

The section header 'Summary of work activities' in a bold, white, sans-serif font, set against a blue background.The author's name 'Rikard Rykkvin' in a white, sans-serif font, positioned below the section header.The full title of the report, 'European Public Health Microbiology Training Programme (EUPHEM), 2015 cohort', in a white, sans-serif font, positioned below the author's name.The section header 'Background' in a bold, blue, sans-serif font.

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 Rikard Rykkvin, cohort 2015 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.

Pre-fellowship short biography

Prior to his EUPHEM fellowship, the fellow worked as a medical doctor specialising in medical microbiology. He had worked several years at the Department of Virology at the NIPH, with a special focus on hepatitis viruses, then at the bacteriology and infection serology lab at Oslo University Hospital, as well as one year as a clinical practitioner at the venereology clinic of Oslo University Hospital. The fellow joined the EU track of the EUPHEM program to gain a greater competency in epidemiologic aspects of public health microbiology, to acquire experience with outbreak investigations, and to increase his knowledge about infectious diseases.

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 projects or activities (on-job services) and partly through participation in the training modules. Results are presented in accordance with the EUPHEM core competencies, as set out in the EUPHEM scientific guide¹.

1. Epidemiological investigations

1.1. Outbreak investigations

Supervisors: Katrine Borgen, Susanne Dudman

A. A norovirus outbreak following a dinner party among healthcare workers (HCWs) in a hospital in Eastern Norway, 2016

On 11 April 2016, the Norwegian Food Safety Authority (NFSA) reported an outbreak of gastroenteritis following a dinner party on 7 April among HCWs from an Eastern Norway hospital department. Leftovers were served to night shift colleagues and at the department lunch the following day. The outbreak was investigated in order to describe its extent and determine its source. A retrospective cohort study was performed among attendees of the dinner, lunch or night shift. Through an online questionnaire information was collected on food exposures and gastrointestinal (GI) illness. Cases were defined as individuals who reported vomiting and/or diarrhea between 7-11 April. Relative risks (RR) were calculated with 95% confidence intervals (CI) using multivariable logistic regression. People with GI-symptoms were asked to deliver a stool sample for enteropathogenic testing. A site investigation was performed at the catering company. The response rate was 65% (36/55). 15 respondents met the case definition (AR 56%). The most frequently reported symptoms were malaise (100 %), nausea (93 %), diarrhea (87 %) and vomiting (73 %). Consumers of pasta salad (RR 7.7, CI 1.1-52) and spinach pie (RR 2.1, CI 1.1-3.9) were more likely to experience illness. No patients at the hospital department became ill. One stool sample tested positive for norovirus. Site investigations showed that catering personnel and building visitors shared bathrooms. We concluded that the pasta salad produced by a local catering company and served during the dinner party, night shift and lunch was the most likely source, and norovirus the most likely agent based on Kaplan Criteria and one fecal sample. Catering companies and food handlers should always practice good hygiene, including having designated toilets for personnel. A final outbreak report was prepared and sent to the NFSA the Municipal Health Office in Lillehammer, who then addressed it with the catering company. The outbreak was accepted for a poster presentation at ESCAIDE in November 2017.

¹ European Centre for Disease Prevention and Control. European public health training programme. Stockholm: ECDC; 2017. Available from: <http://ecdc.europa.eu/en/publications/Publications/microbiology-public-health-training-programme.pdf>

The fellow had the main responsibility for extracting, analysing and interpreting the data, wrote the ESCAIDE abstract and and co-wrote the outbreak report.

B. Large outbreak of mumps virus genotype G among vaccinated students in Norway, 2015-2016

Since 1983, when mumps vaccination (genotype A) was introduced in the Norwegian childhood vaccination schedule, vaccination coverage exceeded 90% and mumps incidence has declined to an annual mean of 0.4 cases per 100,000 population during 2000-2014. We here describe the first large mumps outbreak in Norway occurring from September 2015. We defined a case as a person with clinical mumps notified infection from 01/09/2015 and laboratory confirmation (IgG seroconversion, IgM or PCR) (confirmed) or an epidemiological link (probable). PCR positive specimens were genotyped. We described the cases using notification data and obtained vaccination status from the Norwegian vaccination registry. Between September 2015 and April 2016, 227 cases were notified (225 confirmed). The median age of all cases was 22 years (range 4-66); 89% were 19-28 years old; 62% were male; >75% occurred among students. Of all cases, 5.7% were diagnosed with orchitis; 2.6% were hospitalized. Out of 190 PCR positive specimens, 34% were genotyped, and they were all genotype G. Sequencing data combined with epidemiological data suggested that the index case was a student in Trondheim infected in Italy. 68% of the cases were infected in Trondheim, 25% in Bergen and 7% in other locations in Norway. Of 199 cases with known vaccination status, 96.5% were vaccinated (6% once and 90,5% twice). The health authorities in Trondheim and Bergen vaccinated unvaccinated students and close contacts. This large outbreak occurring among vaccinated students suggests suboptimal protection of the current genotype A vaccine in preventing genotype G mumps outbreaks. However, the outbreak may have been larger if the population was unvaccinated. We therefore recommend maintaining high vaccination coverage and offering the vaccine to all unimmunized individuals.

The fellow was the main investigator from the reference laboratory side in this investigation. The fellow contributed in all stages of the outbreak investigation, participated in outbreak group meetings, co-ordinated diagnostic and genotyping outbreak investigation activities at the reference laboratory, advised outbreak group on significance of microbiological findings, formulated diagnostic advice and information which was communicated to laboratories and health personnel and was co-author on a manuscript. Overall lead investigator was EPIET fellow from cohort 2015 Lamprini Veneti, who performed the epidemiological analysis of the outbreak, wrote the outbreak report, presented the outbreak at ESCAIDE 2016 and wrote a manuscript.

C. Training modules

The EPIET/EUPHEM introductory course familiarised fellows with the methodology and logistical part of outbreak investigations. The Outbreak investigation module allowed fellows to acquire skills and competencies in all practical aspects of both data management and analysis during outbreak investigations, using STATA and data entry software tools such as EPIDATA, and also interpreting and communicating findings. The multivariable analysis module allowed fellows to learn about and build and interpret different models for multivariable analysis in an outbreak situation (as well as others where further analytical interpretation may be needed) as well as how to best communicate the results.

Educational outcome:

The fellow received hands-on experience in outbreak investigations, from case definitions, active case-finding, data collection, data analysis, communicating results in a clear and efficient manner to a multidisciplinary team, and writing outbreak reports. The fellow also experienced the added benefit of a EUPHEM fellow with epidemiological understanding co-operating with an EPIET fellow while co-ordinating the analysis work of the reference laboratory in a national outbreak setting.

1.2. Surveillance

Supervisors: Hilde Kløvstad, Susanne Dudman.

A. Hepatitis C and risk behavior among persons who inject drugs in Norway, 2015

Since 2002, prevalence of HCV (hepatitis C virus) infections among PWIDs (persons who inject drugs) has been surveyed in Oslo. In 2015 this survey was extended to include the City of Bergen. The objectives included measuring the prevalence of HCV infection and risk behavior, in order to provide information to health authorities to evaluate current harm reduction measures and for planning future preventive measures. The health survey was conducted as a cross-sectional study with interview-administered questionnaires and blood tests for anti-HCV with reflex to HCV RNA, at low-threshold centers for PWID in Bergen and Oslo. Informed consent was obtained, and a monetary incentive was given. If HCV was detected, participants were referred for treatment. We calculated HCV prevalence and tested for equivalence between the two cities using a two one-sided test (TOST) with a set equivalence margin of 15 percentage points. In Oslo and Bergen, 227 and 121 participants, respectively were tested for HCV. 68% vs. 81% were male. Median age was 38 vs. 36 years (range 19-62 vs. 18-61). 79% (Oslo) vs. 83% (Bergen) had detectable antibodies against HCV (largest margin 12 percentage points, considered equivalent). Among the anti-HCV positives, 58% (Oslo) vs. 61% (Bergen) had detectable HCV RNA (largest margin

14 percentage points, considered equivalent). 11% (Oslo) vs. 3% (Bergen) of participants stated they had shared syringes, and 27% vs. 19% had shared other paraphernalia during the last four weeks. 43% (Oslo) vs. 35% (Bergen) stated that they had been tested for HCV during the last 12 months. HCV is a major infection among PWIDs in both Oslo and Bergen. Sharing syringes was less common than sharing other paraphernalia. These results highlighted the importance to include paraphernalia in the programs, as well as continue the needle exchange programs. Continued surveillance is necessary to evaluate implemented measures. The study was presented as a poster at the 5th International Symposium on Hepatitis Care in Substance Users, in Oslo September 2016.

The fellow was the main investigator from the reference laboratory for the Oslo part of the study, including co-ordination of laboratory work, verifying assays, interpreting results, producing temporary and final lab result reports for submitters, ordering additional investigations, performing statistical analysis and co-writing abstract and poster (second and corresponding author).

B. Tick-borne encephalitis (TBE) reporting in yearly NIPH reference laboratory report

The Department of Virology at the Norwegian Institute of Public Health has been the national reference laboratory for TBE since 2008, and the laboratory reports on its activities and results in its own section of the collective yearly NIPH reference laboratory report. For the year 2015, the fellow was tasked with writing the TBE report. Tick-borne encephalitis virus (TBEV) is transmitted by ticks, and the disease is common in the areas around the Baltic Sea, in Central Europe and in Austria. In Norway, TBE cases have been detected in the southern parts of the country, particularly around Arendal. The tick vector *Ixodes ricinus* is prevalent along the coast up to Nordland, so one must assume that cases will be detected in other parts of the country as well. The Department of Virology performs analyses every year of TBEV in ticks collected along the coast up to Nordland, and the virus has been detected in several new locations during the last years. The department participates in yearly tick research meetings in Scandinavia and in national and international research projects. The virological surveillance consists of: 1) Serological analysis of blood and cerebrospinal fluid clinical samples with ELISA or immunofluorescence anti-TBE, 2) detecting TBEV with RT-PCR, 3) Participating in external quality assurance programs (Instand) and 4) Participating in the European Network for Diagnosis of Imported Viral Diseases (ENIVD). In 2015 the reference laboratory conducted 421 TBE analyses (IgG and IgM) on 196 samples (serum and cerebrospinal fluid) from 129 patients and 1 EQA sample. The reference laboratory detected IgM antibodies in two patients. In Norway, nine cases of TBE were notified to the Norwegian Institute of Public Health in 2015, and one of these were notified from the reference laboratory. Samples from a few patients were analysed with RT-PCR, but TBEV was not detected.

The fellow extracted, analysed and summarised yearly data for tick-borne encephalitis virus from the reference laboratory results database as well as the Norwegian Surveillance System for Communicable Diseases (MSIS), and updated the TBE chapter correspondingly in the yearly report for the reference laboratories at the NIPH.

C. Bloodborne viral diseases among persons who inject drugs in Oslo 2002 – 15

HAV, HBV, HCV and HIV are defined as infectious diseases of public health importance in the Infectious Disease Control Act in Norway. Therefore, it is necessary to monitor the distribution of these diseases in the general population, as well as in risk groups. PWID are particularly exposed to infection with these blood borne viral diseases. There are an estimated 4200 to 8400 PWID in Oslo. There is a pressing need to describe and analyse the trends of these diseases among Oslo's PWID over time. The main objective was to describe and compare the prevalence of HIV, hepatitis A (HAV), hepatitis B (HBV) and hepatitis C (HCV) among PWID in Oslo, Norway, from 2002 – 2012, and in 2015, using serial yearly point prevalence data gathered at the Department of Virology, Norwegian Institute of Public Health (NIPH). Secondary objective: Analyse if there is an association between prevalence of blood borne viral infections and number of years of injection use or frequency of injections or type of drug used. Tertiary objective: Assess if the average age of drug injection debut for the group has changed through the study period.

Most of the participants were recruited while collecting sterile single-use equipment for drug injections. The health surveys has included a blood sample analysed at the Department of Virology (NIPH) for anti-HAV, HbsAg, anti-HBc, anti-HBs, anti-HCV, HCV PCR, anti-HIV, HIV antigen. We extracted laboratory results and basic demographical data from the participants 2002-12 from the Laboratory Information Management System at NIPH. In addition, injection history data (number of years as a PWID) and data from questionnaires with detailed information about frequency of injections, type of drugs and administration form (injections, oral, etc) were collected. For 2015, part of the project was to conduct the health survey similar to 2012, with recruitment during two weeks in September 2015, and laboratory analysis in the months following. Descriptive epidemiology will be performed for microbiological, demographical and behavioural parameters. Analysis will be restricted to first time participants to obtain mutually exclusive groups of participants for every year. We will analyse with logistic regression if there is an association between prevalence of blood borne viral infections and number of years of injection use or frequency of injections or type of drug used. By calculating age of drug injection debut through the participants' recorded age and injection years, we will find the average age of debut for the group through the period

For the full 2002-15 study, at the end of the EUPHEM fellowship separate prevalence data for first-time participants were not yet available, however, preliminary data were available for all participants by year. The anti-HCV prevalence among all users of the needle exchange site in Oslo steadily decreased from 79% in 2002 to 61% in 2012, but in 2015 the anti-HCV prevalence increased to 75%. For anti-HBc the prevalence decreased from 53% in 2002 to 33% in 2015. The anti-HIV prevalence was less than 3% during the whole period. The preliminary data were presented by the fellow at a scientific meeting with stakeholders. Further analysis will be continued by the fellow after the fellowship ends, including drafting a manuscript for peer-reviewed publication.

D. Training modules

The EPIET/EUPHEM introductory course familiarised participants with the development, evaluation and analysis of surveillance systems. In addition, the "Rapid Assessment in complex emergency situations" module familiarised fellows on 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 epidemiological skills to serve public health interventions such as surveillances.

Educational outcome:

The fellow learned the complexities involved in setting up and evaluating surveillance systems, taking into account the health events under surveillance. The fellow developed understanding and experience of the importance of accurate data entry, how to extract and analyse existing or incoming laboratory surveillance data and select appropriate methodologies learned in the modules, and write reports with interpretation of data and formulate recommendations based on the data.

2. Applied public health microbiology research

A. Possible risk factors for recent transmission of tuberculosis (TB): a cohort study in Norway, 2011-15

Supervisors: Gunnstein Norheim, Anne Torunn Mengshoel, Trude Arnesen.

The majority of TB cases notified in Norway is assumed to be infected abroad. To identify risk groups representing recent transmission in Norway, which may be considered for targeted interventions, we performed a retrospective cohort study including all 1,277 TB patients notified in Norway who had their first culture positive sample taken between 2011 and 2015 with a complete, unambiguous 24-locus MIRU-VNTR (Mycobacterial Interspersed Repetitive Units-Variable Number of Tandem Repeats) genotype available. Cases with identical MIRU-VNTR genotype were defined as clustered. We identified patient and cluster characteristics, and used multivariable logistic regression to calculate odds ratios (OR) with 95% confidence intervals (CI) for factors associated with clustering. 57% of the cases were male, 90% were born abroad and the mean age was 35 years (range 2-94). 61% of the cases had unique genotypes, while 39% cases belonged to 135 different MIRU-VNTR clusters. Being born in Norway by Norwegian-born parents (OR 3.9, CI 2.1-7.1) or being born in Africa (OR 3.0, CI 2.2-4.1) were independent risk factors associated with clustering, compared to being born in Asia. Cases older than 70 years (OR 0.19, CI 0.09-0.42) or who had resided in Norway between one and six months (OR 0.55, CI 0.33-0.91) were less likely to cluster. MIRU-VNTR based strain cluster analyses suggested that being born in Norway or Africa were risk factors for autochthonous TB transmission in Norway. However, the implementation of whole genome sequencing for strain typing is recommended for a refined identification of likely risk groups and inform targeted interventions to reduce ongoing transmission. The fellow wrote the study protocol for this specific project, extracted, cleaned and analysed the data, disseminated the findings, presented results at a NIPH scientific forum and ESCAIDE 2017 (accepted as poster) and wrote a manuscript.

B. Training modules

The EPIET/EUPHEM introductory course familiarised fellows with developing and presenting study protocols, and in the 'Initial management in public health microbiology' fellows learned, time management, team collaboration, how to provide efficient presentation according to target audiences. The Biorisk and Quality management module was also important towards familiarising the fellow in biorisk/biosafety procedures, as well as in performing laboratory risk assessments, essential for good laboratory practices. The "Bioinformatics & Phylogeny" module extended the fellow's knowledge and competence of methods and interpretation of phylogenetic analysis, that were particularly useful while working in projects.

Educational outcome:

The fellow got familiar with all stages of theoretical (through the modules attended) and empirical (hands-on experience) methodology, from identification of the health problem, revising literature, designing the study and detailed protocols for its execution, applying and learning new laboratory methods, collecting and analysing data (including multivariable analysis) and writing scientific articles.

3. Applied public health microbiology and laboratory investigations

A. Comparison of performance of mumps virus RT-PCR vs anti-mumps virus IgM in oral fluid samples

Supervisor: Susanne Dudman

Prior to the large mumps outbreak among mostly fully MMR vaccinated students in Norwegian cities Trondheim and Bergen lasting from September 2015 until April 2016, the first line method for mumps virus reference diagnostics at the national reference laboratory (NRL) of the Norwegian Institute of Public Health (NIPH) was serological testing of oral fluid samples for IgG and IgM antibodies against mumps virus. Due to limited usefulness of serology in this setting, the NRL added mumps virus PCR as a first line analysis on oral fluid samples in October 2015. In order to establish sensitivity and specificity of oral fluid serology and PCR in the NRL diagnostic setting, the fellow performed a retrospective comparison including all oral fluid samples analysed with both serology and PCR at the NRL between Oct 1, 2015 and Dec 31, 2016. Lacking a clinical or laboratory «gold standard», a variable for a true positive result was defined as either having detectable anti-mumps virus IgM and/or mumps virus RNA. Cases with a positive IgM test likely due to recent vaccination, were excluded from the study. 191 samples were analysed with PCR and EIA IgM in parallel. Mumps RNA and IgM were never detected simultaneously in the same sample. Compared against the definition of a true positive mumps case chosen for this analysis, the performance was as follows: overall diagnostic sensitivity for PCR was 70% (14/20) and for EIA IgM 30% (6/20). Age distribution was different among cases detected with IgM: older compared to those that were PCR positive (20-29 years old). Among the 191 oral fluid samples included, 85 (45%) had detectable anti-mumps virus IgG, either as a sign of vaccination, remote infection or recent/current infection. In the specific setting of NRL testing for mumps in Norway, this comparison indicates that RNA detection has a higher diagnostic sensitivity (70%) than IgM (30%). More importantly, however, detections with either method were mutually exclusive, this is probably due to two reasons: 1) sensitivity of PCR and IgM testing are heavily dependent on when the sample is taken in relation to symptom debut. PCR has better sensitivity in the first week of symptoms, while IgM sensitivity increases from the second week. 2) When fully MMR vaccinated individuals acquire a clinical mumps infection (secondary vaccine failure), IgM is usually not detectable in serum. For mumps reference analysis at the NRL, it is recommended to continue to test oral fluid samples in parallel with PCR and IgM, in order to achieve a satisfactory combined diagnostic sensitivity.

The fellow conceived the idea for the internal comparison, collected and analysed the data, interpreted the findings and disseminated the information in an internal report for the reference laboratory.

B. Whole genome sequencing for characterization of Norwegian isolates of *Haemophilus influenzae*

Supervisors: Dominique Caugant and Martin Steinbakk.

Haemophilus influenzae (Hi) may cause upper respiratory tract infections as well as invasive disease. It occurs in an encapsulated and unencapsulated form. Encapsulated Hi have different serotypes (a to f), with the most important being serotype b. Vaccination against Hi serotype b was introduced in the Norwegian immunisation program in 1992. Since then, unencapsulated variants (nontypeable HI, NTHi) and non-b serotype have been the most common cause of invasive Hi disease in Norway. In the period 2008-15, approximately 80 cases of invasive Hi disease have been notified yearly to MSIS. NIPH is the NRL for Hi and receives the majority of isolates causing systemic disease in Norway for confirmation, characterization, and resistance testing. Methods used for characterization include serotyping and MLST. It has been suggested that "if genetic recombination is obscuring the detection of NTHi genetic lineages associated with different disease parameters using the MLST approach, then more detailed analysis such as whole genome sequencing may be required to generate a more reliable phylogenetic population structure and to detect associations between other genetic loci and clinical parameters" (Collins et al, 2016). We aim to establish whole genome sequencing (WGS) of *Haemophilus influenzae* (Hi) as a method for characterising isolates sent to NIPH, in order to have *one* method for providing multilocus sequence typing (MLST) as well as more detailed phylogenetic information and at a later stage antimicrobial resistance (AMR) surveillance data. The objectives were to analyse all Hi isolates received at the NRL during 2015 with WGS, validate MLST results from WGS against available MLST data and identify major clones circulating in Norway. The methodological approach was to assemble the present MLST data from the NRL on isolates received in 2015, then analyse the same isolates with WGS technique (Illumina MiSeq). NRL technicians together with the fellow would produce raw sequences from WGS runs for the fellow to analyse further. After performing MLST on WGS sequences, MLST results from WGS would be compared and validated against existing results, and one would identify major clones through WGS generated data.

The fellow created a dataset of all 107 samples received at the NRL in 2015 for inclusion in the project. NRL technical personnel and the fellow then performed sample retrieval from storage, plating and culturing, colony preparation, DNA extraction, sequencing library preparation with KAPA Hyper plus with a Bravo robot, further

treatment of sequencing library, and sequencing with Illumina MiSeq of the first 48 samples. Due to time constraints, the remainder of the project, including performing MLST on the acquired WGS sequences, will continue after the EUPHEM fellow graduates.

Currently, MLST is the standard method of genetic characterisation of Hi isolates. However, studies of invasive NTHi isolates as well as noninvasive isolates have failed to show clear associations between MLST-based clusters and disease state. After validating and establishing WGS as a routine method for MLST at the NRL when the project completes, WGS data will also provide more extensive characterisation of Hi isolates in Norway, identifying and describing the major circulating clones and facilitate further studies of associations between other genetic loci and clinical parameters, including AMR properties.

C. Laboratory Information Management System solution for registering samples submitted for hepatitis C virus resistance analysis

Supervisor: Anita Kanestrøm

Directly acting antiviral (DAA) therapy for chronic hepatitis C virus (HCV) infection is effective for achieving a sustained virological response. Due to high levels of viral replication and an error-prone polymerase, HCV shows a broad genetic diversity, and some amino acid substitutions will reduce susceptibility to DAAs. The presence of such substitutions, or resistance-associated variants (RAVs), have been shown to predict treatment failure with certain DAA regimens. According to Norwegian national guidelines for HCV treatment, one of the recommended options for HCV patients with genotype 1a and a high viral load (>800 000 IU/ml) is to test for NS5A RAVs prior to treatment. If NS5A RAVs is detected in such a patient, the standard recommended 12 week-regimen of DAA combination grazoprevir/elbasvir should be extended to 16 weeks, and ribavirin added to the regimen, to reduce the risk of treatment failure. In addition, treatment failure with DAAs is often associated with emerging RAVs, and in order to find re-treatment options it is advisable to test for DAA RAVs. There is a need for a surveillance system of HCV resistance in Norway that includes sample data collection for at least patients with relapses and possibly also baseline resistance data. The reference laboratory for viral hepatitis at NIPH in Norway doesn't currently offer HCV anti-viral resistance analyses, but samples may be sent to the Clinical Microbiology Laboratory at Uppsala University Hospital in Sweden for analysis. Because of shipping and analysis costs and procedures, clinicians in Norway often defer from HCV resistance analysis because of this, and choose treatment options not relying on RAV detection where possible. Therefore, there is a need to make HCV DAA resistance analysis available at the viral hepatitis reference laboratory in Norway to make sure the clinicians are able to choose the optimal treatment strategies for HCV patients. The first step is to be able to register incoming samples efficiently and correctly in the Laboratory Information Management System (LIMS). All samples sent to the reference laboratory for viral hepatitis at NIPH are registered in the local LIMS (LabWare LIMS v6), where virological analyses are ordered, results entered and authorized. The fellow designed and programmed the following new elements: 1) A temporary placeholder LIMS analysis for HCV DAA resistance, which will be ordered on all samples where either the submitter or the laboratory wants resistance testing performed. The purpose of the placeholder LIMS analysis is to be a LIMS marker for all samples that in the future will be retrieved and analysed for HCV DAA resistance, once the laboratory analyses are in place. 2) A LIMS component/analysis where information about the patient's current HCV treatment can be registered for the individual samples. This information will be retrieved from the order forms accompanying the samples. 3) A test list package containing the abovementioned two elements. This LIMS implementation was a necessary first step to facilitate effective and correct registering and marking of samples that are due for HCV DAA resistance analysis when the microbiological methods (Sanger sequencing or next generation sequencing) are established. After the sequencing methods are deployed, the LIMS analysis will be changed to accommodate all the possible result alternatives deriving from the sequencing.

D. Zikavirus surveillance project support activities

Supervisors: Dagny Dorenberg and Kaja Sverdrup Borge

Zika virus (ZIKV) is a flavivirus transmitted primarily by the *Aedes aegypti* mosquito. ZIKV may also be transmitted by other mosquitos, e.g. *Aedes albopictus* (tiger mosquito, which has a partly overlapping geographical distribution but also wider presence than *Aedes aegypti*). Norway is located outside the geographical range for both of the primary vectors, but Norwegian residents frequently travel to areas where they may be exposed to ZIKV. The first verified imported case of ZIKV disease in Norway was detected in a female traveller returning from a 2 week trip to Tahiti in 2013. It has also been confirmed that ZIKV can be sexually transmitted by infected men to both female and male partners, raising the possibility for autochthonous transmission in Norway, albeit on a small scale. A project was launched at the NIPH in summer 2016 to describe the natural course of ZIKV disease among patients diagnosed in Norway by clinical, virological and immunological characteristics, in order to strengthen the disease knowledge base relevant for improving antibody-based diagnostics vaccine development, guidelines for counselling of ZIKV patients and prevention/management of short term neurological effects of the disease. One of the specific objectives was to estimate the ratio of symptomatic to asymptomatic ZIKV infections among travellers returning to Norway (particularly after visiting the summer olympics 2016 in Brazil) by comparing serological status pre- and post-travel and linking these to clinical data. This was an observational retrospective and prospective cohort study. Two tasks were assigned to the fellow:

1) to establish procedures and templates in the Laboratory Information Management System (LIMS) for registering samples from the different study participant groups in order to streamline sample registering at the Virology department of NIPH.

2) Producing current Norwegian data on zikavirus testing and results for use in the project protocol and a report to the Ministry of Health (MoH).

At the start of the project, the Virology department at the NIPH was the only laboratory to offer microbiological testing for ZIKV in Norway. All samples received are registered in the local LIMS (LabWare LIMS v6). The fellow would design and program specific templates/scripts for bulk registration of participants' urine samples, pre-travel blood samples and post-travel blood samples in a standardised way, separating these samples from the routine activities of the laboratory. Also, the fellow would extract a result report from the LIMS on all ZIKV testing performed at the Virology department from beginning diagnostic testing in February 2016 until April 2016.

In July and August 2016, the fellow established the requirements for sample registering in co-operation with project personell, and subsequently designed and scripted templates for sample registering. Three different templates were established: 1) urine samples for immediate analysis, 2) pre-travel blood samples for storage awaiting post-travel results, and 3) post-travel blood samples for immediate analysis. The templates enabled project personell to bulk register samples of the corresponding sample material type in the LIMS, with pre-filled analyses, LIMS project tags, dummy project patients, «Start approved» sample status and submitter information. Information that was unique to every project sample, such as participant no., sampling date etc., had to be filled manually. The fellow wrote a detailed instruction for using the system, and held a workshop about system usage for selected project personnel on 27.09.16.

In April 2016 the fellow extracted aggregated data on ZIKV testing in Norway, for use in the project protocol and in an oral report to the MoH by one of the project participants. In the period 25.02.16 until 11.04.16, NIPH had registered 12 laboratory confirmed import cases of ZIKV diseases in Norway, among 222 tested. Of the 48 males tested, 2 were positive with acute ZIKV disease. Ten of the 174 women tested for anti- ZIKV antibodies were positive, of which 5 were reported as pregnant. These were all infected with ZIKV while travelling to countries affected by the ongoing epidemic.

This LIMS implementation enabled effective and consistent registering of ZIKV surveillance project samples. It is important to have a robust, stringent and well described system for registering project samples, in order to ensure that the correct information is registered and the correct set of analyses performed. This in turn will minimize the risk of analyses being delayed or samples being processed erroneously as ordinary routine samples.

Furthermore, the data on ZIKV testing and results produced by the fellow was important to facilitate an updated and accurate analysis on the current ZIKV situation in the project protocol and the MoH report.

E. Training modules

The introductory module, the 'Initial management in public health microbiology' module, the outbreak module (STATA training) and the multivariable analysis module taught many concepts necessary for the fellow to complete his projects successfully, such as communicating efficiently and writing scientific reports, assessing the performance of microbiological methods and learning how to use STATA for data cleaning and advanced analysis.

Educational outcome:

The fellow has deepened his public health microbiology knowledge in terms of laboratory investigations, and collaborating and engaging with different disciplines throughout the projects undertaken. He also gained experience in the preparation of a study protocol, performing statistical analysis, assessing microbiological methods, managing time, formulating recommendations and collaboration within a team.

4. Biorisk management

Before EUPHEM, the fellow had previous experience in biorisk/biosafety procedures, having worked in the mycobacterial BSL3 laboratory at NIPH previously as part of his specialisation in medical microbiology, therefore this core competency was considered as completed by the coordinators.

A. Certifications

- Certificate of Achievement: Basic Security in The Field II (UNDSS)
- Certificate of Achievement: Advanced Security in The Field (UNDSS)
- International Transport of Infectious Substances (WHO)

B. Training modules

The Biorisk and Quality management module familiarised fellows with biorisk and biosafety, such as management, assessment, mitigation, performance, including WHO recommendations on biosafety management in laboratories. A full day was dedicated to the international regulations for dangerous goods, determined by the International Civil Aviation Organisation, and awarded fellows with WHO certified documentation for shipping infectious goods. A visit to the BSL4 lab as part of this module illustrated all concepts learned throughout the module.

Educational outcome:

The fellow understood the principles and practices of biosafety levels 3 and 4 according to WHO and EU directives, and practised safe laboratory procedures and used personal protective equipment according to the Norwegian directives when working in the laboratories.

5. Quality management

A. External quality assessment (EQA) of serologic tests for syphilis (STS) among 23 Norwegian laboratories, 2015

Supervisor: Inger Sofie Samdal Vik, Ingeborg Aaberge and Regine Barlinn

Norway has neither a syphilis reference laboratory nor a national periodical STS EQA programme. However, in May 2015 STS were included in the first round of the biannual general virology/serology EQA programme from the NIPH. Performance and inter-laboratory comparability were assessed, in order to improve diagnostics and surveillance. The EQA scheme was distributed to 23 laboratories, most of which only perform STS screening themselves. Four serum samples were distributed blindly on dry ice, including two samples from patients with recent syphilis infection, one sample from a patient with remote infection and one negative sample. The laboratories were asked to analyse the panel with their standard STS methodology and return results with interpretation and comments. 22/23 laboratories returned results. The laboratories used three different syphilis total antibody chemiluminescence immunoassays for screening, and the qualitative results were fully concordant. Qualitative results from testing with TPPA (*Treponema pallidum* particle agglutination assay) or TPHA (*Treponema pallidum* haemagglutination test) (n=5) were concordant, except for the remote infection sample, where only two laboratories reported concordant results. Quantitative results for Rapid Plasma Reagin (RPR) testing (n=6) were discordant for both RPR reactive samples, with a reported titre range of 4-32 and 2-16, respectively. Thus, results from confirmatory testing of remote infection with TPPA/TPHA varied between laboratories, and RPR testing results were up to eightfold different. We highly recommend that initial and follow-up RPR testing after syphilis treatment are performed at the same laboratory. Preliminary results from this first round of syphilis EQA indicate the need for a reference laboratory, a regular syphilis EQA programme and training of laboratory personnel in TPPA/TPHA/RPR testing, in order to improve consistency for diagnostics and surveillance.

Prior to the fellowship, the fellow had acquired the sample material from real patients and designed the fictitious clinical sample information provided to the participating laboratories. The EQA was then distributed and results received and collected by laboratory personnel at NIPH. For the EUPHEM project, the fellow assembled all the returned results from the laboratories, compared and analysed the data, interpreted the findings, presented the results and made recommendations (accepted for poster at ESCAIDE 2017, and a report for the participating laboratories is due after completion of the EUPHEM fellowship).

B. Developing and troubleshooting NIPH LIMS system

Supervisor: Susanne Dudman

The fellow worked both strategically and with hands-on programming to further develop and improve the LIMS system with regards to handling and analysing microbiological results from the various Public Health virology laboratories at NIPH. Some of the new LIMS elements the fellow developed not described elsewhere in the portfolio: ELISA analyses for Hantavirus that had automatic checks inside LIMS of all required QC criteria, analyses and batches for zikavirus serology and PCR, dengue virus ELISA, quantitative HBsAg, cell culture on RD cells and improved mumps virus PCR solution.

In addition the fellow helped with troubleshooting of numerous issues in the existing system, and advised IT staff on general development of the LIMS system.

C. Adaptation of Norwegian National laboratory code catalog (NLK) at hepatitis/HIV laboratory

Supervisor: Astrid Wester

The Norwegian National laboratory code catalog (NLK) ensures that laboratory analyses are unambiguously defined regardless of whether the patient is treated in primary care or specialist care services. The gradual phasing out in Norway of printed paper for ordering and reporting results of laboratory analyses made standardisation necessary. Establishing universal Norwegian names for analyses is one of several steps on the way towards the goal of the Report to Parliament No. 9 (2012-2013) "One citizen - one journal. Digital services in the healthcare sector». The Norwegian Directorate of Health, and later the Directorate for e-Health, has for several years worked with the health sector to develop the Norwegian National laboratory code catalog. The laboratories have appointed representatives to take care of the professional aspects of updates to the code network. The Directorate for e-Health manages the national version of the code catalog in cooperation with the sector and international actors.

The fellow implemented the NLK framework at the HIV/hepatitis reference laboratory at NIPH, and contributed in regular meetings of a working group at the institute to further develop and improve the NLK.

D. Measurement uncertainty for Hepatitis D virus quantitative PCR

Supervisor: Kathrine Stene-Johansen

The Hepatitis D virus is an incomplete RNA virus that needs HBsAg produced by the hepatitis B genome for its membrane. Transmission of infection occurs together with the hepatitis B virus or in people who are already chronic hepatitis B carriers. The viral hepatitis reference laboratory at the NIPH previously only offered testing for HDV antibodies and antigen, but due to a need for increased analytical sensitivity, HDV quantitative PCR (RoboGene) was established in 2016. The fellow was responsible for ascertaining the correct precision level and measurement uncertainty level of quantitative results in the local laboratory setting, and implementing this in quality documents and in an automatic algorithm for individual LIMS result reports. He was also responsible for designing the analysis in the LIMS, and contributed to the phrasing of standard comments for HDV result reporting.

E. Mumps EQA submittal

The fellow assessed, wrote and submitted an EQA report on mumps virus serological analyses performed at the reference laboratory at the Department of Virology, NIPH. The fellow became familiar with all stages of an EQA, from the application of external quality standards, assessment and final report writing.

F. Annual Norwegian Accreditation Board visit to NIPH

A visit to NIPH from the Norwegian Accreditation Board occurs on a yearly basis, and the fellow revised documents describing kit independent QC controls at the Department of Virology NIPH, in preparation for visit from the accreditation board in late May 2016. Following up on the visit, the fellow established the measurement uncertainty for the anti-HBs analysis based on results from in-house measurements of kit independent controls and information from the kit data sheet, and 1) described the measurement uncertainty in the quality document and 2) programmed the formula for calculating this value in the LIMS.

G. Training modules

In the Biorisk and Quality management module the fellow was familiarised with all aspects concerning quality management in both internal and external quality control.

Educational outcome:

The fellow was involved in both internal and external quality controls and developed understanding of the importance of laboratory quality management programmes to ensure day-to-day laboratory consistency and to be able to produce accurate and reliable results for use in diagnostics, surveillance and research. The fellow was instrumental in providing these standards for the newly established quantitative HDV protocols and through audit and accreditation getting an insight into how standards are maintained.

6. Teaching and pedagogy

A. Measles lecture

The fellow taught current measles diagnostics and epidemiology to medical microbiologists (15 min + Q & A) at the annual Strategy meeting for serology/virology in Norway, Gjestehuset Lovisenberg, Oslo, 29/10-15. The objective was to give an update on measles and to formulate recommendations for diagnostic strategy. The abstract and recommendations is part of a NIPH-published Strategy report on emerging viral infections.

B. Viral infections lecture

The fellow planned, developed and held a 30-minute lecture and Q&A about hepatitis C virus as a model of viral infection, for last year secondary school biology students who interned one week at NIPH.

C. Zikavirus surveillance project procedures workshop

The fellow wrote and taught colleagues (1h) the procedures for registering urine and blood samples and retrieving results and data in the zikavirus surveillance project described under the Surveillance section above.

D. Phenotypic detection of Carbapenemase-producing Enterobacteriaceae lecture

The fellow taught EUPHEM colleagues the principles of phenotypic detection methods for carbapenemase-producing enterobacteriaceae during the introductory module.

E. Facilitator during outbreak course

The fellow facilitated a case study groupwork session on microbiological investigations during a whole day Outbreak investigation course for Norwegian infectious disease control workers at the NIPH.

Educational outcome:

The fellow learned and gained experience in facilitating and planning courses and workshops, and in planning and delivering lectures to multidisciplinary audiences. The fellow experienced the benefits of using diverse pedagogical techniques to stimulate learning.

7. Public health microbiology management

A. Management during outbreak investigations and projects

All projects and outbreak investigations undertaken throughout the fellowship involved public health management, including laboratory and time management, communicating between epidemiologists and the microbiology laboratory, team building and coordination and research collaboration.

B. Epidemic intelligence activities

As part of a biweekly rotation, the fellow acted as the outbreak responsible, performing duties such as daily monitoring the incoming email in the outbreak mailbox, the outbreak reporting system, and the international surveillance network (EWRS/IHR) and forwarding information to the relevant personnel. Weekly outbreak meetings are held at the NIPH, where the outbreak responsible summarises orally for the institute and in a written report.

C. Medical virology officer duty

With his background in medical microbiology, the fellow was able to participate in the rotation duty as medical virology officer on call for the NIPH reference laboratories. This included handling incoming requests and samples at the whole NIPH Department of Virology, ordering the appropriate analyses, prioritising labwork for the technical personnel, technical and medical validation of assays, conferring with external physicians about interpretation of results, and produce written result reports with appropriate explanatory comments from the reference laboratories.

D. Revision of Norwegian guidelines for hepatitis C treatment – resistance testing

The fellow was appointed as the representative for the Norwegian Association of Medical Microbiology in the working group responsible for publishing Norwegian guidelines for diagnosing and treating hepatitis C virus (HCV) infection. He attended meetings, produced background material (HCV genotype distribution) and contributed in revising the sections regarding recommendations for resistance testing and monitoring of HBV re-activation during HCV treatment. The revised 7th version of the guidelines were published at www.hepatittfag.no

E. Laboratory capacity and preparedness for emerging and re-emerging diseases in Norway - 3-minute presentation to ECDC leaders

For the Initial management in Public Health Microbiology module, the fellow analysed and then presented the laboratory capacity and preparedness for emerging and re-emerging diseases in his native country for invited ECDC leaders. The main conclusions were that Norway possessed mostly adequate notification systems and laboratory capacities, however certain de-identified notification sub-systems were ineffective and error-prone, not all emerging diseases were notifiable and many infectious diseases lacked a reference laboratory. The fellow recommended that gonorrhoeae and syphilis were made notifiable with full patient identification instead of de-identified, that emerging diseases such as hepatitis E, enterovirus D-68 and zika virus were made notifiable, and that a syphilis reference laboratory should be established.

F. Designing and implementing a Laboratory Information Management System (LIMS) solution for the rotavirus reference laboratory at NIPH

The Department of Virology receives samples positive for rotavirus from the local and regional microbiological laboratories for reference analysis and genetic characterisation, as part of surveillance of the effect of vaccination against rotavirus. Since the rotavirus reference function is only recently established, the reference laboratory started with a very limited Excel-based system for registering samples and keeping track of results, which did not allow for any reporting to the submitters. There was an acute need for implementing the NIPH LIMS (Labware) for the rotavirus reference laboratory, to ensure a practical and secure way of handling samples, results and result reports back to submitters. There was also a need for queries for extraction of data from the system that the reference lab needed, e.g. number of samples received per month and per submitter, distribution of genotypes, etc. The fellow performed the whole implementation, working together with the laboratory personnel. First, he demonstrated the current implementation of Labware in place at the other sections of the Department of Virology for the laboratory personnel, discussing what kind of implementation would most closely fit their preferred workflow. The laboratory personnel then assembled an Excel file which described all the information about rotavirus analyses that was to be registered in the LIMS: analysis codename, analysis full name, description of method, possible result alternatives, possible result commentaries, cost, number of samples per batch, number of controls per batch, etc. Based on his previous experience with Labware, the fellow then configured and programmed analyses and batches in Labware, according to the specifications received, making sure the design

was consistent with other laboratories' analyses and result alternatives. Along the way, personnel from the rotavirus group tested the new analyses and batches, making sure that they worked as intended. The fellow then also programmed an additional top level analysis, which in an automatic way joined results from the different component analyses, for example merging information from different sub-PCRs to a common rotavirus genotype. When all analyses and batches were designed and ready, the users from the rotavirus group received training from the fellow in how to use them in practise. The users tested all analyses and batches, including the format of result reports sent to submitters. After being accepted by the users, the whole solution was transferred to the actual Labware production platform. After implementation of the system, the users defined for the fellow their needs for extracting data about samples, results and submitters from the LIMS, for use in their reports. According to this, the fellow then defined queries in Labware that could later be used for producing reports. This included for example number of samples received per month and per submitter and distribution of genotypes. The final public health gain was quicker, more efficient and secure analysis of rotavirus samples at the reference laboratory, including reporting back to submitters. The reference laboratory was enabled to make reports on activities and diagnostic results, including results from genotyping and possible shifts in genotype after introduction of vaccination.

G. Training modules

The module 'Initial management in public health microbiology' familiarised fellows in terms of understanding roles and responsibilities in public health management settings. Topics included the identification of different management styles, team roles and team evolution, the delegation of tasks and the provision of structured, clear and efficient feedback.

Educational outcome:

The fellow practised public health management during his projects such as applying principles of scientific communication to peers and stakeholders, recognising the role of different agencies and prioritising daily work of laboratory technical personnel.

8. Communication

A. Publications

1. Rikard Rykkvin, Anne Torunn Mengshoel, Trude Arnesen, Janne Oseberg Rønning, Gunnstein Norheim (2017) Possible risk factors for recent transmission of tuberculosis (TB): a cohort study in Norway, 2011-15 (submitted to Thorax, September 2017)
2. Lamprini Veneti, K. Borgen, K. S. Borge, K. Danis, M. Greve-Isdahl, K. Konsmo, G. Njølstad, S. A. Nordbø, K. S. Øystese, R. Rykkvin, E. Sagvik, Ø. R. Riise (2017). Large mumps virus genotype G outbreak among vaccinated students in Norway, 2015-2016 (submitted to Eurosurveillance, september 2017)

B. Reports

1. Laboratory Information Management System solution for registering samples submitted for hepatitis C virus resistance analysis. R Rykkvin
2. Comparison of performance of mumps virus RT-PCR vs anti-mumps virus IgM in oral fluid samples. R Rykkvin
3. Yearly report of the reference laboratories at the Norwegian National Institute of Health (2015): Tick-borne encephalitis (TBE) section. R Rykkvin
4. Outbreak of gastroenteritis in Lillehammer, April, 2016 (Norwegian). Joanne Michelle F Ocampo, Rikard Rykkvin, Steinar Grue, Ellen Fuglerud.
5. Zikavirus surveillance project support activities. R Rykkvin
6. Haemophilus influenzae whole genome sequencing. R Rykkvin

C. Conference presentations

1. Løvlie A, Rykkvin R, Steen TW, Wüsthoff LE, Ulstein K, Myrvold HF, Soldal LA, Øystese KS, White R, Kløvstad H. Hepatitis C and risk behavior among persons who inject drugs in Norway (Poster INHSU 2016)
2. Rykkvin R. Health survey of persons who inject drugs, Oslo, 2015 (Oral Smitteverndagene 2016)
3. Rikard Rykkvin, Anne Torunn Mengshoel, Trude Arnesen, Janne Oseberg Rønning, Gunnstein Norheim. Possible risk factors for recent transmission of tuberculosis (TB): a cohort study in Norway, 2011-15 (Accepted for poster ESCAIDE 2017)
4. Rikard Rykkvin, Inger Sofie Samdal Vik, Regine Barlinn, Ingeborg Aaberge. External quality assessment (EQA) of serologic tests for syphilis (STS) among 23 Norwegian laboratories, 2015 (Accepted for poster ESCAIDE 2017)
5. Rikard Rykkvin, J. M. F. Ocampo, E. Fuglerud, S. Grue, H. Lange, K. Borgen (2). A norovirus outbreak following a dinner party among healthcare workers (HCWs) in a hospital in Eastern Norway, 2016. (Accepted for poster ESCAIDE 2017)

- Lamprini Veneti, E. Sagvik, S. A. Nordbø, K. S. Øystese, G. Njølstad, K. S. Borge, Ø. R. Riise, K. Konsmo, R. Rykkvin, M. Greve-Isdahl, K. Borgen. Large outbreak of mumps virus genotype G among vaccinated students in Norway, 2015-2016 (Oral presentation by L. Veneti at ESCAIDE 2016)

D. Other presentations

- Rikard Rykkvin. Laboratory capacity for emerging and re-emerging diseases - Norway (Oral, ECDC, IMPHM Module)
- Rikard Rykkvin. Detection of Carbapenemase-producing enterobacteriaceae – phenotypic methods (Oral, Spetses, Introductory course module)
- Rikard Rykkvin, Hans Blystad. A cluster of Bacillus cereus infection among PWID Norway 2016 (Oral, Lisboa, European Monitoring Centre for Drugs and Drug Addiction (EMCDDA)DRID indicator meeting 2016)
- Linda Wüsthoff, Rikard Rykkvin, Tore Steen. Health Survey among PWIDs in Oslo, 2002-15 (Oral, Oslo, Drugs and somatics research meeting 2016)
- Rikard Rykkvin, Kaja S. Borge. Mumps outbreak 2015-16 (Oral, NIPH Scientific forum 2016)
- Rikard Rykkvin. Genetical variation among M. tuberculosis strains isolated from newly diagnosed tuberculosis patients in Norway and epidemiological risk factors for belonging to a genetically defined strain cluster (Oral, NIPH scientific forum 2017)
- Rikard Rykkvin. Influenzavirus mutation associated with severe disease 3-minute presentation (Oral, Spetses, Introductory course module)

E. Other

- Norwegian guidelines for diagnostics and treatment of hepatitis C in adults, March 2017 (Norwegian). Olav Dalgard, Kristian Bjøro, Lars Karlsen, Knut Boe Kielland, Zbigniew Konopski, Magnhild Gangsøy Kristiansen, Rafael Alexander Modahl Leiva, Håvard Midgard, Arild Mæland, Rikard Rykkvin, Per Sandvei.

9. EPIET/EUPHEM modules attended

- EPIET/EUPHEM introductory course, Spetses, Greece (three weeks)
- Bioinformatics and phylogeny, FHM, Stockholm, Sweden (three days)
- Outbreak investigation, Berlin, Germany (one week)
- Biorisk and quality management module, ECDC, Stockholm, Sweden (one week)
- Initial management in Public Health microbiology, ECDC, Stockholm, Sweden (one week)
- Multivariable analysis (MVA), Vienna, Austria (one week)
- Vaccinology, Public Health England, Krakov, Poland (one week)
- Rapid assessment in complex emergency situations, Athens, Greece (one week)
- Project review module, Lisbon, Portugal (one week)
- Project review module, Lisbon, Portugal (one week)

10. Other training

- Mini module project review Stockholm, Sweden (two days)
- National strategy meeting for virology/serology: seminar on emerging viral infections, Oslo (one day)

Discussion

Coordinator's conclusions

EUPHEM programme exposes 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 Rikard Rykkvin during his two-year EUPHEM fellowship (cohort 2015) as a member state track fellow at the Norwegian Institute of public Health (NPHI) in Oslo. The EUPHEM Member State track pathway is unique and represents an excellent opportunity for all Member States to train their own scientists and medical specialists as public health microbiologists and thus strengthen communicable disease surveillance through integrated public health microbiology and epidemiology networks. This has been successfully demonstrated in Oslo by Rikard who after his degree as medical doctor and further specialization in clinical microbiology has substantially contributed to the establishment of key activities for the training site such as the Management System (LIMS) solution for the rotavirus reference laboratory and to the implementation of the existing and "ad hoc" developed systems for a number of viral pathogens (Hanta, Zika, Dengue, Mumps and all Hepatitis viruses), as well as producing guidelines.

Rikard's contribution has strengthened multidisciplinary approaches to epidemiology in outbreak investigations and improved surveillance, while ensuring the validity of diagnostic evidence in projects where epidemiology and microbiology need to go hand in hand like analysing risk factors for recent tuberculosis infection in Norway. The fellow will contribute with his successful training to the 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 and wish him every success in his future career as a public health microbiologist.

Supervisor's conclusions

Rikard has been trained as a specialist in medical microbiology. During his EUPHEM fellowship, he has broadened his expertise with emphasis in Public Health Microbiology including epidemiology. Rikard has contributed to strengthening the collaboration between microbiology and epidemiology at NIPH. One major achievement of the fellowship has been the bridging of the gap between microbiology and epidemiology allowing for communication, networking and close collaborations between the two fields. This is of added national value, in particular since NIPH is engaged in investigating outbreaks at a national level and is giving national advice and recommendations regarding prevention of communicable diseases. The work Rikard has performed during the fellowship has contributed to bring Norwegian data and expertise into a European Public Health Microbiology Network. We regards his work as having had an European added value.

Rikard is very dedicated to his work, friendly and helpful. He has gained a lot of knowledge and experience in the field of Public Health Microbiology during his fellowship. We are unreservedly pleased that Rikard agreed to enter the EUPHEM program, and grateful that the ECDC accepted him. Our thanks are also extended to Rikard's coordinators, collaborators, and supervisors of the various projects.

Personal conclusions of fellow

The EUPHEM programme provided me with the unique opportunity to diversify and work on interesting projects covering a wide range of public health topics. Through the two years of fellowship, I gained valuable experience within fields in microbiology and epidemiology where I was previously inexperienced. Both the concrete output from the projects and the improved skillset that I developed will be a benefit to the public health microbiology work at NIPH. One of the most useful effects of the EUPHEM programme at the local level is the integration of the fellows into the crucial meetingpoint of public health microbiology and epidemiology, and once this is established, experience shows that EUPHEM alumni continue along this path. The carefully designed courses that the fellows attend are instrumental in achieving the fellowship goals of increased competencies across a broad variety of subjects. On top of this comes the added value of the informal European public health microbiology network one becomes part of. As a fellow at the NIPH, I was privileged to have all the tasks, projects, counselling, help and supervision needed to complete the fellowship, and I emerge from it as a more capable and experienced public health microbiologist when faced with the challenges of the coming years.

Acknowledgements of fellow

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