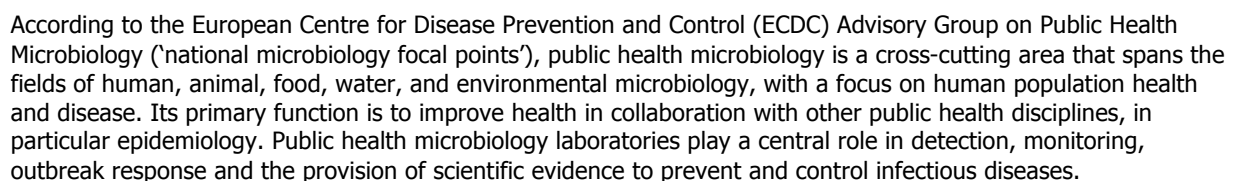
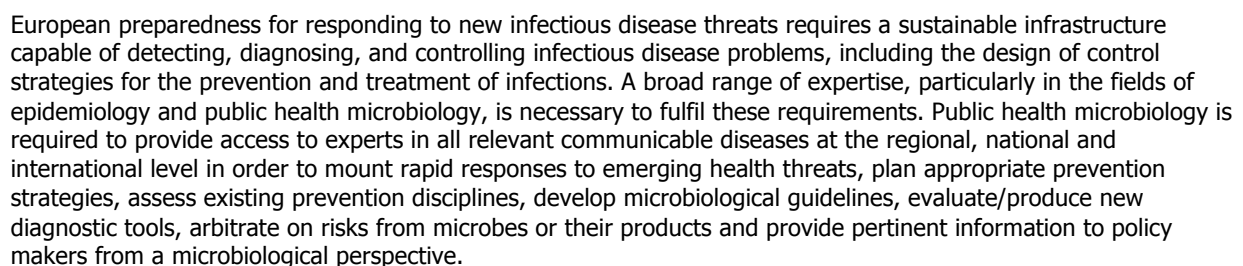
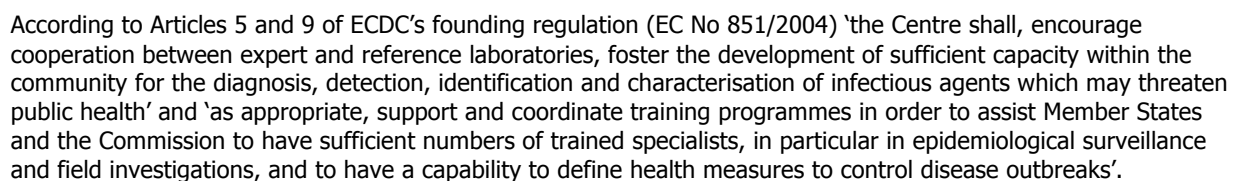
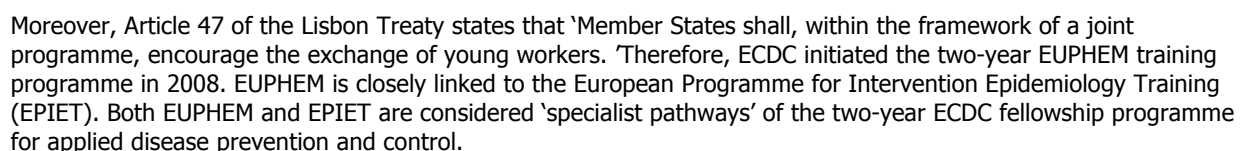


The section header "Summary of work activities" in a bold, white, sans-serif font, set against a blue background.The author's name "Carina Brehony" in a white, sans-serif font, set against a blue background.The subtitle "European Public Health Microbiology Training Programme (EUPHEM), 2018 cohort" in a white, sans-serif font, set against a blue background.The section header "Background" in a bold, blue, sans-serif font.A paragraph of text in a black, sans-serif font, describing the role of public health microbiology as a cross-cutting area spanning human, animal, food, water, and environmental microbiology, with a focus on human population health and disease. It mentions its primary function is to improve health in collaboration with other public health disciplines, particularly epidemiology, and that public health microbiology laboratories play a central role in detection, monitoring, outbreak response, and providing scientific evidence to prevent and control infectious diseases.A paragraph of text in a black, sans-serif font, discussing the need for a sustainable infrastructure to respond to new infectious disease threats. It states that this infrastructure must be capable of detecting, diagnosing, and controlling infectious disease problems, including the design of control strategies. A broad range of expertise, particularly in 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 levels to mount rapid responses to emerging health threats, plan 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.A paragraph of text in a black, sans-serif font, quoting ECDC's founding regulation (EC No 851/2004). It states that 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'.A paragraph of text in a black, sans-serif font, mentioning Article 47 of the Lisbon Treaty. It states that Member States shall, within the framework of a joint programme, encourage the exchange of young workers. Therefore, ECDC initiated the two-year EUPHEM training programme in 2008. EUPHEM is closely linked to the European Programme for Intervention Epidemiology Training (EPIET). Both EUPHEM and EPIET are considered 'specialist pathways' of the two-year ECDC fellowship programme for applied disease prevention and control.

This report summarises the work activities undertaken by Carina Brehony, cohort 2018 of the European Public Health Microbiology Training Programme (EUPHEM) at the Public Health Laboratory (PHL), HSE Dublin, Health Protection Surveillance Centre (HPSC), National Virus Reference Laboratory (NVRL) UCD, St James's Hospital Dublin and the Rotunda Hospital Dublin.

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

Dr Carina Brehony was in academic research for 15 years working on various pathogens. She obtained her PhD on the molecular epidemiology of meningococcal disease at the University of Oxford. Following 12 years in Oxford she moved back home to Ireland to work as a post-doctoral researcher on various projects with the National University of Ireland, Galway including spatio-temporal analysis of shiga-toxigenic *E. coli* infection, carbapenemase-producing Enterobacteriales genomics and antimicrobial resistance, all with a 'One Health' focus. Carina joined the EUPHEM programme to expand her knowledge and understanding in public health and epidemiology and microbiology's role.

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 Carina. The portfolio presents a summary of all work activities conducted by Carina, unless prohibited due to confidentiality regulations.

Results

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

1. Epidemiological investigations

1.1. Outbreak investigations

Supervisor: Dr Eleanor McNamara

Investigation of a COVID-19 outbreak in a residential care facility

Residential care facilities (RCF) and nursing homes became a focus of concern during the COVID-19 pandemic due to the combination of vulnerable patients and exposed healthcare workers (HCW) and the increasing number of case clusters associated with them over time. From March 6th national restrictions were put in place for visitors to all nursing homes. A number of Infection, Prevention and Control (IPC) measures were in place prior to the start of the outbreak as per national COVID-19 guidelines including the implementation of visiting restrictions from 16th March 2020. The use of appropriate personal protective equipment (PPE) for IPC standard, contact and droplet precautions as warranted. Residents were isolated or cohorted according to positivity and suspect status. Other general IPC measures included the requirement for all health care workers to wear surgical facemasks along with standard IPC precautions and to maintain social distancing.

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

An outbreak began in a RCF situated in a large city in Ireland and has a maximum occupancy of 176 residents. The first confirmed case of COVID-19 in the facility was on 23rd March 2020. An outbreak control team (OCT) was convened on March 24th and consisted of: nursing, medical, laboratory and infection control management, household and catering management, public health and occupational health. Weekly or twice weekly OCT meetings were convened for the duration of the outbreak. Laboratory testing was carried out onsite at PHL, HSE Dublin.

A confirmed case was a resident or HCW of the healthcare facility with a clinical specimen (nasopharyngeal swab) with SARS-CoV-2 detected by real-time PCR at PHL during the outbreak period regardless of symptoms. A suspect case was a resident or resident or HCW of the RCF with symptoms (according to national interim guidelines) who was awaiting the results of laboratory testing. There were a total of 72 confirmed cases in 168 residents (43%) with 31 asymptomatic and 41 symptomatic. There were seven deaths associated with COVID-19, six of which were symptomatic and one asymptomatic. This gave a case-fatality rate of 10%. There were a total of 84 confirmed cases in HCWs with 14 asymptomatic and 70 symptomatic. The last positive symptomatic cases were on 27th April (resident) and 2nd May (HCW) and the last asymptomatic positive cases were on 20th May (resident) and 25th May (HCW).

A national screening programme of residents and HCWs for all nursing homes in Ireland was advised and took place in the RCF from 17th to 30th April 2020. A total of 274 asymptomatic HCWs were screened with 14 (5%) positive cases. A total of 108 asymptomatic residents were screened with 29 (27%) positive cases.

The outbreak was declared over on June 22nd 2020. This was as a result of stringent implementation of IPC interventions, clear actions and communication among members of the OCT and all staff across the site. Recommendations to prevent future outbreaks at the facility include: (1) continuing adherence to national guidelines with local onsite risk assessed adaptations/additions; (2) implementation of screening depending on epidemiological situation; (3) continued communication and training onsite; (4) promotion of seasonal influenza vaccine update amongst HCWs.

Carina contributed to lab testing, lab result interpretation and verification. She attended OCTs, collated, analysed and shared data on the outbreak epidemiology with the OCT and wrote a report and a draft manuscript for publication. She presented an ePoster at the European Society of Clinical Microbiology COVID-19 online conference September 23-25 2020.

Training modules

The following modules aided Carina's ability to participate in the OCT:

- During the EPIET/EUPHEM introductory course fellows were taught the basic concepts of logistical and analytical approach to outbreak investigations, including the ten steps of an outbreak investigation.
- The Outbreak Investigations module taught fellows how to perform analytical epidemiological studies within outbreak investigations using various software packages i.e. EpiData and R/STATA. Fellows were also given practical training on when and how to perform analytical studies for an outbreak investigation, including descriptive, cohort and case-control studies.
- The Multivariable analysis module provided a more comprehensive understanding of the principles of statistical analyses, and how to build an optimal model using linear, logistic, Poisson and Cox regression in STATA/R.
- During the Management, Leadership and Communication in Public Health module fellows learned about various aspects and styles of management, leadership and communication within a public health context.

Educational outcome:

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

1.2. Surveillance

Supervisors: Dr Eleanor McNamara, Dr Anne Carroll

A. Sentinel Surveillance of Human *Campylobacter* in Ireland, 2019

The first human national *Campylobacter* Clinical Sentinel Surveillance Reference Laboratory Service provided by the PHL, HSE, Dublin began in early 2019 and involved the participation of 24 clinical microbiology laboratories in different regions from across the country. A sampling frame was devised to provide a representative collection of specimens nationally for 2019. Consequently, Carina coordinated a sampling schedule whereby laboratories sent their *Campylobacter* PCR positive stool specimens/*Campylobacter* isolates to the PHL to be processed. Carina

carried out all whole genome sequencing (WGS) and bioinformatic analysis on cultured specimens to speciate, genotype, identify AMR and virulence determinants and identify clusters.

A total of 453 specimens comprising 366 stool specimens and 75 isolate swabs. A total of 277 *Campylobacter* spp. bacterial isolates were recovered from submitted specimens; 204/366 (56%) from PCR positive stool specimens and 73/75 (97%) from isolate swabs. On the basis of these data human clinical *Campylobacter* in Ireland is associated predominantly with *C. jejuni* with a diverse set of genotypes reflecting many of the major globally distributed lineages.

These data support the current clinical guidelines for the use of macrolides for empiric treatment. The data also reflect what is seen elsewhere with *C. coli* having relatively more multidrug resistance, perhaps a reflection of properties of the species itself or higher antibiotic use in its predominant porcine reservoir. As with many other pathogens, and those with zoonotic reservoirs in particular, increasing antimicrobial resistance is a threat and continued surveillance is imperative to detect trends or novel resistance mechanisms. Genomics has enabled a better understanding of the genetic mechanisms behind antibiotic resistance and here we have shown a strong correlation between genotype and phenotype. However, the correlation is not absolute and phenotypic antibiotic sensitivity testing will not be completely forgone in the short term. Genomics however was shown to be superior to phenotypic testing for species identification and replaced the biochemical assay during the course of the year. Genomics also allowed for the detection of 31 clusters of potential public health interest and alerts were raised for these with the relevant parties. Future opportunities include relating clinical presentation with species, genotype and virulence factor profile. Also, linking with other partners in a 'One Health' framework will help us better understand sources of infection to reduce disease burden and the threat of increasing antimicrobial resistance. The reference laboratory service will continue at PHL.

Carina was involved in all stages of the work. She contributed to the design of the sentinel strategy was involved in all communication with laboratories, carried out all WGS laboratory work and bioinformatics analysis and wrote reports. She presented (oral presentations) at two international and one national conference. The work has been written and submitted as a manuscript to a peer-reviewed scientific journal (under review).

B. Investigation of antiviral resistance in Irish influenza 2018/2019 season

Supervisor: Dr Cillian De Gascun

In the most recent global analysis of human influenza viruses, the level of neuraminidase (NA) inhibitor (NAI) resistance was found to be 0.2%. NAI resistance levels have remained low in Europe since 2008 and this trend persists with less than 1% of viruses tested demonstrating reduced inhibition by oseltamivir in the EU/EEA for the 2018/2019 season. In Europe, the main amino acid substitutions associated with highly reduced or reduced inhibition in influenza A(H1N1)pdm09 are H275Y and Y155H. In spite of current low resistance levels however, with antivirals increasingly being recommended for use, there is the prospect of emerging resistance. The primary aim of this work was to investigate levels of NAI resistance in influenza isolates for the 2018/2019 season in Ireland to guide empirical treatment. A secondary aim was to investigate the presence of substitutions that may be associated with reduced antibody effectiveness to provide insight on vaccine effectiveness (VE).

As a World Health Organisation national influenza centre, the National Virus Reference Laboratory (NVRL) is required to carry out virus characterisation and antiviral susceptibility monitoring. In this study, Irish influenza samples from the 2018/2019 season that were previously typed for the influenza A haemagglutinin (HA) gene (H1 (n=171) and H3 (n=55)) were subject to whole genome PCR followed by Sanger sequencing for H1 and H3 neuraminidase (NA) genes. Of H1 (n=144) samples, one sample (0.7%) harboured an amino acid substitution (Y155H) shown in one study to be associated with highly reduced susceptibility to oseltamivir and zanamivir in H1N1. There were no antiviral resistance related substitutions detected in H3 sample sequences (n=32). As a major protein in the influenza membrane surface inducing an independent immune response to that of the HA protein, the NA protein may also play a role in VE. A recent study demonstrated that a reduction or removal of antibody binding and reduced protection against H3N2 strains was due to mutations on the NA gene. These mutations appear to have widely spread globally and were present in the Irish H3N2 sequences. Its presence in Europe may partly explain the reduced VE seen against influenza A H3N2 for the 2018/2019 season. Routine detailed NA genetic characterisation in Ireland therefore will also facilitate the evaluation of VE and identifying potential factors for ineffectiveness.

Very low levels of NAI resistance here support the current Irish recommendations for NAI use. However, continued monitoring is essential and routine annual NA molecular typing should continue. Monitoring must also be flexible and timely with the release of new NAIs and other influenza antivirals on to the market. Influenza surveillance systems, vaccination programmes and control measures need to be strengthened in order to reduce the burden of seasonal influenza on the population, healthcare system and economy and avoid overwhelming health systems with the possible co-circulation of COVID-19 and influenza.

Carina was involved in all stages of the work. She carried out laboratory work and bioinformatic analysis and wrote and submitted a manuscript to a peer-reviewed scientific journal (under review). The work was presented as a poster at a national microbiology meeting.

Training modules

- During the Introductory course fellows received seminars and case studies of various aspects of surveillance. This included the different types of surveillance e.g. passive, active, syndromic and laboratory surveillance. Fellows discussed what the basic functions were and what elements are required for establishment of a surveillance system.
- Vaccinology module (online) covered various aspects of surveillance related to immunisation including: vaccine coverage and uptake; using surveillance data to plan vaccine campaigns; vaccine effectiveness studies; surveillance of adverse events.
- The Rapid Risk Assessment module covered aspects that are related to surveillance such as rapid risk assessment and surveillance planning in resource poor or crisis situations, geographic information systems and sampling.
- During the Outbreak Investigations module, the fellows had a session on phylogenetic analysis of sequence data. Carina aided the demonstration of this session to other fellows.

Educational outcome:

Planning and development of a laboratory surveillance system. Maintenance of quality service. Communication with service stakeholders. Planning, implementing and monitoring public health interventions using surveillance data. Bioinformatic and sequence analysis and interpretation. Presentations at conferences and writing scientific manuscripts.

2. Applied public health microbiology research

Supervisor: Dr Karen Burns

Carbapenemase producing Enterobacterales (CPE) outbreak in large hospital

Carbapenemase-producing Enterobacterales (CPE) was declared a national public health emergency in Ireland in October 2017. The most prevalent carbapenemase type in Ireland is OXA-48. An OXA-48 CPE hospital outbreak was reported in July 2018. The overall aim of this study was to describe a lengthy CPE outbreak in one ward in a tertiary hospital and investigate potential transmission patterns between patients using microbiological epidemiological and WGS data analysis and provide recommendations for use of these tools.

Cases were all patients admitted to ward A in Hospital X between July 2018 and December 2019 who had a CPE specimen (n=45). Environmental specimens (N=394) of which 26 were positive were taken from a variety of locations within Ward A. Genomic analysis was used to verify isolate species, OXA-48 carbapenemase gene and plasmid presence and genetic background and to describe genetic relationships amongst the CPE isolates using a MLST gene-by-gene approach.

This prolonged outbreak of OXA-48 CPE on a hospital ward exemplifies the complexity and difficulty in the control of these particular organisms. The first outbreak case presented on 31/07/2018 and the last was over a year later on 12/08/19. It involved seven different Enterobacteriaceae species and within each species there was not a single clone that predominated. Genomic species identification identified *Enterobacter hormaechei* (n=35), *Escherichia coli* (n=12), *Klebsiella pneumoniae* (n=5), *Klebsiella oxytoca* (n=1), *Klebsiella michiganensis* (n=1), *Citrobacter freundii* (n=1) and *Serratia marcescens* (n=1). Also, from the relatively short period from which environmental sampling was carried out, five species were detected from various locations within the ward. Even after various IPC measures, including a complete refurbishment, a number of positive environmental screens were obtained. A number of case isolates also were closely related to other OXA-48-carrying isolates from cases elsewhere in the hospital that were unlinked to the outbreak ward. This raises the possibility of a common source in the community or elsewhere in the hospital, or transmission by an individual within the hospital between wards.

Given that several patients harboured isolates that were indistinguishable by WGS, there may have been short chain transmission of the organism amongst patients or it was acquired from a common source, either environmental or another unknown and unsampled contact. Direction of potential transmission between patients and patients and environment is difficult to ascertain particularly in retrospective analysis. But since we know that patient-to-patient transmission occurs and that these organisms, particularly *Klebsiella* and *Enterobacter* species can become adapted to the nosocomial environment, stringent IPC measures must be adhered to. Retrospective genomic analysis can highlight links between apparently sporadic CPE cases in the nosocomial environment.

Two closely related yet distinct OXA-48 plasmid types were found in this outbreak. Both of which have been found

across Ireland over the last number of years and one, called 'plasmid type 2' here, was associated with a prolonged outbreak in another large city centre hospital in Ireland. Within-patient colonisation of multiple OXA-48 species and interspecies plasmid transfer are well documented. For all 12 cases with more than one species isolate, each pair of species, or within three in the case of one patient, shared the same plasmid type. This may indicate the sharing of plasmids between species within patients. Again this highlights the importance of infection prevention to prevent infections and opportunities for such occurrences. As yet there is no means for de-colonisation of CPE patients so IPC is the best current means to do this.

Recommendations from this work which may help to control future CPE outbreaks include: (1) replacement of sink and shower drain pipes that may aid prolonged survival of microorganisms; (2) implementation of regular systematic environmental sampling in the hospital in outbreak and non-outbreak periods; (3) consideration of performing periodic point prevalence surveys for CPE carriage across the hospital, with WGS and detailed analysis carried out on any positive sample isolates in real time and; (4) continued compliance with national CPE clinical guidelines on patient screening for CPE carriage. Future research opportunities could include using metagenomics to index the diversity of microbes and antimicrobial and disinfectant resistance genes across a range of locations across the hospital and compare these to patient microbiomes. Knowledge of the hospital microbiome can aid understanding of the biology of these organisms, potential nosocomial acquisition and transmission and also effectiveness of IPC measures. While some of these recommendations may incur human and monetary resources that are already stretched, prevention of morbidity and mortality from CPE would be hopefully avoid an economic burden in the long term.

Carina carried out, along with EPIET fellow Lisa Domegan, the production of a study protocol and data collection from hospital databases. Carina carried out the descriptive analysis of microbiology testing carried out by hospital clinical microbiology laboratory and analysis of WGS data provided by the National CPE Reference Laboratory, Galway. She produced a report of the microbiology analysis.

Training modules

- The Introductory Course introduced fellows to different study designs, study protocol writing and scientific writing.
- During the Outbreak Investigation module, fellows had a session on sequence and phylogenetic analyses (which Carina also assisted in running) using different software packages. EUPHEMs then had a separate session on next-generation sequencing.
- The Management, Leadership and Communication in Public Health module, Stockholm, Feb 2020 covered aspects such as time and person management or communication, important in research activities and in outbreak control and management.

Educational outcome:

Planning, design of a study and study protocol. Accessing data from hospital and laboratory electronic databases. Data validation. Data security and protection. Writing scientific reports. Presentation of data at scientific meetings.

3. Applied public health microbiology and laboratory investigations

Supervisors: Dr Eleanor McNamara

A. Genomic characterisation of *Escherichia coli* bloodstream infections from a large hospital in Ireland 2017 to 2018

The aim of this project was to characterise a retrospective collection of *Escherichia coli* bloodstream infection (BSI) isolates from a large tertiary hospital by highly discriminatory WGS methods to determine circulating genotypes, antimicrobial resistance (AMR) and virulence determinants. Carina carried out WGS on *E. coli* BSI isolates from the years 2017 and 2018 (n=192). They were characterised genotypically by seven-locus MLST, presence of virulence factors and AMR genes. Relationships amongst isolates were examined using phylogenetics.

A total of 56 sequence types (ST) were found within 10 clonal complexes (cc). ST73cc 21% (n=41) and ST131cc 18% (n=35) were the most frequent. 61 (32%) isolates were phenotypically susceptible to all antibiotics tested for. 13 (7%) isolates were classed as multidrug resistant (MDR). Of these 85% (n=11) were ST131cc. All isolates phenotypically resistant (n=15) to third generation cephalosporins harboured the ESBL-associated beta-lactamase genes *bla*_{CTX-M-15} (n=14) or *bla*_{CTX-M-27} (n=1). WGS prediction of AMR genotype was optimal for beta-lactams and third-generation cephalosporins with positive predictive values of 97% and 100% respectively. The most prevalent virulence genes found were: the protectin *gad* (93%), adhesin *fimH* (92%), siderophore *fyuA* (84%) and protectin *iss* (82%). The uropathogenic specific protein gene *usp* was present in 66% isolates. ST73cc and ST12cc had a

significantly more virulence genes than ST131cc and ST69cc. Two isolates were identified as the enteroaggregative pathotype.

The major globally distributed MDR and pathogenic, predominantly extraintestinal *E. coli* clones, were prevalent in this Irish BSI cohort. This data indicated urological and enteric sources of *E. coli* sepsis. Timely genomic analysis is advantageous to characterise strains, detect emergent strains and drug resistance and identify possible sources of *E. coli* BSI infection in one analysis. This could improve patient outcomes, particularly if such technology was incorporated into routine clinical diagnostic services with as short a turnaround time as possible in order to implement clinical/public health measures that may arise from analyses.

Carina was involved in all stages of the project from the writing and submitting ethics proposal to lab bacterial culture, WGS laboratory work, troubleshooting, bioinformatics analysis and writing of a report.

B. Evaluation of genomics methods for typing of human clinical *Clostridioides difficile*

Supervisors: Prof Tom Rogers, Dr Eleanor McNamara

The ECDC has developed surveillance and lab-testing protocols to harmonise European efforts to monitor healthcare facility based *Clostridioides difficile* infection (CDI) across member states. In Ireland, there has been a voluntary national enhanced surveillance system involving the majority of acute hospitals in the country since 2009. In addition, the 2014 National Clinical Guidelines recommended the establishment of a national reference laboratory and a single national CDI surveillance system.

The current 'gold-standard' discriminatory genotyping method for *C. difficile* is ribotyping. In Ireland however there is limited ribotyping data available and in 2018 it was available for just 19% of notified case isolates. The higher discriminatory power of WGS as well as the simultaneous analysis of virulence and antimicrobial associated factors has obvious benefits for the clinical and public health to CDI. The aim of this project was to evaluate various WGS analysis methods to set a template for the implementation of the method in the laboratory. It will allow us to establish the quality standards and procedures for a regional reference service for *C. difficile* WGS.

Carina validated a WGS methodology to determine the optimum bioinformatics analysis for *C. difficile* in the laboratory by: 1. establishing minimum quality parameters, 2. examining congruence of cgMLST with ribotyping and 3. single-nucleotide polymorphism (SNP)-based phylogenetic clustering method 4. comparing cgMLST schemes within two WGS platforms and 5. examining presence of toxin genes. We showed the overall comparability of the platforms, assembly parameters and cgMLST schemes. However, the SPAdes sequence assembly algorithm within Bionumerics performed better in terms of quality metrics overall than the Velvet algorithm in SeqSphere+. Lower assembly quality can impact, the reconstruction of more complex genome regions and genes including those that are relatively large such as the toxin gene *tcdA*. While lower quality genomes may be able to assign lower discriminatory seven locus MLST STs, they may not be appropriate for use in cluster analysis using the minimum-spanning tree algorithm as this may introduce spurious results. This is crucial in outbreak analysis, when highly discriminatory analysis can rule in or rule out cases. There was a large degree of agreement amongst the methods regarding clustering of isolates. But the SNP phylogeny was most discriminatory than both cgMLST scheme methods. Some of the differences centred on small numbers of SNP and/or cgMLST differences, so each analysis should be taken on a case-by-case basis and include epidemiological information. cgMLST analysis should be used for general molecular surveillance and initial cluster analysis but SNP typing should be employed where possible for the highest resolution in cluster or outbreak or infection recurrence analysis.

WGS can support public health by providing high-quality high-resolution data which can be used nationally and internationally to: track spread of strains, detect emerging (including virulent and/or resistant) strains, investigate outbreaks/clusters, and investigate transmission pathways, thus contributing to focusing the mitigation activities to reduce the burden of *C. difficile* associated disease.

Carina carried out the all WGS validation and analyses and wrote a report on findings.

C. Review of *Mycoplasma genitalium* molecular testing of symptomatic women

Supervisor: Dr Richard Drew

The bacterium *Mycoplasma genitalium* is an emerging cause of sexually transmitted infections (STI) that are associated with non-gonococcal urethritis in men and cervicitis, pelvic inflammatory disease and potentially infertility in women. Little is known about the natural history of *M. genitalium*, due in part to the difficulty in culturing the organism, the smallest known self-replicating organism. However, the advent of nucleic acid amplification testing (NAAT) has aided *M. genitalium* diagnostics and an improved understanding of its epidemiology. The majority of *M. genitalium* infections are asymptomatic and prevalence of infection in the general population is thought to be low. Population-wide screening is not recommended due to the many uncertainties about its benefits as well as the natural history and epidemiology of *M. genitalium*. Unnecessary screening and treatment may also add to further increases in antibiotic resistance. Resistance has increased dramatically since the 2000s and can occur within patients, leading to treatment failure. *M. genitalium* lacks a cell wall and therefore

is untreatable with beta-lactam antibiotics. European and UK guidelines recommend treatment with azithromycin, doxycycline or moxifloxacin. The Rotunda hospital was the first in Ireland to implement routine NAAT testing of symptomatic women. An evaluation of this testing and descriptive analysis was carried out with the following questions to be addressed:

- What are risk factors associated with *M. genitalium* infection in women?
- Should all positives be tested for resistance, or just for treatment failures?

This work's aim was to evaluate the testing program since its implementation and help guide future testing strategies, produce hypotheses for future research and provide data on this emerging disease for communication with public health partners such as the Health Protection Surveillance Centre.

Of 1972 specimens tested between January 2018 and December 2019 10 were confirmed positive (0.5%). Of the positive results, the median patient age was 26 (range 18-34) and 70% were obstetrics or gynaecology patients. Patient symptoms included: discharge in five (50%); pelvic pain on examination in five (50%); abdominal pain in two (20%); pelvic bleeding in two (20%); and dyspareunia in two (20%) patients. Co-infections were present in three patients (30%): one patient had chlamydia; one had bacterial vaginosis and; one patient had chlamydia and bacterial vaginosis. Genotypic antibiotic resistance data were available for seven patients for macrolide resistance. In five patient specimens no resistance markers i.e. mutations in the *23S rRNA* gene were detected but it was in two patient specimens (29%). Neither had a co-infection. One was treated with azithromycin and doxycycline and the other with azithromycin and moxifloxacin. Substitutions in the *parC* gene indicative of quinolone resistance were not present in the seven specimens where this testing information was available.

Recommendations from this work include the following: (1) promotion of *M. genitalium* status to notifiable disease; (2) widespread screening of female population not warranted; (3) *M. genitalium* testing for individuals symptomatic for STIs e.g. multiplex STI assays; (4) antibiotic resistance testing of all positive cases; (5) further research into other potential risk groups

Carina carried out analysis of data from *M. genitalium* testing and wrote report and a manuscript for publication is planned.

Training modules

- The Introductory Course introduced fellows to different study designs, study protocol writing and they performed exercises on scientific writing. It also included an introduction to different types of surveillance e.g. passive, active, syndromic and laboratory surveillance. Fellows discussed what the basic functions were and what elements are required for establishment of a surveillance system.
- During the 'Outbreak Investigation' module, fellows had a session on sequence and phylogenetic analyses (which Carina also assisted in running) using different software packages. EUPHEMs then had a separate session on next-generation sequencing.
- The 'Management, Leadership and Communication in Public Health' module covered topics such as time and person management or communication, important factors in research activities.

Educational outcome:

Consideration of ethics principles. Preparation, submission and communication with Research Ethics Committee. Development and validation of genomics analysis methodologies. Troubleshooting and analysis of next generation sequencing data, phylogenetic analyses. Writing scientific reports and manuscripts.

4. Biorisk management

A. Audit of BSL3 facilities at PHL, Dublin

Carina carried out an internal audit of the Biosafety Level 3 (BSL3) laboratory at PHL. This involved reviewing the laboratory Safety Manual, Quality System documentation relating to the BSL3 laboratory, the BSL3 Code of Practice and interviewing the Quality Manager. The audit focussed on biosafety, process management, quality control indicators and documentation. The audit yielded a general indicator compliance percentage of 96%. The overall quality of operational and facility management was high and no major deviations affecting biosafety in the facility were identified.

B. Training in laboratory testing methods for SARS-CoV-2

As part of the lab team at PHL carrying out SARS-CoV-2 testing, Carina participated in the planning, implementation, validation and verification of the new laboratory testing. With particular focus on biosafety, Carina was trained in use of correct PPE, sample unpacking, labelling and sample inactivation as well as waste disposal.

Training modules

Theoretical material from previous years was provided on EVA.

Educational outcome:

Understanding biosafety regulations, applying biorisk assessment and mitigation methods, learning the implementation of biorisk measures in a laboratory with a new pathogen and test method. Auditing biosafety in BSL3.

5. Quality management

A. External Quality Assessment scheme on antimicrobial susceptibility testing (EQA5-AST) of *Campylobacter*

We participated in the fifth external quality assessment on antimicrobial susceptibility testing (EQA5-AST) for national public health laboratories for *Campylobacter* in the Food-and Waterborne Diseases and Zoonoses Network (FWD-Net). The EQA was organised by Statens Serum Institut (SSI) in 2019. Laboratories were required to carry out antimicrobial susceptibility testing (AST) and species identification on five *Campylobacter* spp. cultures according to the methods used in their laboratories. Carina carried out species identification of the isolates based on WGS using the rmlst.org website. Carina carried out AST by disk diffusion according to EUCAST criteria. The predicted resistance genotype was also carried out according to presence of resistance determinants (gene or mutation presence). Carina successfully completed and submitted the EQA with correct results for both AST and species identification. We were the only participating laboratory in Europe to carry out WGS for AST prediction.

B. Audit of *Campylobacter* molecular testing

The recovery of isolates from PCR positive stool samples was found to be about ~50% during the national human clinical *Campylobacter* sentinel surveillance programme. Carina carried out an audit of the sample processing and testing to determine if any factors were associated with lower isolate recovery. Criteria assessed included: Ct values from submitting labs; date of sampling to date of sample receipt in PHL Dublin; day commenced culture, post receipt in PHL Dublin.

For the criteria tested for, Ct value and number of days between sample date and PHL receipt date, the culture negative samples gave a higher Ct value. Each of these differences was statistically significant ($p < 0.05$ Mann-Whitney U-Test). The mean Ct value for culture negative samples versus culture positive samples was 30.2 (range 17-42) versus 28.4 (range 19-43) in cultured samples. The mean number of days between sample date and PHL receipt date was 5.1 (range 1-21) for culture negative samples versus 3.9 (range 1-11) for culture positive samples. The results for number of days between date of sample receipt and analysis start date were more equivocal and were of borderline significance ($p = 0.054$). The mean number of days between sample date and date of receipt was 2.3 (range 0-6) for culture negative samples versus 2.6 (range 0-5) for culture positive samples.

We shared these data with our service users and recommended that PCR positive stool samples were sent as soon as is possible. *Campylobacter* is known to be a particularly fastidious organism so may be less likely to survive the longer the time from sampling is.

C. Establishment of COVID-19 testing in PHL Laboratory Quality System

In March 2020, the PHL, HSE Dublin in response to the COVID-19 pandemic reduced or paused many of its routine services to join the response to the national emergency. Clients of PHL services were notified and updated of changes to services over the following months. One of the tasks was to validate, verify and then implement molecular testing of SARS-CoV-2 in the laboratory. The PHL is already well experienced in molecular testing for bacterial and viral organisms and is accredited to both ISO17025:2017 and ISO15189 standards. The first step was to assess what testing services could be paused, reduced or transferred to other laboratories. Then advice was sought from the NVRL regarding sample handling, test methods and reporting. Several obstacles were encountered including reagent and plastics supplies for the nucleic acid extraction instrument, supplies of PCR kits and technical glitches with the LIMS software. Several meetings with other laboratory colleagues were convened to discuss and rationalised national supplies. Several companies were contacted with CE and/or FDA approved PCR kits and several were evaluated using a validation panel of SARS-CoV-2 clinical samples provided by the NVRL. A real-time PCR kit was validated and verified and an SOP for the test method was written. A process was established to maintain quality and confidence in the process from sample reception to report resulting. Carina was involved in many of the above aspects of the response but in particular aiding in: assay evaluation, SOP writing, lab testing, lab test result verification and communication.

D. Observing accreditation process for ISO standards ISO17025:2017 and ISO15189 at PHL

Over two days in January 2020 Carina attended as an observer the visit of the Irish National Accreditation Board (INAB) to the PHL. In advance of the meeting Carina attended PHL accreditation meetings and reviewed the ISO standards that were to be assessed i.e. ISO17025:2017 and ISO15189 standards. Carina attended the introductory meeting where schedule for visit was set out, observed discussion on Quality System documentation e.g. personnel training files, User Manual updates, service provider personnel training documentation, review of previous non-conformances. Carina also observed inspectors as they: interviewed staff; reviewed technical aspects such as EQA sample handling, DNA prep, mastermix and Real-time PCR set-ups, media quality control. Carina also observed them review the following: test interpretation; technical validation and result reporting including use of LIMS; checking equipment service and calibration records; assessing preventative action e.g. temperature monitoring of fridges/freezers.

Training modules

Theoretical material from previous years was provided on EVA.

Educational outcome:

During various projects and activities Carina gained experience and further understanding of quality management including: laboratory test method validation and verification, external quality assessments, internal and external auditing and the process of accreditation according to ISO standards.

6. Teaching and pedagogy

A. Problem-Based Learning activity

Carina completed a problem-based learning exercise at the Introductory course. This activity involved collaboration with EUPHEM colleagues over a week period, which involved group learning, researching, planning and practising the teaching activity. It culminated in a four-hour teaching session involving a lecture and interactive session on the topic of CPE.

B. Hepatitis A outbreak case study facilitation

Carina facilitated, along with two EUPHEM colleagues, a Hepatitis A outbreak case study for EPIET and EUPHEM cohort at the Outbreak Investigation Module in Berlin, December 2018. This involved teaching use of software for alignment and phylogeny. We produced a write up and evaluation of our teaching for the practical and also received positive feedback from attendees.

C. Webinar

Carina presented a webinar on EVA for cohort fellows on 'AMR and Genomics'. This activity was an initiative from Carina since there was relatively little formally taught on genomics and AMR during the fellowship and WGS is becoming more widely used in Europe for surveillance, outbreak investigation and other parts of public health including vaccine effectiveness. Carina administered a poll to ask other fellows what they knew about the topics and would like to hear about and this was used to tailor the presentation. The webinar lasted 50 minutes. Carina reflected on the teaching experience afterwards and on the good and bad aspects.

Educational outcome:

These activities involved group learning, planning for teaching, gaining and using feedback and also giving feedback.

7. Public health microbiology management

A. Sentinel Surveillance of Human *Campylobacter* in Ireland, 2019

The establishment of the sentinel surveillance service involved the communication with chief medical microbiologists and consultant microbiologists from 24 clinical microbiology laboratories from across the country. Carina established a rolling monthly schedule whereby the laboratories would send their positive *Campylobacter* samples (PCR positive or isolate cultures) which were then tested for AST and culture confirmed. These laboratory reports were communicated back to each submitting laboratory upon testing completion. Several databases were established by Carina and PHL colleagues and maintained for the service:

- Secure LIMS database containing all submitted samples which could be interrogated
- Secure Excel database of sample records, metadata, test results

- Secure genomic database in Bionumerics platform with genome sequence data with linked metadata for genomics analysis
- Secure culture biobank of retrieved isolates stored in -80° freezer

All aspects of the surveillance service were maintained and managed by Carina over the year. Open communication was maintained with service users who were contacted with any issues or updates. Three quarterly reports and one annual report were prepared by Carina and were shared with users over the course of the years on the outputs of the programme.

B. Outbreak of COVID-19 in residential care facility and implementation of laboratory SARS-CoV-2 testing

Carina was involved in all aspects and challenges of the rapid implementation of COVID-19 testing in the laboratory. Some of the tasks involved re-organising laboratory staff to account for greater lab testing capacity and turn-around-time and also to best maintain social distancing. It involved assisting in the production of lab SOPs, sourcing lab supplies, testing, validation and verification of molecular test kits. It involved communication with other laboratories such as the NVRL on lab methods. It also involved the management and planning of human resources and lab surge capacity. Carina was involved in lab result interpretation and verification and the collation of daily results for dissemination to relevant authorities. Carina also developed a script within the LIMS system which allows for extraction of Ct values for laboratory testing.

As part of the RCF COVID-19 OCT she attended meetings and gained experience in the management of outbreaks. As a member of the team she collated and shared data on the outbreak epidemiology with the OCT, analysed and wrote a report on the outbreak.

C. Management of FWD WGS User Group

Carina took over the running of this user group from previous fellow cohort 2016. This involved communicating with colleagues within Ireland also working on WGS of food and waterborne pathogens and organising TC and face-to-face meetings. Meetings/TC agendas included topics such as: service issues; trouble-shooting; accreditation; data-sharing. At the two face-to-face meetings group members presented on:

- *Campylobacter* sentinel surveillance – Carina Brehony
- CPE genomics – CPE National Reference Laboratory
- Accreditation process in *Listeria* – Dept. of Agriculture
- VTEC WGS service establishment – PHL, VTEC Reference Laboratory
- Food-borne *Listeria* genomics – Dept. of Agriculture
- Bacterial genomics and bioinformatics – University College Dublin

D. Member of subcommittee and technical secretariat for Food Safety Authority of Ireland

Carina was a member of the Food Safety Authority of Ireland (FSAI) subcommittee and technical secretariat for 'Mycobacterium avium subsp. paratuberculosis and the possible links to Crohn's disease' two veterinarian colleagues from the FSAI and Department of Agriculture. The aim was to update the FSAI's previous review of the topic in 2009 with the latest knowledge. The technical secretariat met on several occasions, had TCs and exchanged emails to complete a structured literature review on the topic. Carina established a Mendeley reference manager library and Dropbox folder to facilitate sharing of documents. Between us, we reviewed 82 papers and shared our findings with the subcommittee as a whole at several meetings from June 2019 to January 2020.

E. Other outbreaks/IPC activities

Member of OCT, reviewed and analysed lab data for a number of outbreaks including:

- Control/prevention of Legionella in medical clinical facilities
- Drinking water related outbreak of norovirus in sports club
- Salmonella Java outbreak in care home
- Europe-wide food-borne outbreak of Salmonella Bredeney
- Crèche related VTEC outbreaks

Training modules

- Management, Leadership and Communication in Public Health, ECDC, Stockholm, Sweden (1 week).

- Vaccinology Module (online).

Educational outcome:

As part of *Campylobacter* sentinel surveillance, Carina sent reports of laboratory output to clinical and public health colleagues and reported potential clusters to relevant public health departments and laboratories. As part of COVID-19 OCT she was part of a multidisciplinary public health team. All of this improved understanding of: communication; team management; planning; role and responsibilities; different management styles; motivation of teams; conflict management: structured feedback to improve performance; communicating with authorities and the public.

8. Communication

Publications (EUPHEM)

1. **Carina Brehony**, Linda Dunford, Charlene Bennett, Joan O'Donnell, Lisa Domegan, Eleanor McNamara, Cillian De Gascun. Neuraminidase characterisation reveals very low levels of antiviral resistance and the presence of mutations associated with reduced antibody effectiveness in the Irish influenza 2018/2019 season. *J Clin Virol*. 2020 Oct 1;132:104653. doi: 10.1016/j.jcv.2020.104653.
2. **Carina Brehony**, Donal Lanigan, Anne Carroll and Eleanor McNamara. Establishment of sentinel surveillance of human clinical campylobacteriosis in Ireland (under review at journal)
3. **Carina Brehony**, Maeve Eogan, Jack Lambert, Richard Drew. *Mycoplasma genitalium* molecular testing of symptomatic women at Rotunda hospital, Ireland. (submitted)
4. **Carina Brehony**, Lisa Domegan, Patricia Garvey, Karen Burns. Investigation of a prolonged CPE outbreak in a tertiary hospital Ireland (in preparation)
5. **Carina Brehony**, COVID-19 OCT, Eleanor McNamara. COVID-19 outbreak in residential care home outbreak report (in preparation)

Publications (Other)

1. Mahon BM, **Brehony C**, Cahill N, McGrath E, O'Connor L, Varley A, Cormican M, Ryan S, Hickey P, Keane S, Mulligan M, Ruane B, Jolley KA, Maiden MC, Brisse S, Morris D. Detection of OXA-48-like-producing Enterobacterales in Irish recreational water. *Sci Total Environ*. 2019 Nov 10;690:1-6. doi: 10.1016/j.scitotenv.2019.06.480. Epub 2019 Jun 30. PMID: 31299565.
2. **Brehony C**, McGrath E, Brennan W, Tuohy A, Whyte T, Brisse S, Maiden M, Jolley K, Morris D, Cormican M. An MLST approach to support tracking of plasmids carrying OXA-48-like carbapenemase. *J Antimicrob Chemother*. 2019 Jul 1;74(7):1856-1862. doi: 10.1093/jac/dkz136. PMID: 31225613; PMCID: PMC6587408.
1. Cahill N, O'Connor L, Mahon B, Varley Á, McGrath E, Ryan P, Cormican M, **Brehony C**, Jolley KA, Maiden MC, Brisse S, Morris D. Hospital effluent: A reservoir for carbapenemase-producing Enterobacterales? *Sci Total Environ*. 2019 Jul 1;672:618-624. doi: 10.1016/j.scitotenv.2019.03.428. Epub 2019 Apr 3. PMID: 30974353; PMCID: PMC6525273.
2. Bratcher HB, **Brehony C**, Heuberger S, Pieridou-Bagatzouni D, Křížová P, Hoffmann S, Toropainen M, Taha MK, Claus H, Tzanakaki G, Erdôsi T, Galajeva J, van der Ende A, Skoczyńska A, Pana M, Vaculíková A, Paragi M, Maiden MC, Caugant DA. Establishment of the European meningococcal strain collection genome library (EMSC-GL) for the 2011 to 2012 epidemiological year. *Euro Surveill*. 2018 May;23(20):17-00474. doi: 10.2807/1560-7917.ES.2018.23.20.17-00474. PMID: 29790460; PMCID: PMC6152424.
3. **Brehony C**, Cullinan J, Cormican M, Morris D. Shiga toxigenic *Escherichia coli* incidence is related to small area variation in cattle density in a region in Ireland. *Sci Total Environ*. 2018 Oct 1;637-638:865-870. doi: 10.1016/j.scitotenv.2018.05.038. Epub 2018 May 12. PMID: 29763867.

Reports

1. Genomic characterisation of *Escherichia coli* bloodstream infections from a large hospital in Ireland 2017 to 2018 (draft complete)
2. *Campylobacter* sentinel surveillance in Ireland 2019 Q1, Q2, Q3 and annual reports
3. Investigation of a prolonged CPE outbreak in a tertiary hospital Ireland microbiology report
4. Report of *Mycoplasma genitalium* molecular testing of symptomatic women at Rotunda hospital, Ireland

5. Summary of biosafety audit of BSL3 facilities at PHL, Dublin
6. Report on validation of genomics analysis methodology for laboratory surveillance of *C. difficile*
7. Short piece on EUPHEM fellowship for HPSC Epi-Insight monthly national epidemiology bulletin
8. Short report on activities of FSAI subcommittee and technical secretariat on '*Mycobacterium avium* subsp. *paratuberculosis* and the possible links to Crohn's disease'
9. Summary of communications related to ethics application for *E. coli* BSI project
10. Short report on activities of FWD WGS User Group

Conference presentations

1. **Carina Brehony**, Lisa Domegan et al. CPE OXA-48 hospital ward outbreak in Ireland 2018-2019 - investigation of transmission patterns using social network analysis and genomics. Joint oral presentation at ESCAIDE Conference, Online 2020
2. **Carina Brehony**, Donal Lanigan, Anne Carroll and Eleanor McNamara. Sentinel Surveillance and Genomic Characterisation of Human *Campylobacter* in Ireland, 2019. Oral presentation at One Health, European Joint Programme Meeting, Dublin 2019
3. **Carina Brehony**, Donal Lanigan, Anne Carroll and Eleanor McNamara. Sentinel Surveillance and Genomic Characterisation of Human *Campylobacter* in Ireland, 2019. Oral presentation at Irish Society of Clinical Microbiology Autumn Meeting, Galway 2019
4. **Carina Brehony**, Donal Lanigan, Anne Carroll and Eleanor McNamara. Sentinel Surveillance and Genomic Characterisation of Human *Campylobacter* in Ireland, 2019. Oral presentation at ESCAIDE Conference, Stockholm 2019
5. **Carina Brehony**, Donal Lanigan, Anne Carroll and Eleanor McNamara. Sentinel Surveillance of human clinical *Campylobacter* in Ireland 2019. Poster presentation at Faculty of Public Health Winter Meeting, Dublin 2019
6. **Carina Brehony**, Linda Dunford, Charlene Bennett, Eleanor McNamara, Cillian De Gascun. Investigation of antiviral resistance in Irish influenza 2018/2019 season. Poster presentation at Irish Society of Clinical Microbiology Spring Meeting, Dun Laoghaire 2020
7. **Carina Brehony**, Anne Carroll, Eleanor McNamara. Genomic characterisation of *Escherichia coli* bloodstream infections from a large hospital in Ireland 2017 to 2018. Poster presentation (No. P2924) at ECCMID 2020, Paris (NB: Meeting Cancelled)
8. **Carina Brehony**, Anne Carroll, Eleanor McNamara, OCT team. Investigation of a COVID-19 outbreak in a residential care facility in Dublin. ePoster presentation at ESCMID COVID-19 conference, Online, September 23-25 2020

Other presentations

1. Presented *Campylobacter* sentinel surveillance project at Health Protection Surveillance Centre's monthly Training and Research Seminar. May 2019
2. Presented *Campylobacter* sentinel surveillance project for laboratory staff at PHL, Dublin. October 2019
3. Presented *Campylobacter* sentinel surveillance project at FWD WGS User Group. December 2019
4. Presented CPE outbreak project for review at project mini-review with UK-FETP fellows at PHE office Birmingham, UK, March 2-4 2020
5. Presented Influenza antiviral resistance project and use of sequence data for insights into vaccine effectiveness along with Lisa Domegan, EPIET C2018 who was presenting on VE in Ireland as part of European I-MOVE consortium, 23rd June 2020

Other activities

A. Manuscript Reviewing

Reviewed manuscripts for: *Journal of Medical Microbiology* (on VTEC); *Journal of Antimicrobial Chemotherapy* (on CPE) and *Environmental Pollution* (on CPE).

B. Application for ethics approval for *E. coli* Bloodstream Infection project

For this project Carina prepared a 12-page ethics application for review by the hospital Research Ethics Committee and a four page Data Protection Impact Assessment for the Hospital Research and Innovation Office. Project ethics approval still pending and process paused due to the pandemic.

Training modules

Management, Leadership and Communication in Public Health, ECDC, Stockholm, Sweden (1 week)

9. EPIET/EUPHEM modules attended

1. Introductory Course, Spetses, Greece (3 weeks)
2. Outbreak Investigation Module, Robert Koch Institute Berlin, Germany (1 week)
3. Multivariable Analysis Module, Instituto de Salud Carlos III Madrid, Spain (1 week)
4. Rapid Assessment & Survey Methods, Andrija Štampar School of Public Health, University of Zagreb, Croatia (1 week)
5. Project Review Module, Prague, Czech Republic (1 week)
6. 'Management, Leadership and Communication in Public Health', ECDC, Stockholm, Sweden (1 week)
7. Vaccinology Module (online MOOC, Institute Pasteur) (1 week)
8. Vaccinology Module Webex sessions 22nd to 24th June 2020

10. Other training

1. 'Influenza Bioanalytics' e-Learning pilot course on EVA
2. 'Writing and Reviewing Scientific Abstracts: a field epidemiology focus' online module on EVA
3. 'Influenza vaccination campaigns targeting health care workers' e-Learning course on EVA
4. 'Rapid Risk Assessment (RRA)' e-Learning course on EVA
5. 'PRECEPT' e-Learning course on EVA
6. Open WHO online course: 'Seasonal Influenza: Introduction'
7. Open WHO online course: 'Avian and other zoonotic influenza'
8. Open WHO online course: 'Pandemic Influenza: Introduction'
9. Host site laboratory training in Health and Safety, laboratory methods, Quality System
10. One day meeting of Medical Microbiology Association of 'C. difficile and healthcare infections', November 13th 2019
11. Attended Journal Clubs at National Virus Reference Laboratory on: 'Non-polio enterovirus genotyping systematic review' and 'Mumps outbreak in Marshall Islanders in the USA'. November 15th and 22nd 2019
12. Seminar in HSPC on 'Vaccination and conspiracy theories', November 19th 2019
13. Half-day workshop at St James's Hospital on 'Critical Appraisal of research methodology', January 17th 2020
14. Half-day Next Generation Sequencing Mini Workshop at St James's Hospital, January 28th 2020
15. Project mini-review with UK-FETP fellows and presented CPE outbreak project for review. At PHE office Birmingham, UK, March 2nd to 4th 2020
16. ESCMID Observership Award: Training in *C. difficile* WGS analysis including use of Seqsphere+ software at Prof Maja Rupnik Laboratory, Maribor, Slovenia March 9th to 13th 2020
17. ESCMID Webinar session: 'COVID-19 diagnostics: Lights and shadows', May 7th 2020
18. ESCMID Webinar session: 'The Public health response to the first wave of the COVID-19 pandemic in Europe', June 4th 2020
19. COVID-19 training: sample handling and logging into LIMS; lab testing methods and molecular test analysis and interpretation; result validation and authorisation and reporting

20. One Health EJP Annual Scientific Meeting 2020, May 27th to 29th 2020
21. Online Virtual Public Forum: 'COVID-19 dynamics and evolution'. Hosted by University of California, San Diego, July 31st 2020
22. Online COVID-19 Question and Answer session with Prof Peter Piot Director of London School of Hygiene and Tropical Medicine and Dr John Nkengasong Director of Africa CDC, July 28th 2020
23. Online European Society of Clinical Virology Online conference on COVID-19, September 9th 2020

Discussion

Coordinator's conclusions

One of the main goals of the EUPHEM programme is to expose fellows to diverse and multidisciplinary public health experiences and activities, thus enabling them to work across different disciplines. This report summarises all activities and projects conducted by Carina Brehony during her two-year EUPHEM fellowship (cohort 2018) as Member State track fellow at the Public Health Laboratory in Dublin, Ireland. Carina is the third appointed EUPHEM fellow in Ireland. The projects described in this portfolio demonstrate a diversity of public health microbiology projects. The epidemiological studies consisted from outbreak investigations at regional and national level (including a central role in the response to COVID-19 pandemic in Ireland) to surveillance activities including setting up a national sentinel surveillance system for campylobacteriosis or influenza resistance in Ireland. The laboratory and epidemiologically based projects covered all diverse range of disease programmes involving multidisciplinary working and teamwork on all levels such as physicians, laboratory technicians, epidemiologists, statisticians, government officials and public health officers, showing strength of Carina and ability to work within such an extended environment(s). Carina has shown a high capacity of public health management by working with an active role in interdisciplinary groups and bringing different professionals together. She has strongly supported the introduction of the genomic analysis in the Institute bringing her own skills to her projects. This is an excellent example of collaboration of covering the fellow needs and those of the institute. Activities were in line with the 'learning by doing' of the EUPHEM programme and fulfilled the core competency domains described for professionals in their mid-career and beyond. Activities were complimented by nine training modules providing theoretical knowledge. Projects had a clear outcome, with results communicated in scientific journals and at conferences. The contributions made by Carina to HSE work indicates importance of developing a future critical mass of highly skilled field public health microbiologists within Member States to contribute towards national preparedness as well as being available for responses in the interest of the EU. Thus, the importance of this professional profile has undoubtedly been revealed during the COVID-19 pandemic. The EUPHEM Coordinator Team concludes that the fellow has succeeded in performing all her tasks to a very high standard and with a professional and critical attitude. We wish the fellow every success in her future career.

Supervisor's conclusions

Carina Brehony has completed the two year EUPHEM Fellowship in Public Health Microbiology undertaken at the Public Health Laboratory, HSE, Dublin along with a consortium of National Reference Laboratories and the Health Protection Surveillance Centre. Her personalised Fellowship programme incorporated broad exposure and training opportunities for PHM with supervision provided by a number of Senior Medical Microbiologists and Scientific Specialists. The range of her projects undertaken were varied and together incorporated all the elements for her to achieve the required competencies for this Fellowship. Her Supervisors found her an enthusiastic Fellow, willing to learn and avail of the new opportunities and challenges posed by her PHM projects. Her knowledge and competency to detect, diagnose and control infectious diseases with enhanced PHM competencies and in collaboration with PH Epidemiology colleagues has developed strongly throughout the Fellowship. She worked independently, but also contributed significantly to multi-disciplinary teams as exemplified by her participation in outbreak investigations and the current COVID-19 pandemic management. She relished the analysis of the data produced during her projects, to explore the project aims and substantiate her PHM conclusions. She presented widely at many conferences during her Fellowship and defended her findings confidently. Subsequent papers for publication have been submitted and are under review. She also benefited from visiting another European specialist laboratory facility, expanding her technical expertise and enhancing collaboration opportunities in European PHM. Now as a competent Public Health Microbiology Specialist, she is well positioned to contribute to the national and European capacity of such specialists to address on-going and future communicable threats to public health.

Personal conclusions of fellow

I feel very privileged to have been a part of the EPIET/EUPHEM programme and enjoyed the two years tremendously. It was a unique opportunity to gain public health microbiology training in a structured way through

projects covering a wide array of pathogens and taught modules on a variety of relevant topics. The highlight, and an integral part of the programme, was the formation of personal and professional links with my cohort fellows. These relationships will continue to strengthen national, European and global public health networks.

Acknowledgements of fellow

I would like to thank my site supervisor at PHL Eleanor McNamara for the guidance, support and mentorship over the course of the fellowship. I would also like to thank Anne Carroll (cohort 2013) for her support and valuable experience throughout. Thanks to all my colleagues at PHL for being a really nice group of people to work with. PHL was a great base for the two years and I was glad to be part of the fantastic team that worked so hard to establish and run COVID-19 testing in very trying times.

I would like to thank all my project supervisors for giving me their extremely valuable time especially when there was a pandemic to deal with (!): Cillian De Gascun, Karen Burns, Tom Rogers, Richard Drew Thanks to the very helpful and kind staff at St James' Hospital Clinical Microbiology and the National Virus Reference Laboratory. Thanks to colleagues in the Health Protection Surveillance Centre: Patricia Garvey, Joan O'Donnell and Margaret Fitzgerald

I especially want to acknowledge my cohort fellow Lisa Domegan for being an excellent collaborator and companion through the fellowship. Thanks to my frontline coordinators Silvia Herrera Leon and Aftab Jasir for their guidance throughout the programme. I would also like to thank all the members of the EPIET/EUPHEM programme coordination team for their hard work. Finally I would like to thank my 2018 EUPHEM and EPIET cohort colleagues for being such a lovely bunch of people to have spent two years with...from the Greek Isles onwards! I value their friendships, support and guidance and look forward when we can meet to reflect on the fellowship and also look forward to future.