Summary of work activities
Lin Thorstensen Brandal
European Public Health Microbiology Training Programme (EUPHEM), 2019 cohort

Background

According to the European Centre for Disease Prevention and Control (ECDC) Advisory Group on Public Health Microbiology ("national microbiology focal points"), public health microbiology is a cross-cutting area that spans the fields of human, animal, food, water and environmental microbiology, with a focus on human population health and disease. Its primary function is to improve health in collaboration with other public health disciplines, in particular epidemiology. Public health microbiology laboratories play a central role in detection, monitoring, outbreak response and the provision of scientific evidence to prevent and control infectious diseases.

European preparedness in 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 provides experts in all relevant communicable diseases at the regional, national and international level with the tools they need to mount rapid responses to emerging health threats. This enables them to plan appropriate prevention strategies, assess existing prevention disciplines, develop microbiological guidelines, evaluate/produce new diagnostic tools, assess 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’ which is why 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 Lin Thorstensen Brandal, cohort 2019 of the European Public Health Microbiology Training Programme (EUPHEM) at the Norwegian Institute of Public Health (NIPH).

Lin Thorstensen Brandal is a pharmacist (Cand Pharm), with a masters in microbiology and a PhD in cancer genetics. After a postdoctoral research period in cancer genetics, she started her career at the Norwegian Institute.
of Public Health (NIPH) in 2004, focusing on characterisation and molecular epidemiological surveillance of foodborne pathogens. Since 2005, she has worked as a senior scientist with tasks within surveillance, outbreak detection and investigation, the establishment of molecular epidemiological methods, quality management (EQA’s and accreditation), advisor activities, and research projects associated with enteropathogenic bacteria. Lin has supervision experience both at masters and PhD level. From 2017 until the start of her EUPHEM fellowship she coordinated the National Reference Laboratory for Enteropathogenic Bacteria at NIPH, and she was one of the key people implementing whole genome sequencing in routine surveillance of these pathogens in Norway in 2018.

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.

Methods

This report accompanies a portfolio demonstrating 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 and the summary and communication of 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, with the exception of those prohibited for reasons of confidentiality.

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: Oliver Kacelnik, Hilde Lund, Heidi Lange, and Emily MacDonald

A. Outbreak of ESBL (CTX-M-15)-producing Klebsiella pneumoniae at a surgical ward with national catchment area, Norway, 2019

Supervisor: Oliver Kacelnik, senior medical officer, Department of infection control and preparedness, NIPH

An outbreak of extended-spectrum beta-lactamase (ESBL)-producing Klebsiella pneumoniae (K. pneumoniae) at a Norwegian surgical ward with a national catchment area occurred in 2019. NIPH was asked to assist the outbreak investigation, with a focus on epidemiological analysis. The objectives of the epidemiological investigation were to describe the outbreak, to identify risk factors, and to inform control measures in order to prevent the further spread of the outbreak strain. Between 1 July and 17 December 2019, 20 cases carrying the outbreak strain, sequence type (ST) 307, ESBL (CTX-M-15)-producing K. pneumonia, were detected by whole genome sequencing (WGS). Positive environmental samples continued to be present at the surgical ward, despite comprehensive decontamination procedures.

A descriptive study on patient characteristics, exposures, and movements inside and outside the surgical ward was conducted. Sixty percent of the cases were male, the median age was 65 years, and 11 (55%) developed clinical infections. Seventy-five percent of the cases had stayed in two or more rooms at the surgical ward prior to testing positive.

A retrospective case-control (CC) study was conducted. A single exposure or source could not explain all the cases in this outbreak, but cases more likely had neoplastic disease and an older age than controls. Furthermore, the cases had higher odds of being exposed for specific healthcare workers, ultrasound performed with a transportable machine, dialysis, and arterial catheter compared to the controls.

Based on our findings, several prevention and control measures were recommended.

The fellow was involved in collecting and collating data from patients’ medical record at the hospital, participating in outbreak meetings, framing the case definition, planning and performing descriptive and analytical statistical analysis, communicating with the outbreak team at the hospital, presenting results at NIPH and at the hospital, suggesting control measures to implement, and writing the outbreak report [7].

B. Outbreak of Salmonella Enteritidis linked to bovine carcases imported from Germany, Norway, 2021

Supervisors: Hilde M. Lund and Heidi Lange, senior advisors, Department of infection control and preparedness, NIPH

On 25 February 2021, the National Reference Laboratory (NRL) for enteropathogenic bacteria informed the Department for Infection Control and Preparedness at NIPH of a possible outbreak of Salmonella Enteritidis (S. Enteritidis). In collaboration with the Norwegian Food Safety Authority (NFSA), the Norwegian Veterinary Institute (NVI) and chief municipal medical officers, an outbreak investigation was initiated aiming to identify the source and prevent further transmission. A total of 30 cases were identified, all with S. Enteritidis sequence type 11 and cluster type 5784 based on WGS and core genome multilocus sequence typing. Sixty percent of the cases were female, with a median age of 58 years, and the cases were geographically spread throughout Norway. Fifteen of 19 cases interviewed, with either a trawling questionnaire (n=8) or a targeted questionnaire (n=11) focusing on minced meat and beef products, reported eating bovine minced meat. Eight of these had consumed the minced meat raw. WGS of S. Enteritidis from bovine carcases imported from Germany was conducted by NVI and a match with the human outbreak strain was detected. Meat products from the imported batch were recalled, and all available stock was impounded by NFSA. Denmark, France, and Germany all reported cases with the outbreak strain. Consumers were recommended via the media not to eat raw minced meat, and the routine testing of imported meat to Norway was suggested.

The fellow was involved in framing the case definition, analysing and interpreting microbiological data (including WGS data), participating in multidisciplinary outbreak meetings, communicating with NFSA and NVI as well as to the public through news messages on the website of NIPH [26], posting an urgent inquiry on EPIS (UI-704), supervising Andreas Rohringer, an EUPHEM-fellow from C2020, on outbreak report-writing and scientific writing of an abstract [15, 20].

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

Supervisors: Emily MacDonald, senior advisor, Department of infection control and preparedness, NIPH

In Norway, the first case of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection was confirmed on 26 February 2020. On 27 February 2020, a notification database at NIPH was established in order to survey all identified COVID-19 cases in Norway. The chief municipal medical officers throughout Norway were required to notify all confirmed COVID-19 cases to this database by telephone. The fellow was in the team interviewing, with either a trawling questionnaire (n=8) or a targeted questionnaire (n=11) focusing on minced meat consumption. Sixty percent of the cases were female, with a median age of 58 years, and the cases were geographically spread throughout Norway. Fifteen of 19 cases interviewed, with either a trawling questionnaire (n=8) or a targeted questionnaire (n=11) focusing on minced meat and beef products, reported eating bovine minced meat. Eight of these had consumed the minced meat raw. WGS of S. Enteritidis from bovine carcases imported from Germany was conducted by NVI and a match with the human outbreak strain was detected. Meat products from the imported batch were recalled, and all available stock was impounded by NFSA. Denmark, France, and Germany all reported cases with the outbreak strain. Consumers were recommended via the media not to eat raw minced meat, and the routine testing of imported meat to Norway was suggested.

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Training modules related to the assignment/projects

The three weeks EPIET/EUPHEM Introductory Course provided participants with lectures, interactive sessions, case studies, group work, and writing of a research protocol as training in public health microbiology and intervention epidemiology. The course introduced fellows to the 10 steps of an outbreak investigation. The statistical tool Stata was briefly introduced.

The Outbreak Investigation Module provided an interactive course, including case studies, systematically going through the steps in an outbreak investigation, form data entry and management, designing of questionnaires,
Antimicrobial resistance (AMR) has become a global health crisis. A fundamental component to combatting this crisis is the collection of high-quality AMR surveillance data. Traditionally, this has been anchored in measurement of resistance phenotype, in order to ensure successful antimicrobial treatment. Due to the decline in cost and the advantage of using a truly high throughput method when investigating all relevant parameters, whole genome sequencing (WGS) is increasingly available in public health laboratories. This project aimed to evaluate the advantage of using a truly high throughput method when investigating all relevant parameters, whole genome of resistance phenotype, in order to ensure successful antimicrobial treatment. Due to the decline in cost and the control and vaccines, NIPH

enterocolitica were included in our study and no previous papers comparing phenotypic–genotypic resistance for the following antimicrobials: ampicillin, cefotaxime (third generation cephalosporin), ceftazidime (third generation cephalosporin), meropenem (carbapenemase), chloramphenicol, ciprofloxacin/pefloxacin, and tetracycline. Agar disk diffusion test was used for AST and, after a pilot project testing four different open-access databases, ResFinder and PointFinder from Center for Genomic Epidemiology (CGE) were selected for WGS prediction of AMR. We observed high sensitivity and specificity by comparing predicted resistance from WGS data to phenotypic resistance data for the majority of the antimicrobials examined in Salmonella spp. and Shigella spp. Tetracycline and chloramphenicol in Salmonella spp. and cefotaxime in Shigella spp. showed sensitivity below 90%. Specificities under 90% were seen for ceftazidime and ciprofloxacin in Shigella spp. Few phenotypic resistant pathogenic Y. enterocolitica were included in our study and no previous papers comparing phenotypic–genotypic resistance for this pathogen have been published. More data on this pathogen is needed. We recommended exploring more open-access resources and developing an in-house pipeline, regularly updated and curated, for the prediction of AMR from WGS data before implementing this in routine surveillance of foodborne pathogens.

The fellow was involved in all stages of the project, from planning to the presenting of results. The main tasks included reviewing literature, collecting, analysing and interpreting data, managing the project, and writing a report [8]. Lin suggested recommendations for further improvements in implementing WGS in surveillance of AMR for foodborne pathogens.

B. Bio-behavioural cross-sectional survey among people who inject drugs in Oslo, Norway, 2018

Supervisors: Robert N. Whittaker, research scientist, and Hilde Kløvstad, senior advisor, Department of infection control and vaccines, NIPH

People who inject drugs (PWID) are at increased risk of blood-borne infections such as hepatitis A, B, and C, and HIV. Cross-sectional prevalence studies have been performed regularly in Oslo in order to monitor the transmission of these infections among PWID. The aim of this study was to describe the prevalence of hepatitis A, B, and C, and HIV infections, as well as drug use, among PWID in Oslo in 2018. In addition, we examined if there was an association between hepatitis B or C infection and the number of years injecting drugs. A point prevalence study was conducted among PWID over 18 years attending low-threshold health and social services in Oslo in 2018. Blood samples from the participants were screened for hepatitis A virus (HAV), hepatitis B virus (HBV),
hepatitis C virus (HCV), and HIV. In addition, they answered a questionnaire about drug use. Descriptive analysis was performed. Univariable and multivariable logistic regression were used to examine the association between HBV or HCV infections and the number of years injecting drugs. The study included 299 PWID aged 21 to 69 years (median 41), of whom 75% were male. The median number of injection years was 13.5 and ranged from <1-54 years. The prevalence of HIV, HBV, and HCV infection was 1.4% (4/284), 0.7% (2/283), and 26.1% (74/284), respectively. The prevalence of HAV-antibodies was 65.5% (186/284). Detection of antibodies against HBV core antigen (odds ratio (OR)=1.07, 95% confidence interval (CI) 1.03-1.11), HCV (OR=1.14, 95% CI 1.10-1.18), and HCV RNA (OR=1.04, 95% CI 1.02-1.06), were all associated with increasing years of injection. The prevalence of acute or chronic HCV infection among PWID in Oslo had declined compared to previous years, indicating that the control measures implemented for this risk group have been effective. However, the odds of HCV infection increased with an increasing number of years of drug injection. Thus, it is important to reach this risk group with measures as early as possible. The prevalence of HIV and HBV infections among PWID in Oslo in 2018 were comparable with previous years and remained low. For hepatitis A, the prevalence reflected both previous infection and vaccination and was comparable to earlier years. The results from the study indicated that long-term and targeted infection prevention and control measures towards PWID have been efficient. We recommended that this targeted work be continued as well as the regularly point prevalence studies among PWID in Oslo in order to enhance the surveillance of blood-borne viral infections in this risk group.

The fellow contributed equally to this work along with EUPHEM fellow C2020 Ragnhild Tønnessen. Lin was involved in analysing and interpreting the data using analytical epidemiological methods, and in writing the report [14]. Public health recommendations were suggested.

C. Routine surveillance of enteropathogenic bacteria based on whole genome sequencing

Supervisor: Umaer Naseer, senior scientist, Department of infection control and preparedness, NIPH

Routine surveillance

The National Reference Laboratory (NRL) for Enteropathogenic Bacteria is located at NIPH. All medical microbiological laboratories throughout Norway (n=21) submit Salmonella, Yersinia, Listeria, enteropathogenic E. coli (including Shiga toxin-producing E. coli), Shigella and a selection of Campylobacter isolates to NRL at NIPH. All isolates are verified and characterised by whole genome sequencing (WGS) at NRL. Lin is the professional responsible for molecular methods at NRL and was one of the key people implementing WGS in routine surveillance of these pathogens in 2018. She is closely involved in interpretation of the WGS results and detection of clusters. In addition to her involvement in the Salmonella Enteritidis outbreak linked to beef January to May 2021, Lin has been involved in detecting several clusters during her EUPHEM fellowship. Some examples of clusters leading to an outbreak investigation are: Salmonella Oranienburg, six cases, August to October 2020, no source identified; Yersinia enterocolitica O:3, 10 cases, November 2020, probably linked to pre-washed salad; Listeria monocytogenes, four cases, August to December 2020, no source identified; Salmonella Dublin, six cases, December to January 2020/2021, probably linked to unpasteurised bovine cheese; Yersinia enterocolitica, 15 cases, April to May 2021, ongoing.

Epidemic intelligence activities

In the last year of the fellowship, Lin was responsible for examining and answering all Urgent Inquiries (UIs) received from the Epidemic Intelligence Information System (EPIS) of Food- and Waterborne Diseases and Zoonoses, ECDC. Additionally, she posted three UIs from Norway (UI-704, UI-710 and UI-724).

Training modules related to the assignment/projects

The Introductory Course familiarised participants with the development, evaluation, and analysis of surveillance systems. Lectures and interactive sessions provided the fellows with insights into the challenges of antimicrobial resistance. The statistical tool Stata was briefly introduced.

The Multivariable Analysis Module provided a more comprehensive understanding of the principles of statistical analyses. The Management, Leadership, and Communication in Public Health Module trained fellows in many aspects of management and collaboration including time management and team collaboration.

The Rapid Assessment and Survey methods module introduced fellows to rapid health assessment at the European level, survey methods and spatial analysis, and setting up a surveillance system in complex emergencies situations.
**Educational outcome**

The fellow developed an understanding and experience of the information needed to implement new methods in an existing laboratory surveillance system. Lin also acquired experience in data analysis and the interpretation of surveillance data, as well as how to formulate recommendations and write reports.

**2. Applied public health research**

**A. Molecular epidemiology of Bordetella pertussis in Norway 1996-2019: Allelic variants of vaccine-related antigens**

Supervisors: Didrik Vestrheim, senior medical officer and Anneke Steens, researcher, both at Department of infection control and vaccines, NIPH

Pertussis is an acute respiratory infection caused by *Bordetella pertussis* (*B. pertussis*). The disease can be life-threatening in infants and young children. A shift from whole cell vaccines (WCVs) to acellular vaccines (ACVs) occurred in industrialised countries, including Norway, during the mid-1990s. Despite high vaccine coverage, pertussis continues to be a public health concern globally. A resurgence of pertussis has been described and pathogen adaptation has been suggested as a contributing factor. The aim of this study was to describe the molecular population structure of *Bordetella pertussis* in Norway from 1996 to 2019, and determine if there was an evolutionary shift after the introduction of the ACV in 1998 and pre-school and adolescent boosters in 2006/2007 and 2013/2014.

We included 180 *B. pertussis* isolates referred to the national reference laboratory between 1996 and 2019. The isolates underwent whole genome sequencing. We determined the distribution and frequency of allele variants and temporal changes of genes encoding vaccine antigens.

Two of six different allelic profiles dominated; 47% (n=85) with profile A (introduced 1994) and 42% (n=75) with profile B (introduced 1970), both carrying pertussis toxin (*ptxA1*, *ptxP3*), pertactin (*prn2*), fimbriae (*fim2-1* and *fim3-2* (A) or *fim3-1* (B), respectively). Sixteen percent (n=29) showed deletions in *prn*. Isolates with *pbrP1* and *prn1* disappeared around 2007. The *prn2* allele likely emerged prior to 1972, and *ptxP3* before the early 1980s. Recently circulating clones have the *pbrP3* and *prn2* alleles fixed, with increasing incidence of *prn* deletions.

The Norwegian *B. pertussis* population harbor allelic profiles of ACV antigens with mismatch to components of the ACV. Mutations in ACV antigens occurred perhaps as early as 1950, prior to the ACV era, but ACV might have contributed to the evolution of a more uniform *B. pertussis* population. This could have implications for vaccine efficiency and therefore the prevention and control of pertussis. We recommend continued collection of *B. pertussis* isolates for surveillance purposes, and to further explore the role of genetic adaptation.

The fellow was responsible for reviewing scientific literature, suggesting study design and writing the study protocol. She developed the ethical approval request and the impact assessment due to GDPR regulations. Lin arranged project meetings, selected the material and organised the lab work. In collaboration with the bioinformatician, Lin, collected, analysed and interpreted the WGS data. The fellow drafted a scientific manuscript as the first author [5]. An abstract was submitted to ESCAIDE 2021 [19].

**Training modules related to the assignment/projects**

The EPIET/EUPHEM Introductory Course familiarised the fellow with developing and presenting study protocols for an applied public health research project. This included ethical and governance considerations of the proposed research and proposing public health control measures and recommendations based on research findings.

The Management, Leadership and Communication in Public Health Module was important for the fellows to gain personal skills for professional development, project management, time management, and communication in public health.

The Vaccinology Module introduced the fellows to different vaccine-preventable diseases, vaccine types, vaccination programmes and evaluation of vaccination interventions. Vaccination coverage, the effect of vaccination on the population, and burden of disease were central terms discussed.

**Educational outcome**

The pertussis project ensured experience in all stages of a Public Health Microbiology research project, starting with study design, study protocol/relevant questions, managing a project team of technicians and scientists, method identification, collecting, analysing and interpreting data, through to writing a scientific manuscript. Additionally, Lin gained experience working with a vaccine-preventable disease.
3. Applied public health microbiology and laboratory investigations

A. The role of children in the transmission of SARS-CoV-2 in schools

Supervisors: Brita A. Winje, senior scientist, Department of infection control and vaccines, Hinta Meijerink, senior advisor, Department of infection control and preparedness, and Rikard Rykkvin, senior medical officer, Department of Virology, NIPH

Children with coronavirus disease 2019 (COVID-19) infection are often asymptomatic or have mild symptoms. Symptomatic children shed severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) in comparable quantities as adults and can transmit the virus in a similar manner. However, the role of asymptomatic children in the transmission of SARS-CoV-2 is unknown. In Norway, strict infection prevention and control (IPC) measures were implemented when schools re-opened in April 2020. We aimed to examine transmission of SARS-CoV-2 from confirmed pediatric COVID-19 cases in schools in Norway by systematic testing of all contacts within the school twice during the quarantine period.

We included contact tracings for index cases aged 5-16 years in Oslo or Viken with PCR confirmed SARS-CoV-2, who had attended school within 48 hours prior to symptom onset or date of sampling. We excluded contact tracings with adult COVID-19 index cases. Public health officials identified exposed child and adult school contacts. We distributed equipment and a detailed instruction for self-collection of two saliva samples to consenting participants. The first saliva sample was taken as early as possible, whereas the second saliva sample was taken at the end of the quarantine period. A primary case was defined as a contact who tested positive for SARS-CoV-2 in the first saliva sample, whereas a secondary case was defined as a contact who tested positive for SARS-CoV-2 in the second saliva sample, following a first negative test. All SARS-CoV-2 positive samples were whole genome sequenced. All participants filled out a questionnaire (demographic and clinical data as well as risk factors) at the start and end of the study, respectively, and a daily journal with symptoms was admitted from each participant.

In our first manuscript [1], 13 contact tracings from primary schools were included. Among 234 child contacts, two primary cases (0.9%) and no secondary cases were identified, and among 58 adult contacts one primary case (1.7%) and no secondary cases were identified. Thus, minimal transmission of SARS-CoV-2 from children in primary schools with implemented IPC was observed. In addition, self-collection of saliva for SARS-CoV-2 detection was efficient and highly sensitive (85%). We recommended strengthening IPC measures in schools when transmission level in the community increases.

In our second manuscript [6], a total of 43 contact tracings will be included (29 at primary schools and 14 at secondary schools). We will use WGS data to examine the transmission of SARS-CoV-2 from children in school settings related to different SARS-CoV-2 variants, with a specific focus of variants of concern (VOC). Additionally, we will explore whether the transmission of SARS-CoV-2 is different between children attending primary and secondary schools.

The fellow was one of three scientists developing the study protocol. Lin was responsible for and coordinated the laboratory flow, including collecting, transporting, analysing, and storing all biological material. She put together a laboratory team and arranged meetings. Lin proposed a budget plan for the laboratory work and ordered reagents and equipment. She made instructions for sample collection and transportation. Lin was involved in the interpretation of the laboratory results, including phylogenetic analysis, and was the first author on the first manuscript and the senior author on the second manuscript.

Training modules related to the assignment/projects

The EPIET/EUPHEM Introductory Course familiarised fellows with developing and presenting study protocols, proposing public health control measures and recommendations based on research findings, and communicating relevant public health information.

The Outbreak Investigation Module introduced methods of whole genome sequencing and interpretation.

The Management, Leadership and Communication in Public Health Module trained fellows in management, collaboration and communication, including time management, team collaboration, roles and responsibilities, and effective communication skills.

Educational outcome

The COVID-19 laboratory investigation project was part of a larger research project that gave the fellow increased competencies in microbiological knowledge, specifically within virology and laboratory investigation (microbiological case definition, sampling strategies, laboratory techniques, and team coordination), specimen transportation and laboratory analysis, including WGS. Additionally, Lin increased her knowledge in management and communication.
4. Biorisk management

A. BSL-3 biosafety and biosecurity training

Supervisor: Tone B. Johansen, senior scientist, Department of infection control and preparedness, NIPH

Training for BSL-3 preparedness laboratory staff at NIPH included a general theoretical and a general practical part given by Tone B. Johansen, Irene Rauk, and Veronica K. Jensen. Topics presented were an overview of biosafety and biosecurity, including laboratory safety levels and microbial risk group classification, a general overview of selected highly pathogenic agents and methodology, risk assessments, shipment of dangerous goods, physical barriers in the laboratory, donning and doffing of personal protective equipment, safe working practices and operating procedures following spills, illness, fires etc. In addition, the fellow participated in training on virus RNA-extraction and handling suspicious letters potentially contaminated with Crimean Congo in the BSL-3 laboratory glove box. FilmArray and real-time PCR were demonstrated. Cultivation of risk group 3 bacterial agents in Class 2 cabinet and DNA isolation were performed. The fellow received a BSL-3 training certificate issued by NIPH.

B. Biosafety and SARS-CoV-2; collection and transportation of saliva samples

In the COVID-19 laboratory project, home collection of saliva sample was performed. SARS-CoV-2 is currently classified as a Risk Group 3 human pathogen, and saliva samples that might contain this pathogen require proper handling and transportation.

The fellow was responsible for making guidelines for the collection and transportation of the saliva sample from the participants to the NIPH. The WHO's 2019-2020 guidance and regulations for the transport of infectious substances were read, in addition to the national guidance from the Norwegian Directorate for Civil Protection.

Detailed instructions, written and illustrated, of sampling of saliva in different age groups were developed [29] and transportation of the saliva samples were performed as category B in a sealed leakproof primary receptacle, sealable, leakproof, secondary packaging, and collected and transported in a rigid outer packaging by one of the project members.

Training modules related to the assignment/projects

No training module was run due to COVID-19. The fellow was trained by the Norwegian Institute of Public Health.

Educational outcome

The fellow developed an understanding of the importance of biorisk management, and the requirements necessary to control risks associated with the handling, storage, and disposal of biological agents and toxins in laboratories, understanding the processes associated with BSL3 and BSL4 laboratories as well as biosafety risk assessment and mitigation. Lin had a specific focus on transportation of infectious substances.

5. Quality management

A. External Quality Assessment-8 (EQA) for typing of Listeria in 2020-2021

Supervisor: Umaer Naseer, senior scientist, Department of infection control and preparedness, NIPH

On May 2020, NIPH was invited to participate in the ‘Eighth External Quality Assessment (EQA-8) scheme for typing of Listeria in 2020-2021’ organised by Statens Serum Institut (SSI) on behalf of the European Food- and Waterborne Diseases and Zoonoses Programme, ECDC (ECDC-FWD). The aim of the EQA-8 was harmonisation of the typing methods used by the European laboratory network in order to produce comparable typing data for Listeria strains between laboratories and to ascertain high-quality data submissions to the European Surveillance System (TESSy).

The Listeria EQA included two parts: serotyping of Listeria isolates (conventional and/or molecular) and molecular typing-based cluster analyses (PFGE and/or derived data from the whole genome sequencing (WGS). For this purpose, NIPH received 17 blinded L. monocytogenes isolates. Five of the isolates were included in both serotyping and cluster analysis, whereas six isolates were specific for serotyping and six isolates were specific for cluster analysis.

WGS of the 17 isolates were performed at the National Reference Laboratory for Enteropathogenic bacteria at NIPH.

The fellow analysed, interpreted, and submitted the results through the official online platform.
Training modules related to the assignment/projects

No training module was run due to COVID-19. The fellow was trained by the Norwegian Institute of Public Health.

Educational outcome
The fellow experienced that performing an EQA evenly is an essential aspect of the quality management system for a national reference laboratory. It gives an early warning for systematic problems, provides objective evidence of testing quality, and identifies areas needing improvement as well as specific training needs. Due to increased international trade and travelling, standardised laboratory techniques for comparison of national and international food- and waterborne pathogens are essential.

6. Teaching and pedagogy

A. Main supervisor for PhD student

The fellow has been the main supervisor of a PhD student throughout the two years of the fellowship. The aim as supervisor was to guide the student through the PhD and make the student an independent researcher. This was performed by being a manager, an educator, a coordinator and to be available and supportive. The role of the fellow as supervisor was to introduce the PhD student to the specific research filed, mentor the student to establish critical thinking, hypothesis generation and formulate research questions, guide in time management; support planning and organisation of the projects, present the student to different research environments for collaboration and teach scientific writing skills and communication.

A multidisciplinary supervision team was established and supervision meetings were arranged every second week throughout the PhD period. Lin helped structuring the thesis and organised the defence meeting. Three manuscripts were accepted or submitted during the PhD [2-4]. The thesis was submitted 30 June 2021 [33].

B. Lecture for bachelor students on Shiga toxin-producing Escherichia coli

The fellow developed and delivered a lecture (45 minutes) for bachelor students at the Norwegian University of Life Sciences as part of a course on Food Safety and Hygiene. The purpose of the lecture was to introduce the students to the important foodborne pathogen Shiga toxin-producing E. coli (STEC) by describing its characteristics, reservoir, and route of transmission. STEC infections as a public health concern were covered and the role of NIPH in national surveillance, prevention, and control of STEC infections was demonstrated.

A reflective teaching report and an evaluation of the teaching assignment was written following the lecture.

Training modules related to the assignment/projects

The EPIET/EUPHEM Introductory Course familiarised the fellow with adult learning and how to get the audience interested and active during the session. A key element is to know your audience.

The project review module familiarised the fellow with presenting data clear and concise and to communicate efficiently.

Educational outcome:
As the main supervisor for a PhD student, the fellow was involved in defining projects, describing objectives and strategies to reach appointed targets. Lin also developed competencies in time management and managing the multidisciplinary research team.

The fellow gained experience in teaching by outlining the objectives, developing the lecture, giving the lecture, and receiving feedback from the audience.

7. Public health microbiology management

A. Management during outbreak investigations

Public health management, including time management, communication, coordination, and research collaboration was important during the outbreak investigations. In the K. pneumoniae and the S. Enteritidis outbreaks the fellow acquired team building and negotiation skills by working as a team member. In the K. pneumoniae outbreak, healthcare workers, microbiologists, and epidemiologists worked together and in the S. Enteritidis outbreak NIPH collaborated with Food Safety Authority, Veterinary Institute as well as chief municipal medical officers. The fellow was involved in planning outbreak response and control measures. Reports from both outbreaks were written [7, 15].
**B. Management and coordination of Pertussis research project**

The fellow was involved in planning and managing the project. An application to Regional Committees for Medical and Health Research Ethics (REC) in Norway and a data protection impact assessment (DPIA) to comply with the general GDPR requirements were written by the fellow. A multidisciplinary research team including laboratory technicians, bioinformaticians, researchers and medical doctors was established. Lin arranged both several laboratory and project meetings and was involved in selecting methods used for typing and interpretation of the data. The fellow wrote the first draft of the manuscript [5] and submitted an abstract to ESCAIDE 2021 [19].

**C. Management and coordination of COVID-19 laboratory project**

The fellow was involved in planning and managing the project. Lin was responsible for designing procedures for collecting, transporting, analysing and storing all biological material in the project and coordinating the laboratory work involved in these processes. The fellow participated on project meetings twice a week and was involved in the progress of all parts of the project. Lin applied the principles of scientific communication to peers, stakeholders and the media/public. The fellow was first and last author, respectively, on the two manuscripts from this project [1, 6].

**D. Management and coordination of PhD project**

The fellow was the main supervisor for a PhD student and was involved in planning and managing all the student’s projects. Lin promoted collaboration and partnership between different institutes in all projects. Competencies in different disciplines were important to succeed. The fellow was last author on two of the manuscripts [1, 6] and second author on the third manuscript [3] included in the thesis [33].

**E. Task leader in the One Health Harmony Cap H2020 project**

OH-Harmony-CAP is a One Health European Joint Programme which aims to collect information on current capabilities, capacities, adaptability and interoperability for detection of foodborne pathogens at both the National Reference Laboratory and primary diagnostic laboratory level (https://onehealthjp.eu/jip-oh-harmony-cap). The main goal is to design and test harmonised protocols for characterisation and typing of Shiga toxin-producing *E. coli* (STEC), enterotoxigenic *E. coli* (ETEC), Cryptosporidium spp., *Echinococcus multilocularis*, Toxoplasma gondii, *Trichinella spp.*, *Echinococcus granulosus*, and AMR for *Salmonella* and *Campylobacter* in a One Health perspective. NIPH is task leader of WP2: Development of the OHLabCap, T2: Scoring of collected data and chosen indicators at the National Reference Laboratory (NRL) level. Together with Umaer Naseer, Lin was responsible for the scoring and interpretation of the pilot survey. The results were presented by Lin and Umaer at the OHLabCAP meeting on 11 November 2020. A technical report was written [16] and an abstract was submitted to ASM Microbe 2021 [18]. The fellow was co-author on both outputs.

**Training modules related to the assignment/projects**

The Management, Leadership and Communication in Public Health module familiarised fellows with understanding roles and responsibilities in public health management settings. Topics covered were different management styles, team roles and team evolution, delegation of tasks, and the provision of clear, structured, and efficient feedback, as well as time management.

During the Project Review module, the fellow discussed important study outcomes with public health professionals, to sharpen recommendations and to advance public health communication skills.

**Educational outcome**

General public health microbiology management was an integral component of all projects and activities during Lin’s fellowship. For all projects, the fellow was engaged in scientific communication to peers and stakeholders. Lin collaborated with different agencies and observed the importance of a multidisciplinary team. Time management was central in all projects. Laboratory management was key in several of the fellow’s projects.

**8. Communication**

**Publications related to the EUPHEM fellowship**


Conference presentations


Other presentations

24. Brandal LT. Shiga toxin-producing *Escherichia coli* (STEC) – an important foodborne pathogen, Norwegian University of Life Science, Ås, Norway, 2019.

9. Other activities

26. Together with co-workers the public was informed about the outbreak of *S. Enteritidis* by news messages on website of NIPH: [https://www.fhi.no/nyheter/2021/utbrudd-av-salmonellasmitte/](https://www.fhi.no/nyheter/2021/utbrudd-av-salmonellasmitte/) and [https://www.fhi.no/nyheter/2021/utbruddsstammen-pavist-i-importert-storfekjott-fra-tyskland/](https://www.fhi.no/nyheter/2021/utbruddsstammen-pavist-i-importert-storfekjott-fra-tyskland/)
28. I have been involved in making a web site for the project ‘The role of children in transmission of SARS-CoV-2 in daycare and schools’: [https://www.fhi.no/studier/korona-barn-studien/](https://www.fhi.no/studier/korona-barn-studien/)
29. I have been responsible for making instructions (illustration and guidance) for saliva collection in the COVID-19 project: [https://www.fhi.no/publ/diverse/veiledningsmateriell-for-korona-barn-studien/](https://www.fhi.no/publ/diverse/veiledningsmateriell-for-korona-barn-studien/)
30. I have been involved in developing age-dependent information sheets for participants in the COVID-19 project: [https://www.fhi.no/publ/informasjonsark/informasjonsmateriell-om-korona-barn-studien/](https://www.fhi.no/publ/informasjonsark/informasjonsmateriell-om-korona-barn-studien/)
31. Together with the project leader I have been responsible for writing a news item published on our website in relation to our published article ‘Minimal transmission of SARS-CoV-2 from pediatric COVID-19 cases in primary schools in Norway, August to November 2020’: [https://www.fhi.no/nyheter/2021/barneskoleelever-bringer-i-liten-grad-koronasmitte-videre-pa-skolen/](https://www.fhi.no/nyheter/2021/barneskoleelever-bringer-i-liten-grad-koronasmitte-videre-pa-skolen/)
33. PhD thesis – Main supervisor, title: Shiga Toxin-producing *Escherichia coli* – aspects of their pathogenicity and effects of antimicrobials [Submitted 30 June 2021]
34. Kick-off meeting, OH-Harmony-CAP, 22/01/2020 – 23/01/2020, Surrey, UK

Other training modules

35. Nordic mini project review: Module with feedback from Nordic expert on scientific projects in order to meet EPIET/EUPHEM standards (two days, March 2021, Sweden, online).

10. EPIET/EUPHEM modules attended

1. EPIET/EUPHEM introductory course, 23/09/2019 – 11/10/2019, Spetses, Greece
2. Outbreak Investigation, 09/12/2019 – 13/12/2019, Nicosia, Cyprus
6. Rapid Assessment and Survey Methods, 27/04/21, 05/05/2021 – 06/05/2021, virtual
7. Vaccinology, 14/06/2021 – 18/06/2021, virtual
9. 

11. Other training

Discussion

Coordinator’s conclusions

One of the main goals of the EUPHEM programme is to expose fellows to diverse and multidisciplinary public health experiences and activities, thus enabling them to work across different disciplines. This report summarises all activities and projects conducted by Lin Thorstensen Brandal during her two-year EUPHEM fellowship (cohort 2019) as an MS-track fellow at the Norwegian Institute for Public Health in Oslo, Norway. An accomplished scientist on arrival to the fellowship, Lin further developed her leadership skills as a public health microbiologist and contributed key knowledge and understanding of the risk of transmission of SARS-CoV-2 infection in children and adolescents in Norway. By becoming proficient at applying state of the art epidemiological software, interpretation of epidata and at assessing the impact of WGS applications for surveillance of diverse pathogens at the NIPH, Lin has had the opportunity to provide timely recommendations for improvement of public health policy at national level. Also during this period, whilst applying the fellowship’s “learning by doing” strategy, Lin refined her mentoring and communication skills. As Lin’s front line coordinator, it has been a pleasure and a privilege to collaborate with her during the span of this fellowship.

Supervisor’s conclusions

Lin started the EUPHEM fellowship with experience as a researcher in a national reference laboratory service. During her fellowship, Lin has taken on a wide variety of tasks, activities, and projects. She has demonstrated a very good understanding of the needs and aims of the different tasks she has performed, resulting in outputs that have added to national and international public health activities. In her work she has balanced very well between pragmatic problem-solving and scientific work according to the situation and need. Lin has contributed in the response to the COVID-19 pandemic, both in the initial response by setting up systems and performing contact tracing, and in later research projects to provide evidence for transmission among children. She has performed and participated in quality management, delivered several lectures, and supervised other fellows and a PhD student. Lin has compiled and analysed laboratory and epidemiological surveillance data for enteropathogenic bacteria, and has looked into behavioural risks for blood-borne infections among people who inject drugs. In her research project on molecular epidemiology of Bordetella pertussis in Norway in the period 1996-2019 she has developed protocols, analysed NGS-data, and interpreted the results.

In all her projects and activities, Lin has collaborated with supervisors and co-workers from several departments of the institute during a time. Lin has established good and strong relationships and has masterfully managed to engage her co-workers. She has worked independently and in a structured manner with a high workload and several tasks in parallel. She has pulled through different projects during a challenging time due to the pandemic response. Her work has strengthened the public health microbiology at NIPH and contributed to collaboration across disciplines.

Personal conclusions of fellow

The EUPHEM fellowship has been an excellent experience and has broadened my knowledge within various areas of public health. This pertains especially to epidemiology and the use of analytical epidemiological methods, but also microbiology in which new pathogens have been explored and different laboratory methods applied. The importance of bringing microbiological and epidemiological knowledge together is a key factor in public health for effective infectious disease control and prevention. The learning by doing approach with the mix of high-quality training modules and different projects and activities has been inspiring and increased my professional skills within public health. I have gained increased competencies within communication and public health management. Collaboration with public health experts at NIPH as well as international experts and EPIET/EUPHEM fellows has been encouraging and valuable. The fellowship has provided me with a network of European public health experts, which is important since increased globalisation and transmission of communicable diseases emphasise the necessity of international collaboration for effective infectious disease control and prevention.

Acknowledgements of fellow

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and a friendly working environment. A specific thanks to my colleagues at NIPH for giving me the opportunity to focus on my EUPHEM fellowship even though everyone was also involved in COVID-19-related work.

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