management; understand time management; plan, schedule and organise research projects; organise and participate meetings; communicate through scientific writing and oral presentations; give and accept feedback.

8. Communication

A. Publications relating to EUPHEM fellowship

- Harvala H, Wiman Å, Wallensten A, Zakikhany K, Englund H, Brytting M. 2016. The role of sequencing of the heamagglutinin gene and the hypervariable region in the measles outbreak investigations in Sweden, 2013-2014. *Journal of Infectious Diseases* 15;213(4):592-9.
- Harvala H, Ydring E, Brytting M, Söderblom T, Mäkitalo B, Wallensten A, Tegmark Wisell K, Jernberg C. 2016. Increased number of *Campylobacter* bacteremia cases in Sweden, 2014. *Clinical Microbiology and Infectious Diseases 22:391-393.*
- Harvala H, Rosendal T, Lahti E, Engvall OE, Brytting M, Wallensten A, Lindberg A. 2016. Epidemiology of Campylobacter jejuni infection in Sweden, November 2011 – October 2012 – Is the severity of infection associated with C. jejuni sequence type? Infection Ecology & Epidemiology 6:31709.
- 4. Harvala H, Rizzardi K, Alm E, Åkerlund T. The emergence and spread of moxifloxacin-resistant *Clostridium difficile* ribotype 231 in Sweden. *New Microbes, New Infection 14:58-66.*

- Harvala H, Ögren J, Boman P, Riedel H, Nilsson P, Winiecka-Krusnell J, Beser J. Cryptosporidium infections in Sweden – understanding the regional differences in reported incidence. Clinical Microbiology and Infection, in press.
- Harvala H, Jasir A, Penttinen P, Pastore Celentano L, Greco D, Broberg E. Surveillance and laboratory detection for non-polio enteroviruses in the EU/EEA region – are we ready for the next enterovirus outbreak? Manuscript submitted to CMI.
- 7. Pastore Celentano L, Broberg E, Harvala H, Greco D. Future insight into environmental poliovirus surveillance in the EU/EEA region. Manuscript.
- 8. Harvala H, Carnahan A, Brytting M. Evaluation of RSV surveillance in Sweden. Manuscript in preparation.

B. Other publications

- 1. Kokki I, Smith D, Simmonds P, Ramalingam S, Wellington L, Willocks L, Johannessen I, Harvala H. 2015. Hepatitis E virus is the leading cause of acute viral hepatitis in Lothian. *New Microbes, New Infection.* 15(10):6-12.
- Smith DB, Ijaz S, Tedder R, Hogema B, Zaaijer H, Izopet J, Bradley-Stewart A, Gunson R, Harvala H, Kokki I, Simmonds P. 2015. Variablity and pathogenicity of Hepatitis E virus genotype 3 variants. *Journal of General Virology 96(11):3255–64*.
- 3. Harvala H, Hyypiä T. 2016. Parechoviruses. *Reference Module in Biomedical Sciences. (review article)*
- 4. Harvala H, Simmonds P. 2016. Viral meningitis in children. Lancet Infectious Diseases 16(11):1211-1212.

C. Reports

- 1. Folkhälsomyndigheten. Ökning av invasiv campylobacterinfektion en konsekvens av ändrade odlingsmedium. 2016. ISBN 978-91-7603-633-4. Published in Swedish only.
- 2. Report of survey results on laboratory testing for Salmonella, Yersinia, Campylobacter, Cryptosporidium and EHEC in Swedish microbiology laboratories. In preparation, in Swedish only.

D. Teaching materials

- 1. Case study on the molecular investigations of the outbreaks of hepatitis A in Europe for the EUPHEM Module on Bioinformatics and Phylogenetics, Stockholm, Sweden, 16-18 November, 2015. This included also collating all sequence data to be used in the case study.
- Case study on the molecular surveillance for influenza in Sweden for the EUPHEM Module on Bioinformatics and Phylogenetics, Stockholm, Sweden, 16-18 November, 2015. This included also collating all sequence data to be used in the case study.
- 3. Case study on the molecular investigations of the outbreaks of hepatitis A in Europe modified for the ECDC Summer School, Stockholm, Sweden, 9-10 June, 2016. This included also collating all sequence data to be used in the case study, and developing step-by-step guide for data analysis.
- 4. Case study on the molecular surveillance for influenza in Sweden modified for the ECDC Summer School, Stockholm, Sweden, 9-10 June, 2016. This included also collating all sequence data to be used in the case study, and developing step-by-step guide for data analysis.
- Case study on the molecular investigations of the emergence and spread of Clostridium difficile in Sweden for the ECDC Summer School, Stockholm, Sweden, 9-10 June, 2016. This included also collating all sequence data to be used in the case study, and developing step-by-step guide for data analysis.
- Introductory lecture on Ten Steps in Outbreak Investigations (45 minutes) and modified case study on Norovirus outbreak in Denmark for the first EUPHEM training session organised for the Annual meeting of the European Society for Clinical Virology, Edinburgh, UK, 9 September, 2015.

E. Conference presentations

- Harvala H, Ydring E, Brytting M, Söderblom T, Mäkitalo B, Wallensten A, Tegmark Wisell K, Jernberg C. Increased number of *Campylobacter* detections in blood samples in Sweden from June to October in 2014 – artefact or true increase? Oral poster presentation at the European Scientific Conference on Applied Infectious Disease Epidemiology (ESCAIDE), Stockholm 11-13 November, 2015.
- 2. Harvala H, Wiman Å, Wallensten A, Zakikhany K, Englund H, Brytting M. Should sequencing of the heamagglutinin gene or the hypervariable region be part of outbreak investigations in the measles elimination end-game? Oral poster presentation at ESCAIDE, Stockholm 11-13 November, 2015.
- Harvala H, Rosendal T, Lahti E, Engvall OE, Brytting M, Wallensten A, Lindberg A. Epidemiology of *Campylobacter jejuni* infection in Sweden between 2011 and 2012 – are infections caused by *C. jejuni* ST677 more severe than others? Oral poster presentation at ESCAIDE, Stockholm 11-13 November, 2015.

F. Submitted abstracts

- 1. Harvala H, Jasir A, Penttinen P, Pastore Celentano L, Greco D, Broberg E. European enterovirus surveillance and laboratory detection are we prepared to detect an enterovirus outbreak? Selected as poster presentation to ESCAIDE, Stockholm, Sweden, 28-30 November, 2016.
- 2. Harvala H, Rizzardi K, Alm E, Åkerlund T. The emergence and spread of moxifloxacin-resistant *Clostridium difficile* ribotype 231 in Sweden. Selected as oral presentation to ESCAIDE, Stockholm, Sweden, 28-30 November, 2016.
- Harvala H, Ögren J, Boman P, Riedel H, Nilsson P, Winiecka-Krusnell J, Beser J. *Cryptosporidium* infections in Sweden – understanding the regional differences in reported incidence. Selected as poster presentation to ESCAIDE, Stockholm, Sweden, 28-30 November, 2016.
- 4. Harvala H, Jasir A, Penttinen P, Pastore Celentano L, Greco D, Broberg E. European enterovirus surveillance and laboratory detection are we prepared to detect an enterovirus outbreak? Selected as oral presentation to the International Meeting on Picornaviruses (EUROPIC), les Diablerets, Switzerland, 4-8 September, 2016.
- Harvala H, Jasir A, Penttinen P, Pastore Celentano L, Greco D, Broberg E. European enterovirus surveillance and laboratory detection – are we prepared to detect an enterovirus outbreak? Selected as oral presentation to the Annual meeting of the European Society for Clinical Virology (ESCV), Lisbon, Portugal 14-17 September, 2016.
- 6. Harvala H, Carnahan A, Brytting M. RSV surveillance in Sweden can we improve it? Selected as a poster presentation, ESCV, Lisbon, Portugal 14-17 September, 2016.

G. Selection of other presentations

- 1. Harvala H. Introduction what is EUPHEM program? Microbiology seminar at the Public Health Agency of Sweden. 12 November, 2014.
- 2. Harvala H. Microbiological Surveillance. Lecture to the Master's Students at the Karolinska Institute, Stockholm Sweden. 16 December, 2014 and 13 January, 2015.
- 3. Harvala H and Pini A. Ebola preparedness in Sweden. Presented to the Director of ECDC during the Initial Management in Public Health Microbiology Module, Stockholm, Sweden. 3 February, 2015.
- 4. Harvala H. Should sequencing of the heamagglutinin gene or the hypervariable region be part of outbreak investigations in the measles elimination end-game? Presented at the Nordic Mini Project Review Module, Copenhagen, Denmark. 13 April 2015.
- 5. Harvala H. Increased number of *Campylobacter* detections in blood samples, Sweden 2014 artefact or true increase? The Nordic Mini Project Review Module, Copenhagen, Denmark. 14 April 2015.
- 6. Harvala H and Tryfinopoulou K. Issue with developing vaccine against HIV. Presented during the Vaccinology Module, Krakow, Poland. 22 April, 2015.
- 7. Harvala H. Should sequencing of the heamagglutinin gene or the hypervariable region be part of outbreak investigations in the measles elimination end-game? Mini Project Review Module, Lisbon, Portugal. 25 August 2015.
- 8. Harvala H. Increased number of *Campylobacter* detections in blood samples in Sweden from June to October in 2014 artefact or true increase? Mini Project Review Module, Lisbon, Portugal. 26 August 2015.
- 9. Harvala H. Ten steps in the outbreak investigations. The EUPHEM training session at the Annual meeting of the European Society for Clinical Virology, Edinburgh, UK, 9 September, 2015.
- 10. Harvala H. Overview of EUPHEM projects 2014-2015. Microbiology seminar at the Public Health Agency of Sweden. 25 September 2015.
- 11. Harvala H and Pini A. What are the EPIET and EUPHEM programs? Presentation for the Gymnasium Students, ECDC, Stockholm, Sweden. 14 December 2015 and 18 January 2016.
- 12. Harvala H and Rizzardi K. The emergence and spread of C. difficile ribotype 231 in Sweden between 2006 and 2015. Microbiology seminar at the Public Health Agency of Sweden. 18 March 2016.
- 13. Harvala H. RSV surveillance in Sweden can we improve it? Presented at the Nordic Mini Project Review Module, Stockholm, Sweden. 18 April 2016.

9. EPIET/EUPHEM modules attended

- EPIET/EUPHEM Introductory Course, Spetses, Greece (three weeks)
- Outbreak Investigations, Robert Koch Institute, Berlin, Germany (one week)
- Initial Management in Public Health Microbiology, ECDC, Stockholm, Sweden (one week)
- Biorisk and Quality Management, ECDC, Stockholm, Sweden (one week)
- Multivariable Analysis, Austrian Agency for Health and Food Safety, Vienna, Austria (one week)
- Vaccinology Module, Regional Institute for Public Health, Krakow, Poland (one week)
- Rapid Assessment and Survey Methods, Athens, Greece (one week)
- Project Review Module, Lisbon, Portugal (one week)
- Bioinformatics and Phylogenetics, Stockholm, Sweden (three days)

10. Other training and meetings

- Nordic Mini Project Review Module, Copenhagen, Denmark (two days)
- Introduction to the Clinical Microbiology in Sweden, Karolinska Hospital, Stockholm, Sweden (one day)
- Annual Meeting of the European Society for Clinical Virology, Edinburgh, UK (four days)
- Bionumerics Course by Applied Maths, Stockholm, Sweden (one week)
- Biosafety Course, Public Health Agency of Sweden, Stockholm, Sweden (two days)
- Nordic Study Group Meeting on Campylobacter Source Contributions, Copenhagen, Denmark (two days)
- ECDC Workshop on Burden of RSV disease in Europe, Stockholm, Sweden (two days)
- Nordic Mini Project Review module, Stockholm, Sweden (two days)
- UK Clinical Virology Network Annual Meeting, Liverpool, UK (two days)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 Heli Harvala during her two-year EUPHEM fellowship (cohort 2014) as an EU track fellow at the Swedish Institute of Public Health, Stockholm, Sweden. Heli is the first appointed EU track EUPHEM fellow in Sweden. The projects described in this portfolio demonstrate the breath of public health microbiology work of Heli. Epidemiological studies consisted from regional to national outbreak investigations while surveillance activities extended from Cryptosporidium infections in Sweden to EU wide study of non-polio entrovirus surveillance. The laboratory and epidemiologically based projects covered all diverse range of disease programmes involving multidisciplinary working and teamwork on all levels such as physicians, veterinary experts, 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). Heli has shown a huge ability in bringing together different profetionals toward a common goal. She has assisted ECDC in two projects, and designed and implimanted a course in phylogeny. Activities were in in line with the 'learning by doing' and 'on the job training' ethos 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 this EUPHEM fellow to ECDC 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 her tasks to a very high standard and with a professional attitude which indicates her developmment in leadership. We wish the fellow every success in her future career as a public health microbiologist.

Supervisor's conclusions (Mia Brytting on behalf of supervision team)

Heli is a cheerful and friendly person who doesn't have any difficulties to cooperate with other people. When she came to Sweden she managed to settle herself and her family very quickly.

She sees opportunities instead of problems. She has an incredible scientific excellence and a curiosity to pick up new topics. Due to her previous experiences she has an overview that makes it possible for her to pinpoint the interest of public health.

She is fully engaged in each project, is actively involved in planning, and she is open for new projects. She runs her projects independently but ask when needed. She has been able to plan her work well and has run the projects in parallel without any problems. During these years she has published several articles, reports and posters.

She has done projects in collaboration with different departments at the public health agency of Sweden, with other Swedish agencies and clinical laboratories, as well at ECDC. She has organized a new EUPHEM module (Bioinformatics and Phylogeny Module) and the first EUPHEM training session at the Annual Meeting of the European Society for Clinical Virology (ESCV). She and the EPIET fellow Alessandro Pini also organized the Nordic mini project review module.

During these two years Heli has done outbreak ingestions by genotyping for hepatitis A virus and EHEC 0130 and by questionnaires for *Campylobacter* and *Cryptosporidium*. The study of increasing numbers of *Campylobacter* bacteremia showed the impact of culturing media used at the diagnostics laboratories. Heli also used a questionnaire involving diagnostic method used to evaluate the Swedish RSV surveillance system. The outcome of these studies showed the importance of the methodology used for diagnostics and its impact of the surveillance in Sweden for *Campylobacter* and RSV. Heli also performed whole genome sequencing with the aim to study the transmission of moxifloxacin-resistant *Clostridium difficile* ribotype 231. The data from this study had impact of the Swedish recommendation of *Clostridium difficile* surveillance and moxifloxacin prescription policy. By genotyping of

Campylobacter jejuni was the association of severity of infection and type investigated. Heli showed that *C.jejuni* ST-257 was significantly associated with hospitalisation. This study was performed in collaboration with National Veterinary Institute. To be able to have complete picture of zoonotic *C.jejuni* infections a collaboration between the agencies performing human and animal surveillance are of importance. This study strengthen this collaboration in Sweden.

In the global surveillance of measles, genotyping of the nucleoprotein (N) is used. However, the gene segment used is conserved among the different genotypes. To be able to increase the resolution between outbreaks with the same N genotype Heli studied other gene segments. The use of combination of sequences from the nucleoprotein, hemagglutinin and the hypervariable region, increased the resolution so different outbreaks with the same N genotype could be differentiated. We have already discussed the outcome of this study with other countries in Europe since several countries have struggled with the same problem. Heli have also investigated the laboratory preparedness in Europe for detection of new enteroviruses. Knowing the gaps in the European surveillance of non-polio enterovirus surveillance is importance to be able to improve it. Heli's deep knowledge in bioinformatics did it possible to organize the first Bioinformatic and Phylogeny Module within the EUPHEM program and for the ECDC summer school. By increasing the knowledge how the use of molecular methods can improve outbreak investigation and surveillance in country, European and global level, the public health will improve. Heli has learned new topics, but also been giving a helping hand when needed so we have also learned from her.

Personal conclusions of fellow

The EUPHEM programme provided me with an excellent opportunity to be involved in diverse projects covering the different aspects of public health microbiology, from outbreak investigations and surveillance to the public health microbiology management and teaching. Although public health microbiology focuses on human health and disease, it is a cross-cutting subject spanning the fields of human, animal, food, water and environmental microbiology. During the fellowship I was fortunate to be part of different outbreak investigations and multidisciplinary research teams, which often included members from human, animal and food national agencies. It clearly broadened my view of medical microbiology, and how broadly it can impact public health. The programme brings together different disciplines; the effective communication and collaboration between microbiologists and other people from different background, especially from epidemiology, is one of the key elements in public health microbiology. The structure of EUPHEM training with specific modules and 'learning-by-doing' approach with continuous feedback and self-evaluation provides a good foundation to perform these tasks. From this fellowship, I have gained valuable experience in epidemiology and working together with epidemiologists, and consequently have a deeper understanding of public health within and beyond the laboratory. Furthermore, I have also experienced that the fast developing field of microbiology has set the need for even closer collaboration between microbiologists than ever before.

The EUPHEM programme also encourages a network of European public health laboratories, and contributes to the field of public health microbiology. It has been a privilege to become a part of the public health microbiologist network in Europe, and beyond. I truly hope I can continue to contribute to this growing field of public health microbiology.

Acknowledgements of the fellow

I would like to thank my EUPHEM supervisor, Mia Brytting, for her encouragement, support and excellent mentorship throughout the programme. I am also grateful to Katherine Zakikhany for encouraging the start of the programme at the Public Health Agency of Sweden, and for her continued support during this fellowship. I would also like to thank my EPIET supervisor Anders Wallensten and project supervisors including Cecilia Jernberg, Åsa Wiman, Jessica Beser, Kerstin Falk, Kristina Rizzardi and Thomas Åkerlund for providing interesting opportunities within the field of public health microbiology, and for sharing their knowledge especially in the field of bacteriology with me; and all co-authors I have had a pleasure to work with. I wish to acknowledge everyone at the microbiology and epidemiology departments for the great collaborations, with special mention to Karin Tegmark Wisell for her valuable contributions to my projects and Erik Alm for his continued support in the field of bioinformatics.

I would also like to acknowledge the support and opportunities provided by external collaborators Ann Lindberg, Elina Lahti and Thomas Rosendal at the National Veterinary Institute of Sweden, as well as Eeva Broberg and Pasi Penttinen at the ECDC. My special thanks go to Eeva – it has been such a pleasure working with you! I am especially grateful for the support, availability, constructive feedback and excellent mentoring provided by the EUPHEM coordinator Aftab Jasir (ECDC); you especially have given me several amazing opportunities to develop as a teacher in the field of public health microbiology. I would also like to thank the other members of EUPHEM and EPIET coordinator teams, as well as fellowship programme office for their support and practical guidance throughout the fellowship. My warmest thanks go to the all EUPHEM and EPIET fellows, from the cohort 2014 as well as from cohorts before and after, for the friendship and fantastic team spirit. I would very much like to thank specifically the fellows at the Public Health Agency of Sweden; EPIET fellow Alessandro Pini for the caring friendship and previous EPIET fellow Viktor Dahl for the practical guidance. I am also very grateful to Teija Korhonen from EPIET cohort 2012 for introducing and recommending me the EUPHEM program. Last but not least, I would like to thank my family for the fantastic commitment and love throughout this fellowship. My warmest gratitude belongs to my parents, who travelled from Northern Finland to Sweden to look after children during the every training module and meeting summing up over 3 months spend here; and to my dear husband, who travelled from UK to Sweden almost every weekend to remind me of true life. Our children are thanked for the enjoyable time spent together; you are simply a powerful source of inspiration and energy!