

The text "Summary of work activities" in a bold, white, sans-serif font, set against a blue background.The name "Tone Bjordal Johansen" in a white, sans-serif font, set against a blue background.The text "European Public Health Microbiology Training Programme (EUPHEM), 2018 cohort" in a white, sans-serif font, set against a blue background.The text "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.

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Stockholm, September 2020

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This report summarises the work activities undertaken by Tone Bjordal Johansen, cohort 2018 of the European Public Health Microbiology Training Programme (EUPHEM) at the Norwegian Institute of Public Health (NIPH).

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

Tone is educated as a veterinarian (DVM), with a PhD in microbiology. After graduating from The Norwegian Veterinary College in 2000, she worked as a researcher at the Department of Bacteriology at the Norwegian Veterinary Institute until 2015. Her focus areas were mycobacteriology, highly pathogenic bacteria and zoonotic agents. In 2009, she finished her PhD at the Norwegian College of Veterinary Medicine. Since 2015, she worked at the Norwegian Institute of Public Health (NIPH) as a senior researcher at the Department of Zoonotic, Food- and Waterborne Infections. Tone has competence in general veterinary and public health microbiology, special competence in mycobacteriology and highly pathogenic agents (RG3 and RG4 agents), and experience in biosafety and biosecurity. She joined the EUPHEM programme to broaden her knowledge on public health microbiology and intervention epidemiology, to gain experience on outbreak investigation and to learn more about infectious diseases and infectious disease control in Europe.

Methods

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

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

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

Results

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

1. Epidemiological investigations

1.1. Outbreak investigations

Supervisors: Umaer Naseer, Emily Macdonald, Heidi Lange

A. A case of botulism following intake of commercial fermented fish

On the 4th of January, the NIPH was notified about a suspected case of botulism in a male patient from a municipality in Trøndelag. The patient had been sick with symptoms starting on the 26th of December, following a meal of fermented fish ("rakfisk") the previous day. Three other persons had eaten the same fish, but were not ill. We communicated with the local food authorities and the municipal health authorities, as well as the doctor treating the patient, and ensured that antitoxin was sent to the hospital the same day and that patient samples were sent for toxin analysis. Leftovers of commercially prepared fish consumed by the patient was available for testing. No other food items that could be suspected for botulism had been consumed by the patient. Patient samples and fish samples were sent for toxin analysis by the mouse bioassay test at the Norwegian University of Life Science. The patient sample (serum) was confirmed positive on the 10th of January. The fish sample was negative for *C. botulinum*. No further samples of fish were available for analysis.

The producer of the fish decided in cooperation with the local food authorities to withdraw this product from the market on 11 January. The product had been sold at Christmas markets and to selected grocery shops. A short notice to inform the public was published on the institute's webpages.

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>

The fellow participated in all stages of the case investigation, and was responsible for contact with the involved stakeholders, as well as writing the short notice published

B. Outbreak of Salmonella Agbeni, Norway 2019

An outbreak of *Salmonella* Agbeni occurred in Norway early in 2019. The NIPH led the outbreak investigation in collaboration with the Norwegian Food Safety Authority (NFSA) and the Norwegian Veterinary Institute (NVI). Between 31 December 2018 and 16 March 2019, 56 persons were reported with the *S. Agbeni* outbreak strain, of which 21 were hospitalized. The cases resided in different municipalities in Norway.

A case-control study was conducted, and cases were found more likely to have consumed a commercial mix of dried exotic fruits than controls (cases=8, controls=31, OR 50, 95% CI 3-2437). The outbreak strain was confirmed by whole genome sequencing, and was isolated from the fruit mix linked to the cases, resulting in withdrawal from the market on 6 March 2019. The fruit mix consisted of fruits from different countries and continents. It was packed in Italy and distributed to several European countries, including Norway. However, no cases were reported from other countries.

Epidemiological and microbiological investigations confirmed the fruit mix as the source of this outbreak, which was characterized by severe clinical presentation. This was the first report of an outbreak of *S. Agbeni* in Norway. Exotic dried fruit products are increasing in popularity as healthy alternatives to sweets. This outbreak highlighted that dried fruits could represent a risk in terms of foodborne infections, which is of particular concern because these are ready-to-eat products.

The fellow participated in all stages of the outbreak investigation, including descriptive and analytic statistical epidemiological analyses, interpreting microbiological genotyping data, conducting interviews (CC study), communicating with NFSA and the municipal health authorities, communication to the public by news messages on the institute's website, and writing updated status reports and a final outbreak report [4]. A final manuscript describing the outbreak is approved for publication in Eurosurveillance with the fellow as first author [2]. The outbreak was also presented at ESCAIDE 2020 [12] and at the yearly national conference in medical microbiology at NIPH in December 2019 [18].

C. Outbreak response group, COVID-19, Norway 2020

The fellow was involved in the outbreak response group from the early phase of the COVID-19 pandemic in January 2020. At this time point, it was still regarded as a national Chinese outbreak of a new coronavirus (called 2019-nCoV) that had similarities to SARS, primarily affecting Wuhan city and the Hubei province. An outbreak response group was established at NIPH to follow the situation carefully and to prepare for international spread that could affect Norway. The outbreak team prepared daily reports to the Norwegian Directorate of Health and the Ministry of Health (MoH) describing the development of the epidemic based on international epidemic intelligence data (primarily based on data from WHO and ECDC and other important information like media reports, reports from Chinese public health authorities CDC and others). Norway reported its first COVID-19 case on 26 February 2020.

The fellow was responsible for writing minutes from outbreak meetings and to write and update advice and public information published on the institute's websites. The fellow alternated in the team that prepared daily reports to the Norwegian Directorate of Health and the MoH. Before writing the daily report, the fellow needed to search different web platforms and to follow up Early Warning and Response System (EWRS) alerts to have updated data to present. As the pandemic developed, and the outbreak group at NIPH expanded, the fellow was enrolled in other tasks that are accounted as separate activities that are described under the different core competencies; laboratory investigation, management and communication and biorisk management.

Training modules

The three week EPIET/EUPHEM Introduction Course provided participants with the basic concepts of logistical and analytical approach to outbreak investigations, including the ten steps of an outbreak investigation. Lectures, interactive sessions, case studies, group work and writing of a research protocol was included for public health microbiology and epidemiology training. Stata as a tool was introduced briefly at this course. The Outbreak Investigation Module provided more insight in outbreak investigations, and covered data entry and management, designing of questionnaires, descriptive and analytical data analyses using Stata, communication of the findings and implementation of control measures. Case studies were used for practical training in analytical studies for an outbreak investigation, including descriptive, cohort and case-control studies. The EUPHEM fellows had a separate session focusing on whole genome sequencing (WGS) and analysis, which gave very good insight in this topic and how ECDC works on harmonizing WGS in Europe. The Multivariable Analysis Module provided a more comprehensive understanding of the principles of statistical analyses, and how and when to use linear, logistic, Poisson and Cox regression. Case studies were used for practical training. The Management, Leadership and Communication in Public Health Module trained fellows in many aspects of management and collaboration including time management and team work. The PRM in Prague 2019 included a session on scientific writing and an exercise on STROBE guidelines that was useful for preparation of scientific manuscripts.

Educational outcome:

Botulism: The case was a useful experience in the management and investigation of a case of botulism which is rarely observed in Norway, and provided experience in multidisciplinary team work.

Salmonella Agbeni: The fellow received hands-on experience in all parts of an outbreak investigation, 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.

COVID-19: The work in the outbreak management group gave valuable experience for the fellow following the development of this global pandemic from the early phase as a national Chinese outbreak and until a global pandemic was declared. The need to constantly keep updated on the international development and to summarize the most important epidemic intelligence data to the stakeholders, gave invaluable learning and understanding of the importance of epidemic intelligence and the role of different stakeholders and organizations involved in global health.

1.2. Surveillance

Supervisors: Oliver Kacelnik, Petter Elstrøm and Umaer Naseer

A. Analysis of the non-travel related cases infected with Carbapenemase Producing Organisms in Norway (2012-2019)

Carbapenems are used as last-resort treatment for infections caused by multidrug resistant bacteria. However, extensive use of these antibiotics is driving the emergence and rapid spread of resistance against carbapenems. Carbapenemase-producing organisms (CPOs) are considered a serious health threat and are responsible for a major on-going public health problem globally. In Norway, the level of CPO infections is low as compared to other countries, with an incidence rate in 2017 of 0.82. The yearly number of reported cases has however increased the last years.

The aim of this project was to describe the non-travel related cases infected with CPO in Norway (2012-2019) and to identify epidemiological and microbiological links between the cases in order to recommend improved surveillance and preventive measures against spread. Data and isolates were collected as a part of the national surveillance system. All human cases of CPO are mandatorily reported to the Norwegian Surveillance System for Communicable Diseases (MSIS), and all reported cases (clinical infections and colonization) covering the period 2012–2019 were included. K-res is the national reference laboratory (NRL) for CPO. Bacterial isolates were sequenced at the reference laboratory, and the sequences were shared with NIPH by a secure platform for a data sharing that was established as part of the project.

The results showed that in the period 2012-2019 a total of a total of 425 notifications (364 persons) with CPOs were registered in the surveillance system. Amongst these, approximately 1/4th were registered as autochthonous cases. During the study period there has been a significant increase in the annual number of persons registered in MSIS, and also in the number of cases with no travel history. Sequencing showed that we could detect clusters that might indicate smaller outbreaks or domestic transmission chains previously not recognized. The establishment of a secure platform for data sharing between surveillance site (NIPH) and reference laboratory (K-res) will be useful for rapid outbreak detection and investigations in the future. Due to delay of ethical and GDPR approvals, and due to other tasks that the fellow was assigned to during the COVID-19 pandemic, the finalisation of this project has been delayed. The results will be presented in a report to the MoH. The project has also been extended, and will be continued until at least 2025, with yearly evaluation of data.

The fellow was involved in all stages of the project from planning to data preparation and analysis (STATA and Seqsphere), including writing ethical approval request and GDPR impact assessment and drafting the study protocol. The fellow will continue working with the project and will draft the final the report to MoH.

B. Epidemic Intelligence activities

Epidemic Intelligence is the process to detect, verify, analyse, assess and investigate public health events that may represent a threat to public health. Epidemic intelligence provides early warning signals as one of the main objectives of public health surveillance systems. In Norway epidemic intelligence is both event based and indicator based, and NIPH is the national focal point for International Health Regulations (IHR) for WHO and Early Warning and Response System (EWRS) for the EU.

The fellow was a part of the Epidemic Intelligence group and participated in the weekly meetings. The fellow was partly involved in the daily monitoring of the main mailbox for incoming alerts. The fellow's tasks were then to distribute information to relevant employees and to write a report to be presented at the weekly Epidemic Intelligence meeting.

Training modules

The introductory course familiarised participants with the development, evaluation and analysis of surveillance systems. Lectures and interactive sessions familiarized the EUPHEM fellows with the challenges of antimicrobial resistance. The Multivariable Analysis Module in Madrid in March 2019, provided a more comprehensive understanding of the principles of statistical analyses. The Rapid Assessment and Survey methods module introduced fellows to the multidisciplinary and international response to complex emergencies situations.

Educational outcome:

The fellow was introduced to different surveillance systems and gained knowledge in extracting data and combine data from different surveillance systems. The fellow developed understanding and experience on how to analyse existing laboratory surveillance data and select appropriate methods, interpret, formulate recommendations and write reports. The fellow also gained experience in analysis of sequence data.

2. Applied public health microbiology research

Supervisors: Umaer Naseer, Emily MacDonald, Hilde Kløvstad

A. Evolution of *Salmonella* Typhimurium in Norway, 2005-2018: The emergence and expansion of new epidemic clones

In the last decade, the monophasic variant of *Salmonella* Typhimurium (MVST) has increasingly been identified as a cause of food-borne outbreaks in Europe. Compared to *S.* Typhimurium (ST), the monophasic variant shows more resistance to antimicrobials, and might also be more virulent. MVST has mostly been associated with pork products, but its reservoirs are unknown in Norway. This project aimed to investigate the population dynamics of ST and its MVST in Norway from 2005 to 2018, to describe the most prevalent clones, how they change over time and how MLVA data and WGS data are linked, in order to understand the evolution of strains and to identify local reservoirs for timely detection and prevention of future outbreaks.

In Norway, all cases of salmonellosis are mandatorily reported to MSIS and the isolated pathogens are sent to the National Reference Laboratory for Enteropathogenic Bacteria (NRL). At the NRL, all *Salmonella* isolates are typed for surveillance purposes. From 2004 to 2018, molecular typing of *Salmonella* spp. was performed using MLVA. Since March 2018, whole genome sequencing has replaced MLVA as the standard method for molecular surveillance.

We extracted data for all non-travel associated cases of ST and MVST notified to MSIS from 2005 until 2017, and complemented with data from the NRL database. Preliminary analyses showed that domestically acquired infections caused by MVST were increasing in Norway, while the proportion of cases with ST decline. Antibiotic resistance was observed at a higher frequency for MVST isolates than for ST. Observed differences in age groups and geographic distribution indicate different reservoirs for MVST and ST.

The analyses were not completed due to delay of ethical and GDPR approvals, and due to other tasks that the fellow was assigned to during the COVID-19 pandemic.

The fellow was responsible for reviewing scientific literature and to write the study protocol including developing dummy tables. In addition, the fellow developed the ethical approval request and the impact assessment due to GDPR regulations. The fellow participated in data analysis of surveillance data with STATA and excel and analysis of MLVA data using BioNumerics.

B. Investigation of presence and spread of new variant of *Chlamydia trachomatis* resulting in false-negative test results by Aptima Combo 2 CT/NG assay (Hologic) in Norway, 2019

In April 2019, Finnish experts informed through Epidemic Intelligence System for Sexually Transmitted Infections (EPIS STI) that a new variant of *Chlamydia trachomatis* (CT) had been detected in Finland. This "Finnish new variant CT (FI-nvCT)", with a C1515T mutation in the 23S rRNA gene, caused false-negative CT results in the nucleic acid amplification test Aptima Combo 2 (AC2) (Hologic). The FI-nvCT was later reported also from Sweden. The aim of this activity / project was to investigate if the new variant was present in Norway, and if detected to assess the need to recall patients for re-testing.

In Norway, 6 out of the 17 laboratories diagnosing CT samples routinely use AC2, accounting for approximately 50% of the CT test volume across Norway. From May to August 2019, 97 possible FI-nvCT cases from five Norwegian laboratories were available for 23S rRNA gene sequencing. In 81 (83.5%) of these samples, the CT 23S rRNA C1515T mutation was detected, and accordingly those were confirmed as FI-nvCT cases. The patients with the FI-nvCT originated from 11 different counties across Norway. A retrospective analysis based on samples with

elevated test signal in the laboratories was performed. The results indicated that the FI-nvCT might have been present at least in some regions of Norway from July 2018 or earlier.

Based on the high proportion and widespread geographic distribution of confirmed FI-nvCT samples, NIPH recommended a six month recall of patients, to ensure correct diagnosis for patients that might have received a false negative test. In total, the laboratories identified 1360 samples that fit the case definition for recall. One laboratory decided to extend the recall period back to July 2018 and, accordingly, 1377 patients were offered re-testing.

The public health relevance of this project was partly to secure necessary diagnostics and treatment for patients that had received a false negative test result, and in addition to correct national surveillance data, thus ensuring a better and more correct surveillance of *Chlamydia*.

The fellow was responsible for the communication with the laboratories and for data collection and data analyses on the retrospective analysis. She took part in information exchange on the situation in the EPIS-STI network communication platform. The fellow drafted the manuscript and was the first author of the Rapid Communication that was published in Eurosurveillance in October 2019 [1]. The results were also presented on the yearly national conference in medical microbiology at NIPH in December 2019 [17].

Training modules

The EPIET/EUPHEM Introductory Course familiarised fellows with developing and presenting study protocols and identification of the public health added values of research results, and gave good advice for scientific writing. In a group exercise, the fellows developed a protocol in order to answer a research question. The Management, Leadership and Communication in Public Health Module was important for the fellows to gain personal skills for professional development, project management and communication in public health.

Educational outcome: The two projects together ensured experience in all stages of a public health microbiology research project, starting from formulating the research question, plan the project, performing the necessary data analyses and writing the manuscript of interest to the relevant public health scientific community. The fellow gained more insight in the microbiological typing tools that are routinely used for Enteropathogenic bacteria and particularly for *Salmonella*. She additionally got acquainted with the field of STDs, and in particular diagnostic challenges for *C. trachomatis*.

3. Applied public health microbiology and laboratory investigations

Supervisors: Siri Feruglio and Olav Hungnes.

Establishing diagnostics for SARS-CoV-2 in the 24/7 preparedness laboratory

The 24/7 preparedness laboratory at NIPH has the national reference function for diagnostics of Risk group (RG) 3 and some RG 4 agents. The laboratory has a team of trained microbiologists and technical staff on-call duty. The aim of this project was to establish a diagnostic assay for detection of SARS-CoV-2 at the 24/7 preparedness laboratory to ensure a national diagnostic capacity for urgent samples. The assay was a real-time PCR test described in a publication from Corman et al 2020 and recommended by WHO.

The fellow was responsible to plan and perform the validation and to write the validation plan and report. In addition she contributed to develop the SOP and to the practical implementation in the 24/7 laboratory diagnostic capacity at NIPH, including training of personnel. The assay was implemented in the 24/7 preparedness laboratory from 31 January. The full validation report is in Norwegian [7].

In addition, the fellow took part in the group that initiated and coordinated capacity building for diagnostics of SARS-CoV-2 in Norwegian medical microbiological laboratories. This work was led by the reference laboratory for coronaviruses with outbreak potential at NIPH. The group developed advice to the laboratories, and had weekly skype meetings with representatives from all the laboratories to discuss progress and challenges. Major challenges were contamination of primers and probes and lack of equipment and reagents, as also was reported from other countries. Per 15 March, most Norwegian medical laboratories had implemented PCR for SARS-CoV-2.

Training modules

The EPIET/EUPHEM Introductory Course discussed robust laboratory investigations. In group work and case studies, different aspects of laboratory investigations were addressed. The "Management, Leadership and Communication in Public Health" module provided fellows with tools to use during multidisciplinary team projects.

Educational outcome: The fellow had the opportunity to learn and apply new laboratory competencies, and specifically increased her knowledge on laboratory methods for detection of viral pathogens. Additionally, she gained knowledge in how to identify and proceed with the best approach when time is limited. The communication with primary medical microbiological laboratories gave good insight in the various diagnostic challenges they experienced, from contamination of primers and probes to lack of equipment and reagents.

4. Biorisk management

Supervisors: Ingeborg Aaberge and Siri Feruglio

The fellow has several years of experience from work in biosafety level (BSL)-3 laboratories, is trained for work at the preparedness laboratory at NIPH, and have previously performed training for international transport of infectious substances. The fellow also leads the biosafety committee at NIPH.

A. Smallpox; Threat and preparedness in Norway.

The project and report is regarded as confidential / exempt from public disclosure and is therefore not further described here.

The fellow was assigned as the project leader and coordinated the multidisciplinary group that was assigned to the project. She performed literature searches to gain necessary scientific background, and presented the results for the group. The fellow together with colleagues developed scenarios for modelling of outcomes of different situations, and interpreted the results of the models. The modelling was performed by the department for advanced modelling and biostatistics at NIPH. She drafted the report and was responsible for the final version of the report that was sent to the MoH [5].

B. Literature review and recommendations for biosecurity in Norway.

Norway has committed to comply to the UN Security Council Resolution (UNSCR) 1540 (Biological and Toxin Weapons Convention (BTWC)) and to the EU Council Decision ((CFSP) 2016/51 of 18 January 2016 in support of the BTWC in the framework of the EU Strategy against Proliferation of Weapons of Mass Destruction).

The Norwegian Institute of Public Health (NIPH) was assigned a task from the MoH to: (i) review existing regulations on biosecurity in Norway, (ii) describe gaps and shortages, (iii) use relevant international biosecurity guidelines for comparison and (iv) elaborate recommendations for implementation and strengthening of biosecurity in Norway

A working group at NIPH was responsible for the project. We performed a review of international regulations, and focused on countries that have implemented good practise and regulations on this subject, as well as international guidelines. After performing a review of current recommendations, we organized a peer to peer one day meeting with all the relevant stakeholders from the four health regions in Norway, the Defence and Veterinary sector to agree upon the following recommendations: (i) Biosecurity regulations must include highly pathogenic agents, primarily those in RG3 and 4, (ii) The regulations must apply for all sectors that might handle such biological agents, both public sector laboratories (Public Health, Medical, Defence, Veterinary), research institutions, private laboratories and industry, (iii) The regulations should be compiled in one law or one act, (iv) Institutions or facilities that will handle the listed biological agents must apply and get approval before they start the work and (v) A biosecurity program must be established at the facility /institution. The report was delivered to the MoH on 30 November.

The fellow performed the literature review of relevant publications and legislative documents and prepared a summarized background document. She participated in the working group that together identified gaps and concluded on relevant measures for improved biosecurity. She participated in meetings with the MoH and the national stakeholders. The fellow contributed to the writing the final report [6].

C. Biosafety and SARS-CoV-2, national risk assessment

SARS-CoV-2 was regulated as a risk group (RG) 3 agent by The Norwegian Labour Inspection Authority 19 March 2020. The Norwegian primary medical microbiological laboratories needed advice on how to work with samples suspected for SARS-CoV-2 in a safe way, but also in a way that allowed an efficient flow of samples. The fellow together with the COVID-19 laboratory group at NIPH therefore did an overarching national risk assessment for work with SARS-CoV-2 and developed biosafety advice for the medical microbiological laboratories. The assessment was built on guidance from WHO, ECDC, CDC and the Public Health Agency of Canada. The risk assessment was communicated to The Norwegian Labour Inspection Authority in form of a letter, and presented to representatives from all the Norwegian medical microbiological laboratories in a web meeting on the 25 March. Our advice was also published on the institute's websites

The fellow was responsible to lead this work. She performed the literature review based on advice from international organizations, led the risk assessment, drafted the letter to The Norwegian Labour Inspection Authority, presented the results and advice to the medical microbiological laboratories and drafted the information published on the institute's webpage.

D. Biosecurity course

The fellow participated in a one day biosecurity course arranged by the Centre for Biosecurity and Biopreparedness in Copenhagen, Denmark on the 25 October 2019.

Training modules

The Management, Leadership and Communication in Public Health Module was valuable for all projects, training the fellow to adapt public health communication to different stakeholders and in project management. The Vaccinology module gave increased knowledge in vaccine preventable diseases and different vaccines, which was relevant for the smallpox project.

Educational outcome:

The fellow had pre-experience on biosafety and work at BSL-3 level laboratories, but more limited knowledge in biosecurity. The project on biosecurity therefore gave training in this field that is becoming more important worldwide. The smallpox project gave insight in scenario based modelling and introduced the fellow to the field of vaccine preventable diseases. The fellow was trained in assessment of risk to a potential health threat, and planning of response. The topic gave valuable learning in the importance but also the challenges of vaccine preparedness. This project gave the fellow experience as a project leader of a group with multidisciplinary background. All three projects gave experience in working in multidisciplinary teams, and interaction with different stakeholders from various sectors.

5. Quality management

Supervisor: Siri Feruglio and Didrik Vestrheim

The fellow has former background and experience on quality management from several years of work in both the Veterinary and the Public Health sector, and did therefore not need extensive work in this area.

A. Validation of real-time PCR for diphtheria

Diphtheria is a vaccine preventable disease that can cause serious disease classically affecting the upper respiratory tract, and is caused by toxigenic strains of *Corynebacterium diphtheriae* and occasionally toxigenic *Corynebacterium ulcerans* or *Corynebacterium pseudotuberculosis*. The bacteria can also cause skin lesions (cutaneous diphtheria). Non-toxin-producing strains can also cause disease, but the disease is less severe, and does not require infection control measures. Diphtheria is notifiable in Norway, with one to two cases reported per year, mainly the cutaneous form. The national reference laboratory at NIPH have observed an increased amount of samples the last years, especially from skin lesions, and there was a need to implement rapid detection of the different species and the toxin gene. A recent gap analysis from ECDC also highlighted the need for methodology that targets both toxigenicity and the three pathogens.

The current real-time PCR in use for the toxin detection of *C. diphtheria* at the NRL at NIPH only targets the toxin, not the species. The aim of this project was to identify a suitable new real-time PCR method for *C. diphtheria* to ensure early and accurate diagnosis of suspected cases. A quadriplex real-time PCR method published by the WHO reference laboratory for diphtheria at Public Health England that included targets for both toxin and species identification, and in addition include an internal PCR quality control was identified as the method to implement. The validation plan was finalized, but due to the COVID-19 pandemic, this work was paused due to prioritizing of resources and personnel at the reference laboratory and as the fellow was needed on other tasks. The plan described 1) validation of in silico specificity of primers and probes, 2) validation of PCR efficiency and linearity, 3) validation of analytical sensitivity, 4) validation of specificity, 5) validation of different matrices and 6) validation of precision and stability.

The fellow was responsible for performing literature search to identify the best method to implement and to write the validation plan. The fellow also performed the first step of the validation (in silico analysis) [8].

B. EQA highly pathogenic bacteria and viruses

The fellow participated in an external quality assessment exercise (EQAE) arranged by the Robert Koch Institute and the Marburg Institute of Virology as a part of the European Joint Action for health aims to ensure a safer

environment for all EU citizens (SHARP). The aim for the EQAE was to assure high quality and correct diagnostics for highly pathogenic bacteria and viruses, and at the same time evaluating the time used before submitting results.

The EQAE targeted risk group (RG)3 and RG4 bacteria and viruses and was analysed at the 24/7 preparedness laboratory at NIPH. Target bacteria for the EQAE were *Bacillus anthracis*, *Brucella* spp, *Burkholderia mallei*, *B. pseudomallei* and *Francisella tularensis*. Target viral agents were Ebola virus, Marburg virus, Crimean Congo Haemorrhagic Fever Virus and Lassa virus. Live samples were sent for RG3 agents, while RG4 agents were inactivated. Samples with bacterial agents were examined by both molecular methods and culture, while viral samples were only examined by molecular methods (real-time PCR). The submitted report is confidential.

The fellow participated in analyses of samples and in reporting of results.

Training modules

The Vaccinology Module introduced fellows to different vaccine preventable diseases, which was relevant for the work with diphtheria, although the focus was primarily on diagnostics. Additionally, EUPHEM fellows had a session on vaccine-preventable diseases in the Project Review Module in 2019.

Educational outcome: The fellow was familiarized with the institute's laboratory quality and accreditation system from before, but gained additional knowledge in how to best plan a method validation and to write the report. The required literature review gave increased knowledge on diphtheria, and how to assess and identify the best method for the purpose.

6. Teaching and pedagogy

A. Workshop on disease outbreak investigation across sectors with a One Health approach

The aim of this teaching assignment was to develop and host a case study that would be the basis of a one-day course in outbreak investigation on 24 April 2019, hosted by the department. The main objective of the workshop was to bring together stakeholders at the local and national level to train cooperation across sectors in the response to a disease outbreak within zoonotic, food-and waterborne diseases.

The workshop case study focused on cooperation and communications between stakeholders at the local (municipality) and the national level between One Health actors in Norway, mainly Municipality Medical Doctors (MMD) and the Food Safety Authority (FSA), and other actors locally, regionally, and nationally.

The objectives of the teaching assignment were to: (i) plan the schedule for the day with a mix of lectures and case study work, (ii) define the objectives of each lecture (but not develop the lectures), (iii) develop a case study (participants version and facilitator version) and (iv) decide which parts of the case study to complete in each session so that it fits with the lectures.

The case scenario was an outbreak of EHEC in children in two day care facilities. The content covered: detection of an outbreak, notification, case finding, case definition, descriptive epi, design of a cohort study, how to calculate and interpret relative risks, control measures, contacts with media, and in addition, the responsibilities of each actor and collaboration in the investigation. Upon completion of this training, participants should know and be able to exercise their role and responsibilities in an outbreak of a zoonotic, food- or waterborne disease from a One Health perspective.

The fellow's role was to develop the case study [19] together with EPIET fellow Cohort 2017, Cecilia Wolff. During the course, the fellow guided the participants through the case study inject by inject, and was also one of the facilitators. Both fellows participated in the design of the workshop, and planned the lectures and discussions presented together with the case study, in order to make the full course fit nicely together.

B. Problem-based learning: Importance of AMR as PH threat

This task was a group assignment for all EUPHEM fellows during the introduction course at Spetses. Together the group followed the principles for problem based learning, and developed a joint presentation about carbapenemase resistance and the public health implications. The joint presentation was rounded up with a self-assessment from the fellows and feedback from the tutors. The fellow's task was specifically to prepare and present molecular methods for diagnostics of carbapenemase producing organisms in session 3 of the final presentation.

C. Biosafety and biosecurity course for participants from Moldova

As a part of the NIPH's work in Global Health and International Health Regulations, a course in biosafety and biosecurity at BSL-3 level was arranged for five persons from the Public Health Institute in Moldova and for one

EUPHEM fellow at NIPH. In all, we arranged a four day course, with both theoretical and practical parts. In the last day of the course, there was oral feedback and summary of the course.

The fellow participated in the planning of the course agenda and content, and planned and delivered two presentations [15], one covering general principles for biorisk management and how to work in a BSL-3 laboratory, and one introducing risk assessment. The fellow also planned and arranged a risk assessment workshop for the participants together with a colleague.

Training modules

The EPIET/EUPHEM introductory course provided fellows with a platform for presentation skills and different ways of teaching. The EUPHEM-specific activity in problem-based learning enabled fellows to prepare their own lectures and was valuable training for teaching. The many case studies that were introduced, gave experience in how to develop and deliver a case study to participants. The Management, Leadership and Communication in Public Health Module covered topics on how to communicate effectively within a multidisciplinary teams. At the Project Review Module, the fellows received critical feedback on their presentation styles, which gave room for improvement and new ideas.

Educational outcome:

The fellow gained experience in planning and delivery of single lectures as well as organisation of a full course, to communicate and train public health and laboratory professionals, to define learning objectives and to assess own performance through feedback. The One Health workshop was valuable for training in moderation of a case study and gave additional training in the ten steps of outbreak investigation. The exercise at the introduction course gave experience in problem based learning. The course for colleagues from Moldova gave valuable interactions and discussions around differences between countries regarding laboratory systems, and challenges when resources are limited.

7. Public health microbiology management

A. Risk communication and infection prevention and control guidance for COVID-19

Norway reported its first COVID-19 case on 26 February 2020. On 12 March, the government announced a series of restrictive infection control measures after a rapid increase in cases and evidence of community transmission. These included border control and a travel ban, closure of daycares, schools, universities and businesses; and a ban on mass gatherings. A strict lockdown was never imposed, but the general rule was to work from home and to avoid public transportation. The population mobility dropped dramatically overnight.

The fellow has, during the development of the outbreak of COVID-19, been a part of the group responsible for risk communication and infection prevention and control guidance. The group developed advice to the general public and to the national authorities based on available guidance from WHO, ECDC, CDC and others. In addition, the group has been responsible to develop national infection prevention and control (IPC) guidance documents requested by the MoH for different sectors in the society.

The fellow was responsible to write and update advice on the website. Examples are advice for mass gatherings, advice for workplaces, advice for schools and daycare facilities and facts about COVID-19. The fellow has contributed to the national guidelines for IPC for aviation, public transport, workplaces, schools and daycare [9,10,11]. A rapid communication with the fellow as the first author describing the infection prevention guidelines and considerations for paediatric risk groups when reopening primary schools during COVID-19 pandemic in Norway was published in Eurosurveillance [3].

B. Leading the biosafety committee at NIPH

The biosafety committee includes participants representing the different laboratories at NIPH. Relevant issues and problems regarding biosafety are discussed in the meetings and communicated to the relevant department directors at NIPH. The committee evaluates risk assessments and gives advice to all laboratories handling infectious agents at NIPH. The fellow is the leader of this committee at NIPH, arranges meetings and writes minutes from meetings. The meetings have been held approximately every second month.

C. Ethical approval request and Impact assessment for GDPR for Surveillance and Research projects

The fellow was responsible to write the ethical approval request to the regional ethical board in Norway and the impact assessment for GDPR to the data protection officer at NIPH for Surveillance and Research projects.

Training modules

The Management, Leadership and Communication in Public Health Module familiarised fellows in terms of understanding roles and responsibilities in public health management settings, and gave experience in the best way to deliver public health messages and results to different audiences. During the Project Review module, the fellow had the chance to discuss important study outcomes with public health professionals, to sharpen recommendations and to advance public health communication skills.

Educational outcome: These projects and activities has improved the fellow's management and communication skills, and she gained the ability to professionally and effectively communicate with higher authorities, stakeholders and the public. The projects on smallpox and biosecurity in Norway described under biorisk management gave experience in managing Public Health projects in collaboration with multidisciplinary teams. The fellow had pre-experience with developing ethical applications, but the impact assessment for GDPR was a new and challenging task, that provided new knowledge both for the fellow and the institute.

8. Communication

Publications

1. Johansen TB, Kløvstad H, Rykkvin R, Herrfurth-Erichsen EB, Sorthe J, Njølstad G, Ebbesen MH, Nygaard RM, Sandmoen EK, Thilesen C, Onken A, Liljedal I, Hadad R, Unemo M. The "Finnish new variant of *Chlamydia trachomatis*" escaping detection in the Aptima Combo 2 assay is widespread across Norway, May-August 2019. *Eurosurveillance*. Volume 24, Issue 42, 17/Oct/2019
2. Johansen TB et al. Exotic dried fruits caused *Salmonella* Agbeni outbreak with severe clinical presentation, Norway, December 2018 to March 2019 (Accepted for publication in *Eurosurveillance*)
3. Johansen TB, Astrup E, Jore S, Nilssen H, Dahlberg BB, Klingenberg C, Berg AS, Greve-Isdahl M. Infection prevention, guidelines and considerations for paediatric risk groups when reopening primary schools during COVID-19 pandemic, Norway, April 2020. *Eurosurveillance* Volume 25, Issue 22, 04/Jun/2020.

Reports

4. Johansen, TB et al. Outbreak report. An outbreak of *Salmonella* Agbeni, Norway, 2019 (in Norwegian)
5. Report to MOH, 2018. Vaccine preparedness. Exempt public disclosure (in Norwegian)
6. Report on biosecurity in Norway to MoH, 2018 (in Norwegian)
7. Validation plan establishment of Diphtheria PCR (in Norwegian)
8. Validation plan and report real-time PCR for SARS-CoV-2 (in Norwegian)
9. Guidance for IPC in day care, primary schools and secondary schools during COVID-19, Norway 2020 (three reports in Norwegian, two are translated in English)
10. Guidance for IPC in aviation during COVID-19, Norway 2020 (in Norwegian, translated to English)
11. Guidance for IPC in public transport during COVID-19, Norway 2020 (in Norwegian)

Conference presentations

12. Johansen TB et al. Outbreak of *Salmonella* Agbeni with severe clinical presentation linked to exotic dried fruit mix, Norway, 2019. ESCAIDE 2020

Other presentations

13. Johansen TB. Brucellosis in Norway. A study on whole genome sequencing and antimicrobial susceptibility testing. Outbreak Investigation Module. Berlin, 2019.
14. Johansen Linkevicius M, Angermeier H, Gonçalves P, Amato E, Thomas-Lopez D, Brehony C, Riess M, Johansen TB. Problem-based learning. Importance of AMR as PH threat. Spetses. 2018
15. TB. Overview Biosafety and Biosecurity and Risk assessment. Course in Biosafety and Biosecurity. Oslo 2019.
16. Johansen TB. Risk assessment planning and management. Course in Biosafety and Biosecurity. Oslo 2019.
17. Johansen TB. The "Finnish new variant of *Chlamydia trachomatis*" escaping detection in the Aptima Combo 2 assay is widespread across Norway, May-August 2019. National conference in medical microbiology, NIPH, Oslo December 2019.
18. Johansen TB. Exotic dried fruits caused *Salmonella* Agbeni outbreak with severe clinical presentation, Norway, December 2018 to March 2019. National conference in medical microbiology, NIPH, Oslo December 2019.

Other

19. Johansen TB and Wolff C. Case study for workshop in outbreak investigation of foodborne pathogens, NIPH, 24 April 2019.

Training modules

The EPIET/EUPHEM Introduction course covered the topic scientific writing and introduced fellows to communication strategies. Scientific writing and best approach strategies for abstracts were also discussed at the Multivariable Analysis Module. The PRM modules gave fellows experience how to best present scientific data and to give and receive feedback. The Management, Leadership and Communication in Public Health Module further trained the fellows in communication strategies, and used role play and group work to train for different audiences.

9. EPIET/EUPHEM modules attended

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

10. Other training

1. The European Scientific Conference on Applied Infectious Disease Epidemiology (ESCAIDE), Malta, 18-30 November 2018.
2. Nordic Mini Project Review Module, Copenhagen, Denmark. 3-4 April 2019.
3. Nordic Biopreparedness Forum. Workshop in Risk Assessment in the Context of BSL 3 Operations. Oslo, 21-22 March, 2019.
4. Cohesive Workshop, outbreak investigation of foodborne pathogens. Oslo, 24 April, 2019.
5. Course in biosecurity. Centre for Biosecurity and Biopreparedness, Copenhagen, Denmark. 25 October 2019.
6. The European Scientific Conference on Applied Infectious Disease Epidemiology (ESCAIDE), Stockholm, Sweden, 18-30 November 2019

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 Tone Bjordal Johansen during her two-year EUPHEM fellowship (cohort 2018) as a member state track fellow at the Norwegian Institute of Public Health (NIPH). The EUPHEM Member State track pathway is a 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 by Tone who enthusiastically embraced the fellowship showing her value in several fields from extended outbreak investigations to surveillance and lab investigation but also in response to Covid-19 pandemic. Her former experience in the field of highly pathogenic organisms has been invaluable both in supporting her country MoH and providing cascading expertise through training. The contribution made by Tone indicates the importance of developing a future critical mass of highly skilled field public health microbiologists within Member States to contribute towards national preparedness. The EUPHEM Coordinator Team concludes that the fellow has succeeded in performing all her tasks with a high professional attitude and remarkable commitment. Tone has been an intelligent, dedicated person and a fellow with whom was a pleasure to work with: I wish her every success as a public health microbiologist.

Supervisor's conclusions

The EUPHEM fellowship has been an opportunity for Tone to increase her knowledge and experience into various fields of public health microbiology. For the Norwegian Institute of Public Health (NIPH), her fellowship has provided an invaluable asset to the team of public health professionals.

Tone has been an exceptionally strong candidate. During her fellowship, she has displayed eagerness to expand her knowledge base and learn new skills. She has shown a great degree of versatility and flexibility, and managed

to complete most tasks of high quality and within set timeframes. She has been a determined individual who has taken on the EUPHEM fellowship, even during difficult times. Especially during COVID-19, she has demonstrated her excellent communication skills and has been an invaluable member of the Norwegian COVID-19 response team. Her projects covered all core domains within the programme and showed that she was able to work and manage these projects independently. Her scientific knowledge, technical and organisational skills and team spirit has been very much appreciated by all supervisors along with her open-mindedness, positivity, diligence and goal-oriented personality.

It was a great pleasure to have Tone as a EUPHEM fellow at NIPH and we highly appreciate her contribution and achievements within the fellowship programme. Tone is a great ambassador for the EUPHEM program and for Public Health Microbiology. I wish her every success for the future.

Personal conclusions of fellow

The EUPHEM fellowship has been a valuable experience for me, and has provided very good training in public health microbiology and epidemiology. The learning by doing approach with the mix of training modules and projects has been excellent for increasing my professional skills and knowledge. The modules arranged by ECDC covered important aspects of public health and have been very relevant for my projects. Through the daily work with projects and other activities at the Norwegian Institute of Public Health, I was able to gain a solid basis of knowledge in different areas of public health and to advance my skills in microbiology and epidemiology together with highly skilled colleagues. And finally, the fellowship provided me with a network of public health colleagues all over Europe, a network that is important for coordinated future public health action for the benefit of population health in Europe.

Acknowledgements of fellow

I would first like to thank my EUPHEM supervisor, Umaer Naseer, for excellent guidance and constant support and supervision throughout the fellowship. I am grateful to Didrik Vestheim and Ingeborg Aaberge for introducing me to the EUPHEM programme and encouraging me to apply, and Emily MacDonald that through her coordinating role and general positivity, created a good environment for all the fellows at NIPH. All my project supervisors have been invaluable for my professional development and for fulfilling my projects, and I thank them for their guidance and expert input and for their general positivity, making the fellowship a very good experience. I would also like to thank the many EPIET and EUPHEM fellows at NIPH, present and former, for fruitful interactions and collaboration, shared learning and a friendly environment. Many appreciations to all my colleagues at NIPH for providing a warm and friendly working environment. A special greeting goes to all my co-fellows in Cohort 2018, for their friendship, knowledge and support throughout these two years, it has been a privilege to do the fellowship experience together. A pandemic prevented all travels and physical meetings, making the fellowship different, but we still kept the spirit up in the group. I would especially like to thank my frontline coordinator, Loredana Ingrosso, for guiding me through the fellowship in an excellent way and for being supportive and understanding for the challenges faced during the fellowship, and Aftab Jasir for her constant support and commitment to all the EUPHEM fellows. Last but not least, I thank my family for all their support and patience with my long working hours and many travels during these two years.