



FELLOWSHIP REPORT

Summary of work activities

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Intervention Epidemiology path (EPIET)

Cohort 2014

Background

The ECDC Fellowship Training Programme includes two distinct curricular pathways: Intervention Epidemiology Training (EPIET) and Public Health Microbiology Training (EUPHEM). After the two-year training EPIET and EUPHEM graduates are considered experts in applying epidemiological or microbiological methods to provide evidence to guide public health interventions for communicable disease prevention and control.

Both curriculum paths are part of the ECDC fellowship programme that provides competency based training and practical experience using the 'learning by doing' approach in acknowledged training sites across the European Union (EU) and European Economic Area (EEA) Member States.

Intervention Epidemiology path (EPIET)

Field epidemiology aims to apply epidemiologic methods in day to day public health field conditions in order to generate new knowledge and scientific evidence for public health decision making. The context is often complex and difficult to control, which challenges study design and interpretation of study results. However, often in Public Health we lack the opportunity to perform controlled trials and we are faced with the need to design observational studies as best as we can. Field epidemiologists use epidemiology as a tool to design, evaluate or improve interventions to protect the health of a population.

The European Programme for Intervention Epidemiology Training (EPIET) was created in 1995. Its purpose is to create a network of highly trained field epidemiologists in the European Union, thereby strengthening the public health epidemiology workforce at Member State and EU/EEA level. Current EPIET alumni are providing expertise in response activities and strengthening capacity for communicable disease surveillance and control inside and beyond the EU. In 2006 EPIET was integrated into the core activities of ECDC.

The objectives of the ECDC Fellowship - EPIET path are:

- To strengthen the surveillance of infectious diseases and other public health issues in Member States and at EU level;
- To develop response capacity for effective field investigation and control at national and community level to meet public health threats;

The views expressed in this publication do not necessarily reflect the views of the European Centre for Disease Prevention and Control (ECDC).

This portfolio does not represent a diploma. Fellows receive a certificate acknowledging the 2-year training and listing the theoretical modules attended. Additionally, if all training objectives have been met, they receive a diploma.

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- To develop a European network of public health epidemiologists who use standard methods and share common objectives;
- To contribute to the development of the community network for the surveillance and control of communicable diseases.

Fellows develop core competencies in field epidemiology mainly through project or activity work, but also partly through participation in training modules. Outputs are presented in accordance with the EPIET competency domains, as set out in the EPIET scientific guide¹.

Pre-fellowship short biography

Isidro Carrion graduated as a nurse in 2002. After finalizing his Masters in International Cooperation and Economic Development, in 2009, he worked with Doctors Without Borders (MSF). In 2012, he completed his Masters in Public Health, and worked for two years with MSF as an epidemiologist.

Fellowship assignment: Intervention Epidemiology path (EPIET)

On 15th of September, Isidro started his EPIET fellowship at the Centre for Infectious Disease Surveillance and Control (CIDSC) in Public Health England (PHE), London, United Kingdom, under the supervision of Richard Pebody. This report summarizes the work performed during the fellowship.

Fellowship portfolio

This portfolio presents a summary of all work activities (unless restricted due to confidentiality regulations) conducted by the fellow during the ECDC Fellowship, EPIET path. These activities include various projects, and theoretical training modules.

Projects included epidemiological contributions to public health event detection and investigation (surveillance and outbreaks); applied epidemiology field research; teaching epidemiology; summarising and communicating scientific evidence and activities with a specific epidemiology focus. The outcomes include publications, presentations, posters, reports and teaching materials prepared by the fellow.

This portfolio also includes a reflection from the fellow on the field epidemiology competencies developed during the 2-year training, a reflection from the supervisor on the added value of engaging in the training of the fellow, as well as a reflection by the programme coordinator on the development of the fellow's competencies.

Fellowship projects

1. Surveillance

Environmental surveillance for poliovirus in the United Kingdom (UK)... getting ready.

BACKGROUND

WHO recommends Poliomyelitis Environmental Surveillance (PES) in populations where acute flaccid paralysis surveillance is not in place and where conditions exist that render the population at potential risk for poliovirus circulation. The UK has close links with geographical areas where endemic wild (WPV) and circulating Vaccine Derived Poliovirus (cVDPV) are still present. We describe a protocol for implementing PES in the UK as part of the National Polio Plan.

METHODS

We reviewed the WHO guidelines and literature on PES, obtained information from colleagues in countries using PES and sewage network companies in the UK. We developed a protocol for sewage sampling procedures, proposed

¹ European Centre for Disease Prevention and Control. European public health training programme. Stockholm: ECDC; 2013. Available from: http://ecdc.europa.eu/en/epiet/Documents/Scientific%20guides/EPIET%20Scientific%20Guide_C2016.pdf

scenarios of poliovirus detection, based on mathematical modelling, and described the required public health actions following detection.

RESULTS

We propose using grab method sampling to collect raw sewage at least once a month from converging sewers networks serving populations of optimal size: 100,000–300,000. WPV or cVDPV detected through this environmental surveillance would represent a public health emergency warranting immediate further investigation and notification to the Public Health Authorities and WHO. To determine if there is local poliovirus transmission, actions would include: enhanced environmental sampling (more frequently, smaller target populations, more sites), active search for poliovirus-infected persons, estimating local polio immunisation coverage in target groups and genome characterization to determine length of transmission chains and possible source. We present four levels of possible detection scenarios and associated public health actions, including mop-up vaccination when genetic and epidemiological evidence indicate widespread transmission of WPV or cVDPV.

CONCLUSIONS

This new surveillance system will allow the early identification of poliovirus transmission in the UK and inform optimal implementation of a rapid public health response.

Role and outputs: Responsible of the protocol development. Abstract accepted for oral presentation at ESCAIDE 2016 (1). The protocol will be published in the PHE web site in the next months (2).

Supervisor(s): Richard Pebody

The PHE Surveillance Standards within Surgical Site Infection Surveillance Service

BACKGROUND

Infections acquired in hospital are recognised as being associated with significant morbidity. The Surgical Site Infection Surveillance Service (SSISS) enhance the value of surveillance providing high quality comparative data based on a standardised approach to data collection, analysis and interpretation. We evaluated the surveillance system according to the Public Health England Surveillance Standards (aims, objectives, operation of systems, data analysis, dissemination of information, quality assurance and information governance, and capacity) in order to guarantee that the SSISS complies with national legislation and guidance on best practice.

METHODS

We reviewed the protocol, the evaluations documents, the data sets, the standard operational procedures (SOP) for data reconciliation, the data storage, transfer and analysis system level security policy, the software used, letters to hospitals, and publications derived from the SSISS data.

RESULTS

The SSISS aims and objectives have recognisable public health goals, agreed through regular consultation with internal and external stakeholders. There is not regular or programmed review of the objectives. There has not been a program of regular evaluation; ad hoc external evaluations have been done. The SSISS used appropriate and standardised denominators. There are effective protocols and quality assurance checks on data collections and a surveillance manual including data flows, SOP for data access and user manuals. Appropriate statistical analyses are used to investigate trends and associations, which are communicated adequately. Surveillance information is stored complying with the Data Protection Act and adhering to good information governance practice. Data is stored in a robust and resilient way, ensuring access for all those with a legitimate need, minimisation of duplication, and business continuity arrangements ranging from back-ups to disaster recovery.

CONCLUSION

The SSISS highly complies with the PHE standards. We recommend to establish a program of regular evaluation so that the SSISS maintain these high quality surveillance standards.

Role and outputs: Main investigator. Report submitted and accepted by the Head of Information Management of the PHE Field Epidemiology Service (3)

Supervisor(s): Theresa Lamagni

Title: Review of the surveillance data of Guillain–Barré syndrome (GBS) presentations in England and time series analysis of GBS and laboratory reports, April 2004 to August 2015.

BACKGROUND

Public Health Wales reported a cluster of 10 atypical GBS temporally related to a cluster of four children with acute flaccid paralysis in January 2016. As a response to this situation, Public Health England undertook a review of routine surveillance sources, to investigate any potential changes in the epidemiology of GBS across England, and describe the seasonal patterns of GBS.

METHODS

We extracted the data for admissions to hospitals in England using a GBS diagnostic Hospital Episodes Statistics database (January 2014 to December 2015). We examined the association between increases in GBS episodes and increases in laboratory reports for *Campylobacter* spp., Cytomegalovirus, Epstein-Barr virus, *Haemophilus influenzae* (B and non B), *Mycoplasma pneumoniae*, Influenza, Adenovirus, Varicella Zoster virus, Parainfluenza and Enterovirus from 2004 to 2016 using multivariable time series analysis.

RESULTS

Between January 2004 and August 2015, the incidence of GBS was 2.45 (95%CI: 2.32-2.59) per 100,000 inhabitants per year. From 2004 to 2015, the number of GBS cases increased significantly ($p < 0.01$). During the study period, GBS cases increased every January. The rest of the multivariable analysis is on going.

CONCLUSIONS

We observed seasonality in GBS presentations. We recommend further time series analysis from an ecological perspective to understand better the reasons behind the yearly peak in GBS cases in England.

Role and outputs: Main investigator. Wrote the protocol. Preliminary report written. Protocol for further time series analysis written. Analysis on going. The results of this study will be submitted to a peer review journal.

Supervisor(s): Richard Pebody and Nick Andrews

Competencies developed:

The polio environmental surveillance project helped me to learn about the environmental surveillance of polio and its use as part of the polio eradication program. I reviewed epidemiological data of other systems and literature in order to guide public practice and to set up a new surveillance system. I learnt how to coordinate different institutions and partners for the logistics and technical issues of the surveillance system, including the collaboration with the laboratory colleagues and the mathematical modelling team which gave me a good learning experience in these fields. I monitored the progress of the projects and prepared activity reports. I also had to establish communication with different countries in order to find out about the different systems in place in Europe.

With the review of the SSISS project, I got to know all the details of the system (e.g. data and information systems, SOPs, information governance, etc.). I understood the importance of an adequate surveillance objective and the challenge of establishing uniform data collection systems for all the hospitals of the country. Furthermore, I learnt to evaluate all these aspects according to different indicators and standards.

Finally, the GBS project gave me the opportunity of participating in the teleconferences of the outbreak control team in a high profile investigation. It also helped me to consolidate my technical skills on the management of big data sets (i.e. data cleaning and recoding). By working on this project I could further develop my technical knowledge and skills on time series analysis. I wrote the study protocol for this epidemiological study identifying the public health problem. By doing so, I gained my first experience in PHE on the aspects related to the ethics of a research: confidentiality, protection of individuals and conflict of interest.

2. Outbreak investigations

Epidemiological description and implications for control of an outbreak of NDM-producing *Klebsiella pneumoniae* in two hospitals in United Kingdom (UK), 2015.

BACKGROUND

Carbapenem-resistant Enterobacteriaceae (CRE) are a growing challenge within hospitals due to limited therapeutic options and difficult infection prevention and control. In March 2015, two patients infected with an indistinguishable *Klebsiella pneumoniae* ST14 strain with a New Delhi metallo-beta-lactamase (KP-NDM) were identified in hospital A. We reviewed the epidemiological-molecular links of the patients to understand the transmission patterns.

METHODS

We screened all hospitalised and newly-admitted patients in a large renal unit and associated vascular unit. We analysed rectal screening samples using chromogenic agar, and multiplex real-time PCR, with further typing (Variable Number Tandem Repeat, VNTR, analysis and Whole Genome Sequencing, WGS) and colistin resistance testing. Confirmed cases were persons infected or colonized with the outbreak VNTR profile, between 01/04/2014 and 03/08/2015, with previous attendance to hospital A or B. Probable cases were the same, but without VNTR confirmation. We calculated frequencies of exposures potentially associated with KP-NDM acquisition (clinical conditions, procedures, previous hospitalizations, contact with positive patient).

RESULTS

We identified 38 cases (32 confirmed, 6 probable); 11 infected, 27 colonised. Median age: 68 years (range 26-85); 21 (55%) were male. All were long-stay patients in renal or vascular wards, with complex medical histories and no recent foreign travel history. Of the cases, 70% (16/23) had a colistin-resistant strain. Initial negative screen sample followed by a positive one and contact between cases indicated that transmission likely occurred in three different wards. Control measures were implemented :enhanced screening, wards closure, isolation/cohorting of cases, enhanced environmental cleaning, cleaning/disinfection protocol review, antimicrobial policy review and stewardship.

CONCLUSIONS

VNTR and WGS typing helped identify this large outbreak of KP-NDM. We could not establish the potential source or initial transmission point. We recommend early identification of cases with robust screening on admission, rapid implementation of control measures and detailed epidemiological-microbiological investigations to understand the spread and reduce the risk of transmission of CRE within hospitals.

Role and outputs: Main-investigator. Report written (4) and poster presented at ECCMID 2016 (5).

Supervisor(s): Charlotte Anderson and Yimmy Chow

National outbreak of verocytotoxigenic Escherichia coli (VTEC) amongst adults exposed to prepacked salad detected by whole genome sequencing in England and Wales, July – September 2015.

BACKGROUND

In August 2015, Public Health England detected a phylogenetic cluster of VTEC cases widely dispersed across England with one case in Wales. We investigated to identify the vehicle of infection and determine suitable control measures.

METHODS

We defined cases as those with VTEC serotype O157 phage type 8 verotoxin 2a clustering within five single nucleotide polymorphisms of the outbreak sequence by whole genome sequencing (WGS). Standardised VTEC Enhanced Surveillance Questionnaires were completed for all cases. Exposures common to 70% or more were assessed further with a focused questionnaire. A case – case study was conducted to compare primary outbreak cases with non-outbreak cases from 2015, aged over 18, resident in England or Wales, without history of foreign travel in the week before onset. Sporadic (non-outbreak) controls meeting these criteria were selected from the National VTEC database. We used multivariable logistic regression to calculate odds ratios (OR) and 95% confidence intervals (95%CI) .

RESULTS

Forty-four cases were identified; 73% were female (median age 36, range 2-73 years). Thirty-six cases and 78 controls were included in the case-case study. Consumption of prepacked salad from one national supermarket-chain was identified as the primary exposure associated with illness (OR: 54, 95%CI: 11-247). Further investigations implicated two prepacked salad products, with one common ingredient, processed by one distributor who was supplied by six salad leaf producers during the outbreak period.

CONCLUSIONS AND RECOMMENDATIONS

A national VTEC outbreak was successfully detected using WGS. The routine application of a standardised questionnaire to all VTEC cases facilitated a rapid investigation which identified prepacked salads as the likely vehicle of infection. Protection of salad leaves from possible sources of contamination from harvest to distribution is strongly recommended.

Role and outputs: Co-investigator. Isidro performed the analysis, identified the source, wrote the report (6) and presented it in the outbreak control meetings.. Poster presented at ESCAIDE 2015 by Amy Mikhail (7)

Supervisor(s): Richard Elson, Neville Verlander and Amy Mikhail.

Insidious risk of severe mycobacterial infection in cardiac surgery patients

BACKGROUND

An urgent UK investigation was launched to assess the risk of invasive *Mycobacterium chimaera* infection in cardiothoracic surgery and a possible association with cardiopulmonary bypass heater-cooler units following alerts in Switzerland and the Netherlands.

METHODS

Parallel investigations were pursued: i) identification of cardiopulmonary bypass-associated *M. chimaera* infection through linkage of national laboratory diagnoses to prior hospital admissions combined with prospective case finding (2007-2015) ii) cohort study to assess patient risk iii) microbiological and aerobiological investigations of heater-coolers in situ and under controlled laboratory conditions iv) whole genome sequencing (WGS) of clinical and environmental isolates.

FINDINGS

Eighteen probable cases of cardiopulmonary bypass-associated *M. chimaera* infection were identified, all except one adults. Cases had undergone valve replacement in 11 hospitals between 2007-2015, a median 19 months prior to onset (range 3 months-5 years). Risk to patients increased after 2010 from <0.2 to 1.65/10,000 person-years in 2013, a nine-fold rise for infections within 2y of surgery (RR=9.08, 95% CI 1.81-87.76). Endocarditis was the most common presentation (n=11); to date, 9 cases have died. Of 16 isolates tested, 15 were confirmed as *M. chimaera*. Investigations identified aerosol release through specific breaches in heater-cooler tanks. *M. chimaera* and other potential pathogens (including *Legionella*) were recovered from water and air samples taken in situ. Phylogenetic analysis of WGS data found close clustering of strains from probable cases.

INTERPRETATION

We identified low but escalating risk of severe *M. chimaera* infection associated with heater-coolers with cases in a quarter of cardiothoracic centres. Our investigations strengthen aetiological evidence for heater-coolers' role in transmission and raise the possibility of an ongoing, international point-source outbreak. Active management of heater-coolers and heightened clinical awareness are imperative given the consequences of infection.

Role and outputs: Co-investigator (case search, case investigation and review of manuscript) Submitted to Clinical Infectious Diseases (under review) (8)

Supervisor(s): Theresa Lamagni

Uncovering the scale of a reptile associated salmonellosis outbreak in United Kingdom (UK), 2015: a recent history.

BACKGROUND

Salmonella enterica serotype Enteritidis has been associated with reptiles in the United States, but until now not documented in UK. Transmission of reptile associated salmonellosis occurs through contact with reptiles or contaminated reptile feed such as feeder mice. A cluster of cases of *Salmonella* Enteritidis was detected using whole genome sequencing (WGS) in August 2015. We investigated the events to identify the source.

METHODS

Routinely collected information was reviewed to develop a hypothesis which suggested a possible link with reptiles. A case-control study was conducted. A case was defined as a laboratory-confirmed *Salmonella* Enteritidis within a five single-nucleotide polymorphisms difference of the outbreak WGS profile. We randomly recruited controls from a consumer survey panel, frequency matched with cases on age. Cases and controls with history of travel within seven days of onset or interview were excluded. Standardised questionnaires on exposures (food and animal contact) were completed online. We calculated odds ratios (ORs) for different exposures.

RESULTS

Between January and August 2015, 70 cases were reported; median age was 18 years (range: 1-72), 36% were under 10 years of age and 54% were females. 26 cases and 56 controls had completed the questionnaire, twenty (80%) of these cases owned a snake, 23 (50%) required hospitalization. Exposure to snakes was the only variable independently associated with infection (Odds Ratio 810 95% CI (85-7715) p<0.001). Isolates of *S. Enteritidis* PT8 belonging to the outbreak profile were recovered from reptile feeder mice (but not from rats, mice and chicks) sampled at the retail and wholesale level.

CONCLUSION

Cases were associated with owning a reptile, particularly corn snakes. We believe this to be the first *S. Enteritidis* outbreak associated with snakes reported. Further investigation is essential to identify the source and the real extent of this outbreak.

Role and outputs: Co-investigator. Isidro conducted the case-control study, performed the analysis, identified the source, wrote the final report (9) and presented the results during the outbreak control team meetings. He presented this work as a late breaker oral at ESCAIDE 2015 (10) and submitted to Food Microbiology (11).

Supervisor(s): Richard Elson, Neville Verlander and Sanch Kanagarajah

Title: *Outbreak of gastrointestinal illness following a wedding at a restaurant in London, January 2016.*

BACKGROUND

On the 04/02/2016, the Field Epidemiology Services of South East and London (FES Sea) was alerted by North West London Health Protection Team (NWL-HPT) of reports of gastrointestinal illness among attendees at a wedding at the restaurant A, in London. The outbreak control team (OCT) investigated to: describe the outbreak in terms of time, place and person; estimate the risk of illness among attendees; identify factors associated with illness among attendees and determine a possible vehicle and route of transmission, to provide suggestions for future prevention and management actions

METHODS

A confirmed case was a guest or staff, who attended the A venue on January 16th, with a positive sample (laboratory confirmation) for *Campylobacter* Spp. taken during the two weeks after the wedding. A probable case was a guest or staff, who attended the A venue on January 16th and developed diarrhoea and/or vomiting with onset during the 10 days after attending the event. We used an online questionnaire to collect information on symptoms and exposures among all attendees (guests and staff, cohort study), possible prior common experiences and other possible sources of illness as well as about any secondary transmission.

RESULTS

The study was not finalized as the wedding party organiser refused to send the online questionnaire link to the guests.

Role and outputs: Co-investigator. Isidro wrote the protocol, designed the cohort study and developed the online questionnaire.

Supervisor(s): Sooria Balasegaram, Geraldine Leong, Helen Maguire, Maria Saavedra-Campos.

Title: *Salmonella enteritidis outbreak in England and Wales, 2015.*

BACKGROUND

Since April 2015, Whole Genome Sequencing (WGS) has been the routine test for *Salmonella* identification, surveillance and outbreak investigation at the national reference laboratory in England and Wales. In May 2015, an outbreak of *Salmonella* Enteritidis cases was detected using WGS data and investigated.

METHODS

A case was defined as a laboratory-confirmed *Salmonella* Enteritidis within a five single-nucleotide polymorphisms difference of the outbreak WGS profile. Cases residing in the UK were interviewed to obtain a food history; links between suppliers were mapped to produce a food chain network for chicken eggs. The association between the food chain network and the phylogeny was explored using a network comparison approach. Food and environmental samples were taken from premises linked to cases and tested for *Salmonella*.

RESULTS

Within the outbreak Single Nucleotide Polymorphism (SNP) defined cluster, 136 cases were identified in the UK and 18 in Spain. One isolate from a food containing chicken eggs was within the outbreak cluster. There was a significant association between the chicken egg food chain of UK cases and phylogeny of outbreak isolates.

CONCLUSION

This is the first published *Salmonella* outbreak to be prospectively detected using WGS. This outbreak in the UK was linked with contemporaneous cases in Spain by WGS. We conclude that UK and Spanish cases were exposed to a common source of *Salmonella* contaminated chicken eggs.

Role and outputs: Co-investigator. Isidro described the outbreak in terms of time, place and person and produced the weekly report for the Field Epidemiology Services (12)

Supervisor(s): Thomas Inns and Paul Cleary.

Investigation of a national outbreak of VTEC *Escherichia coli* O157 using online consumer panel control methods - Great Britain, October 2014

BACKGROUND

In October 2014, Public Health England (PHE) identified a cluster of *Escherichia coli* O157 PT8 (VTEC) which shared a Multiple Locus Variable-number Tandem Repeat Analysis (MLVA) profile. Due to increased cluster detection it has become necessary to find less resource-intensive investigation methods. During 2013, an online consumer panel, which rewards members for completing surveys, was trialled as a novel recruitment method. It was found to be comparable to traditional methods. The aims of this investigation were to identify the vehicle of infection using online survey methods.

METHODS

We conducted a case-control study, recruiting two controls per case. Cases were identified as Great British residents, aged 18 or over, with the outbreak MLVA strain. A consumer survey panel randomly recruited controls by emailing members an online survey link. PHE contacted cases first by phone and then email. We excluded participants with history of travel within seven days of symptom onset. We performed multivariable logistic regression to calculate adjusted odds ratios (aOR) and 95% confidence intervals (95%CI).

RESULTS

We recruited 36 (75%) of 48 contactable cases and 96 controls over five days; only several hours were needed to prepare data for analysis. Cases had greater odds of consumption of pre-packed salad (aOR 13; 95%CI 4.2-42). Additionally, they were more likely to have purchased salad (aOR 28; 95%CI 5.0-157) or potatoes (aOR 3.3; 95%CI 1.0-10) from a specific retailer.

CONCLUSIONS

This study demonstrates a strong epidemiological link between consumption of pre-packed salad and disease. The use of consumer panel controls in conjunction with online surveys was less resource intensive than traditional data collection methods. Therefore we recommend this as a plausible method for use in future outbreak investigations.

Role and outputs: Co-investigator (data collection). Poster presented by Chantil Sinclair in ESCAIDE (Stockholm) and in TEPHINET (Mexico), 2015

Supervisor(s): Bob Adak

Competencies developed:

The NDM-producing *Klebsiella pneumoniae* project gave me the opportunity to get involved in a high level outbreak and to further develop my negotiation and communication skills when working with other partners. I learnt how to collect information in a nosocomial outbreak (i.e. reviewing charts and creating patient forms) and how to use the I2 network analysis software and R. By presenting this outbreak in ECCMID, I had the opportunity to attend a big and prestigious conference and to learn how to write abstracts for these events. I developed evidence based recommendations for the prevention and control of future outbreaks.

In the *Salmonella enteritidis* outbreak in England and Wales, I was responsible, for the first time, of writing the descriptive epidemiological situation report. I used R for automated report writing.

In the VTEC outbreak amongst adults exposed to prepacked salad, I applied the different technical skills that I had acquired in the multivariable analysis module. It was the first time, I was involved in an analytical study in PHE (i.e. case-control). I run the whole analysis using Stata, identified the source, wrote the report and presented it in the outbreak control meetings. Furthermore I learnt how to design online questionnaires using the PHE online survey system.

With the investigation of the outbreak of severe mycobacterial infection, I had the opportunity to get involved in an outbreak of international dimensions. It helped me to improve my skills on the case investigations. I examined charts and test results and interviewed different clinicians and infection control staff. By working on this outbreak, I learnt the importance of reaching consensus about the case definition.

The outbreak of reptile associated *Salmonella* gave me the opportunity to consolidate my technical skills in multivariable analysis for outbreak investigation. By presenting this outbreak at ESCAIDE I gained experience on orally presenting outbreak investigations at an international conference.

Finally, the outbreak of gastrointestinal illness following a wedding gave me the opportunity to get involved in a more local investigation since the beginning of the outbreak. I participated in the OCT meetings and was responsible for establishing communication between FES and HPT concerning the cohort study. I learnt how to write a protocol for a cohort study in this type of setting and how to develop an online questionnaire.

3. Applied epidemiology research

Depression-Anxiety: the most prevalent co-morbidity among people living with HIV in England and Wales, 2014.

BACKGROUND

HIV infection has become a long-term condition associated with other chronic conditions. We present the first population-level estimates of self-reported prevalence of selected co-morbidities in people living with HIV (PLHIV) in England and Wales.

METHODS

'Positive Voices' is a cross-sectional probability survey of healthcare needs and sexual behaviour in PLHIV, conducted between May and November 2014. We obtained a random sample of PLHIV from 30 HIV clinics purposively sampled, using the SOPHID (Survey of Prevalent Infections Diagnosed) census. Participants completed the online questionnaire on sociodemographics, diagnoses of non-HIV comorbidities, and quality of life. Data was weighted to the age, sex, ethnic and risk group distribution in the SOPHID dataset, to improve representativeness. We calculated adjusted prevalence of comorbidities, and compared these with the prevalence of co-morbidities in the general population obtained from the Health Survey in England (HSE) 2012.

RESULTS

We obtained 779 questionnaires (response rate 26%). Prevalence of depression-anxiety among PLHIV was 27% (95%CI 22-34), (19% in women, 32% in men), higher than the HSE estimates for the general population: 14% (17%,11%, respectively). Statin use for high cholesterol was reported by 19% (95% CI 16-22) of PLHIV (11% in women, 21% in men) compared with 9.4%, (8%, 11% respectively) in the general population. Prevalence of hypertension was 12% (95%CI 10-15) (13% in women, 12% in men) compared with 21% (22%, 21% respectively) in the general population. Age specific prevalence (18 to 59 years) in our survey was: depression 31% (95%CI 28-35), statin use for high cholesterol 15% (95%CI 13-18), and hypertension 13% (95%CI 11-16). Compared to the general population, respectively: 18% (CI95% 17-19), 9% (CI95% 9-10) and 16% (CI95% 15-17). Comparing by risk group, within our surveyed population, men who have sex with men (MSM) had a higher prevalence of all three co-morbidities (37% for depression-anxiety, 25% for high cholesterol, and 14% for hypertension).

CONCLUSIONS

Depression-anxiety was the most prevalent self-reported comorbidity among PLHIV and MSM in particular. In keeping with other studies depression and high cholesterol appear higher in PLHIV compared to the general population. Monitoring the changing pattern of comorbidities among PLHIV can inform health planning and models of care.

Role and outputs: Main investigator. Poster presented at the British HIV Association (BHIVA) conference in Brighton, 2015 (13), manuscript in preparation.

Supervisor(s): Meaghan Kall, Erica Pufall and Valerie Delpech

The emergence of enterovirus D68 (EV-D68) in the English population: The necessity for reinforcing enterovirus respiratory screening.

BACKGROUND

In autumn 2014, EV-D68 associated with severe respiratory disease and neurological presentation emerged in North America and in some European countries. We describe the epidemiology of EV-D68 in England, between October and December 2014.

METHODS

In England, enterovirus cases presenting with acute neurological symptoms are reported to the Enterovirus Surveillance System (ESS). From September 2014, reports were extended to include enterovirus positive cases hospitalised with respiratory symptoms. We collected clinical information on all laboratory confirmed EV-D68 cases. In primary care, respiratory swabs from patients consulting with influenza-like-illness were tested for EV-D68 from

September 2013 to January 2015. We further characterized EV-D68 strains by amplification and partial sequencing of the VP1 coding region.

RESULTS

From October-December 2014, 36 EV-D68 cases were detected through ESS (age range: 0-71 years (median: 3); 55% male). 31 cases presented with respiratory and two with neurological symptoms (EV-D68 negative in cerebral spinal fluid); 18 were immunocompromised or had other underlying diseases. 29/36 (81%) cases were hospitalised; 12/29 (33%) were in ICU and one died. Seven were outpatients or only seen in emergency department. In primary care, EV-D68 positivity increased from 0.2% (4/1,757) (95%CI: 0.08-0.6) before September 2014 to 2.0% (8/385) (95%CI: 1.0-4.0) after (p-value<0.001). EV-D68 strains genetically similar to those detected in 2014 in USA have been circulating in England since 2012 and were also detected in 2014/2015.

CONCLUSIONS

EV-D68 circulation in primary care in England increased after September 2014. In secondary care, EV-D68 presented mainly with severe respiratory symptoms, particularly in those with underlying diseases. We recommend reinforcing enterovirus surveillance through screening of respiratory samples of suspect cases to better understand the epidemiology of EV-D68 and to inform surveillance and laboratory-testing guidance.

Role and outputs: Main investigator. Status: Poster presented at ESCAIDE (2016)(14) and manuscript submitted to Epidemiology and Infection (under review) (15)

Supervisor(s): Richard Pebody and David J. Allen.

Understanding the culture to stop Ebola Virus Disease (EVD): social and cultural factors behind community resistance and a super spreading event in the village of Fogna, Guinea Forrest.

BACKGROUND

Attending funerals and having contact with a case in community settings are the most common modes of Ebola Virus (EV) transmission. We investigated a cluster of EV in Fogna, Forest Guinea to identify socio-cultural determinants and their relation with community resistance.

METHODS

We present the extent of the cluster and the results of qualitative studies: observant participation, interviews with five key informants and two focus groups conducted during February-March.

RESULTS

On 19th of February 2015 the first case of EV in Fogna, a 65 year old woman, community and religious leader died leading to 20 secondary cases(15 females, age range: 16-70 years (median 37), sixteen died (case fatality: 80%)) and 148 contacts were identified in total. Qualitative findings regarding nature of the exposure were: During the animist funeral ceremony, only women washed and prepared the body. No coffin was used. Regarding reasons for resistance: Most of the infected people fled to the forest because of fear of the Ebola Treatment Centre: rumours said people were killed there for their organs to be sold, and this made the villagers reluctant to interventions of the response team. The four secondary cases who survived were accompanied back to the village. They shared their experience to educate and reassure villagers. This decreased community resistance and yielded contact tracing: the only two subsequent cases occurred among followed contacts and were identified with no delay.

CONCLUSIONS

Engaging EV survivors from the same community decreased community resistance and improved surveillance. In reluctant communities understanding the socio-cultural local context, the nature of the exposure and community perceptions may improve community involvement and prevent EV transmission.

Role and outputs: Main investigator. Poster presented at ESCAIDE (2016), (16) and article published in International Health (17)

Supervisor(s): Tarik Derrough, Josep Jansa and Guenaël Rodier

Description of Hepatitis A outbreaks and subsequent public health actions in England, 2011-2015

BACKGROUND

In developed countries, the most common mode of Hepatitis A virus (HAV) transmission is from person to person. We described HAV outbreaks that occurred in England from April 2011 to April 2015 and the public health actions taken in response to inform the revision of public health guidance on HAV management.

METHODS

We defined an outbreak as any situation i) with >1 HAV laboratory-confirmed epidemiologically linked cases with at least one case occurring outside the household of the primary case or ii) any school child not linked to an identified HAV case for whom we assumed transmission in school. The local health protection teams completed a questionnaire describing these outbreaks in terms of place, time, person, HAV genotype and public health actions taken.

RESULTS

We collected information on 19 HAV outbreaks. Median age of primary and secondary cases was 9.5 years (range: 2-52, n=16), and 9.5 (range: 0-58, n=39), respectively. Thirteen (68%) outbreaks occurred in an educational setting (school/nursery), four in households, one in a care home and one during a choir trip. Genotype was obtained in 10 outbreaks: three were genotype 1A, seven genotype 1B. Oral fluid test (OFT) to identify asymptomatic cases was used in 3/19 outbreaks. Vaccination beyond household contacts was done in 16 outbreaks (14 schools/nurseries, one care home, and one choir trip contacts); the definition of a contact varied according to the setting.

CONCLUSIONS

Children and school/nursery settings play an important role in the spread of HAV in England. In view of the potential unknown transmission of virus from asymptomatic cases in children, OFT should be used to determine the real extent of HAV community outbreaks and provide evidence for extended vaccination

Role and outputs: Main investigator. Report written (18). Poster accepted for ESCAIDE (2016) (19). Manuscript to be submitted to a peer-reviewed journal.

Supervisor(s): Sema Mandal

Seroprevalence of Hepatitis A in England

BACKGROUND

The documented age shift in hepatitis A (HAV) susceptibility has implications for the overall burden of HAV morbidity and associated health and social costs. The objective of this study is to explore changes in the seroprevalence of HAV in England in order to help inform public health control strategies of HAV and inform healthcare planning.

METHODS

We will conduct a cross-sectional seroprevalence study using specimens collected in 2014 and stored by PHE seroepidemiology programme. We will use a sample of 4000 specimens, 500 per age group (10 year age groups from 0 to 60 years).

DISCUSSION

This study will provide data on HAV currently susceptible groups, which will allow the comparison with previous studies, to look for any discernible trends and to identify shifts in HAV seroprevalence in different age groups. The findings will be of great importance, especially considering the current context of Hepatitis A vaccine shortage, as they will help informing modelling to predict future outbreaks and improve health care planning.

Role and outputs: Main investigator. Protocol finalized. Isidro wrote the protocol, will analyse the data and prepare a manuscript.

Supervisor(s): Sema Mandal

Field epidemiologist with Epicentre-MSF Switzerland in a measles seroprevalence study, Katanga, DR Congo, 2016

BACKGROUND

Despite the repeated vaccination campaigns organized by the government and NGOs and the reported vaccine coverages the province of Katanga in DR Congo is regularly affected by measles outbreaks. Seroprevalence data offer reliable information about the immunity of the population, but this data are rarely available in DR Congo. MSF conducted a cross-sectional study to estimate the measles seroprevalence in children under 15 years old in order to help the planning of future vaccination campaigns and the mathematical modelling for outbreaks forecasting.

METHODS

We used two-stage cluster sampling, randomly selecting 20 clusters of 20 children (10 children 6- 59 months, 10 children 5-14 years). The sample size was calculated for an estimated seroprevalence of 50%, alpha error of 5%, a 10% precision and a design effect of 2. We collected dried blood spot samples from the selected children to test for measles IgG.

RESULTS

All the information and samples were collected on March 2016. The analysis are ongoing at the moment of writing this abstract.

Role and outputs: Co-investigator. Isidro contributed to the writing of the protocol, organised the training and the fieldwork participated in the data collection and will contribute to the data analysis and writing the report/manuscript.

Supervisor(s): Alexandre Blake and Sandra Cohuet.

Competencies developed:

With the positive voices survey, I gained experience on the data analysis in surveys. I created the different strata and used Stata for the epidemiological analysis with post-stratification weights. Furthermore, I had my first experience on creating a poster .

By working in the EV-D68 project, I had the opportunity to be involved in all the stages/steps of an applied epidemiological research. I identified the surveillance data needs for the risk assessment. I gained experience on preparing risk assessments and on the creation of a research project as a response to an international outbreak. I further developed my skills on scientific writing and poster design.

The Ebola project in Guinea gave me the opportunity to use other approaches of outbreak response in a complex context. I had the opportunity to use my knowledge in qualitative and anthropological research.

By doing the Hepatitis A outbreaks review project, I had the opportunity to be part of the Hepatitis A guidelines review working group. I learnt the details of the Hepatitis A outbreak investigation and the relevant public health actions. Furthermore, I gained experience on public health guidance developing and how to find scientific evidence to orientate the recommendations, and how to identify gaps in scientific evidence and propose the subsequent research needed.

By participating in the measles seroprevalence study in DRC, I gained experience on the logistical issues related to the organization and conduct of a study like this in such a different and complex setting. I had to manage the financial and operational planning aspects of this epidemiological project. Being the team leader, I also had to work in a team and enhance my negotiation skills. I learnt how to use mobile data collection tools using ODK based software. I also learnt how to use R for the analysis of survey data and improve my skills in automated reporting.

4. Communication

Publications in peer reviewed journals

One manuscript published (14)

Manuscripts submitted to peer reviewed journals (in review process)

Two manuscripts submitted (11, 15) both under review.

Conference presentations

Three oral presentations at ESCAIDE (2015 and 2016) (1, 10, 16).

Two posters at ESCAIDE 2015 and 2016 as first author (14, 19). One poster at ESCAIDE 2015 as co-author (7)

One poster at the BHIVA conference 2015 (13).

One poster at ECCMID 2016 (5)

Reports

Five outbreak reports: Salmonella enteritidis outbreak in England and Wales, 2015 (12)); outbreak of Klebsiella Pneumonia NDM in two Hospitals in London (4) ; national outbreak of verocytotoxigenic Escherichia coli (VTEC) amongst adults exposed to prepacked salad detected by whole genome sequencing in England and Wales, July – September 2015 (6); reptile associated salmonellosis outbreak in United Kingdom (UK)(9), 2015; description of Hepatitis A outbreaks and subsequent public health actions in England, 2011-2015 (19).

One surveillance system evaluation report: The PHE Surveillance Standards within Surgical Site Infection Surveillance Service (3)

Other

One new surveillance protocol developed: Environmental surveillance for poliovirus in the United Kingdom to be published in the PHE web site (2).

5. Teaching activities

Lecture on "Introduction to surveillance in public health" for students of the Master in Immunology of the University College of London

The session was 45 minutes long and it took place in one of the seminar rooms of Public Health England (PHE) on the 27th of November 2014. Around 20 students of the Masters in Immunology of the University College of London (UCL) attended this session.

Instructional Design: This teaching activity was part of a course that is run every year by PHE in collaboration with UCL as part of the Masters curriculum. We obtained a list of the students with the academic background of each of them in order to adapt the level and contents of the session to their knowledge or field of interest. I used a power point presentation with interactive slides and many questions inserted on the slides to stimulate discussion and active participation.

Learning objectives: At the end of this exercise participants will be familiar with the purposes and uses of surveillance in public health, the different key surveillance concepts and types of surveillance. The students will be able to explain why and how surveillance is the corner stone of public health.

Evaluation: All students returned a completed evaluation form, using scores from 1 to 4 (1=very poor , not met, 2=poor/partially met, 3= average/ moderately met, 4 Good/mostly met, 5= very good fully met). The mean score of this activity was 4.2.

Supervisor(s): Ruth Ruggles

Two practical sessions on Epidemiology of Tuberculosis and Epidemiology of HIV and Sexual Transmitted Infections (STI) in the London School of Hygiene and Tropical Medicine (LSHTM)

The sessions were 1.5 hours long and took place in a classroom of the LSHTM on the 18th and 19th of May 2015.

The target audience were the students of the Masters in Immunology of the University College of London.

Instructional Design: This teaching activity was part of a course that is run every year by the LSHTM. I asked the participants to briefly explain to me their background in order to adapt the level and contents of the session to their knowledge or field of interest.

I used different exercises and case studies. The students were asked to organize themselves in groups of 5 and to discuss each question of the exercises or case studies in group. Then we all came back together to discuss the solutions to the exercises.

Learning objectives: At the end of this exercise participants will be familiar with different epidemiological concepts related to the epidemiology of TB and HIV/STIs (e.g.: birth cohorts, annual risk of infection, molecular epidemiology and tracing of infection, transmission probability, transmission risk factors). The students will be able to create and interpret birth cohort's graphs, calculate the annual risk of infection, the risk of not being infected after X episodes of sexual, and basically interpret molecular test result for the investigation of transmission chains

Evaluation: There was an evaluation done by the organizers of the LSHTM for the overall module. Only 11 students filled it in. The commentaries about the practical sessions were very positive.

Supervisor(s): Paul Fine

Session about Overview of disease determinants and public health response in the PHE training "Hitchhikers Guide to Epidemiology".

The session was 45 minutes long and took place in one of the seminars rooms of PHE on the 13th of May 2015. The target audience was around 20 PHE colleagues and some external people working in non-epidemiologist positions.

Instructional Design: This teaching activity was part of a module that is run every year by PHE. We obtained a list of the participants with their job position of each of them in order to adapt the level and contents of the session to their knowledge or field of interest.

I used a power point presentation with interactive slides and many questions inserted on the slides to stimulate discussion and active participation.

We organized the participants in groups of 5 or 6 for some short case studies about different scenarios and public health actions.

Learning objectives: At the end of this exercise participants will be familiar with the concepts of disease determinants and public health actions (e.g. infectious period, incubation period, attack rates, prophylaxis, etc.). After this session the participants will be able to think in terms of the triangle host, agent and environment.

Evaluation: All participants returned a completed evaluation form, using scores from 1 to 4 (1=very poor, not met, 2=poor/partially met, 3= average/ moderately met, 4 Good/mostly met, 5= very good fully met). The mean score of this activity was 4.3.

Supervisor(s): Ruth Ruggles

Session on Principles of surveillance in the "Public Health England (PHE) Introductory course on the epidemiology and surveillance of infectious diseases"

The session was 45 minutes long and took place in one of the seminars rooms of PHE on the 5th of October 2015. The target audience was around 20 newly arrived PHE colleagues working in different positions.

Instructional Design: This teaching activity was part of an introductory course that is run twice per year by PHE. We obtained a list of the participants with the job position of each of them in order to adapt the level and contents of the session to their knowledge or field of interest.

I used a power point presentation with interactive slides and many questions inserted on the slides to stimulate discussion and active participation.

Learning objectives: At the end of this exercise participants will be familiar with the purposes and uses of surveillance in public health, the different key surveillance concepts and types of surveillance. The students will be able to explain why and how surveillance is the corner stone of public health.

Evaluation: All participants returned a completed evaluation form, using scores from 1 to 4 (1=very poor, not met, 2=poor/partially met, 3= average/ moderately met, 4 Good/mostly met, 5= very good fully met). The mean score of this activity was 4.1.

Supervisor(s): Ruth Ruggles

Educational outcome: These different teaching activities in PHE helped me to get to know better the PHE surveillance systems. I identified some gaps in my knowledge about the different systems in place in PHE, which I addressed before the sessions and therefore I consolidated my knowledge about the concepts I taught. The teaching activities in LSHTM helped me to be exposed to a very high academic level of epidemiology with very experienced and knowledgeable students. It also helped me consolidate the knowledge about the concepts I was teaching

6. Other activities

Epidemiologist in the World Health Organization (WHO) Ebola response mission, Guinea 2015

The mission objective was to contribute to the control of the outbreak and prevention of further spread by breaking the cycle of transmission in the community and health care facilities through: reinforce of the epidemiologic surveillance system; establishment of a system for data management, storage and dissemination for decision making and action; and documentation and preparation of information products including daily situation reports.

By working in this mission, I consolidated my knowledge about the concepts of R0, incubation period and transmissibility of a disease in outbreak control. (See research section for more details)

Field epidemiologist with Epicentre-MSF Switzerland in a measles seroprevalence study, Katanga, DR Congo, 2016.

See research section.

On call duty for the Centre for Infectious Disease Surveillance and Control, Public Health England.

Health protection on call for the PHE national centre. This on call service is mostly used for other PHE colleagues or other health professionals seeking support or advice regarding public actions in communicable disease control. I had to provide advice (in collaboration with a PHE consultant) for these situations. By covering the on call rota I was exposed to a range of communicable diseases and subsequent public health actions, I learnt a lot about the different protocols. It also helped me to gain confidence on assuming responsibilities and providing advice to other highly qualified colleagues in complex situations.

7. EPIET/EUPHEM modules attended

1. *Introductory course , 29 September to 17 October 2014, Spetses, Greece*
2. *Outbreak investigation module, 8 to 12 December 2014, Berlin, Germany.*
3. *Multivariable analysis module, 23 to 27 March 2015, Vienna, Austria.*
4. *Project review module, 24 to 28 August 2015, Lisbon, Portugal.*
5. *Time series analysis module, 24 to 27 November 2015 , Utrecht, Holland.*
6. *Vaccinology module, 16 to 20 May 2016, Paris, France.*
7. *Rapid assessment and sampling module, 20 to 26 June 2016, Athens, Greece.*
8. *Project review module (PRM), 22 to 26 August 2016, Lisbon, Portugal.*

Supervisor's conclusions

Isidro has had an extremely productive two-year EPIET fellowship. He has achieved all of his EPIET training objectives, being very pro-active and engaged in all his projects. He has made important contributions to a wide range of areas including a large number of national and international outbreak investigations; strengthening of UK national polio surveillance and further our understanding of Enterovirus D68. He can be proud of what he has achieved.

Coordinator's conclusions

Isidro was involved in a wide range of public health relevant projects (including many outbreak investigations, research and surveillance projects and two international missions in complex emergency settings), undertook an impressive amount of work, and achieved a large amount of outputs. He was able to work independently and effectively, but also in a team, and delivered high quality work. He demonstrated a positive attitude towards scientific review and was always ready to accept constructive criticism. During his fellowship, Isidro managed to enhance his

capacities, improve considerably his epidemiological skills and has achieved a high level of competence in all the required domains. I believe that Isidro is committed to field epidemiology and has excellent professional skills for any epidemiological and public health related work, both at national and international level.

Personal conclusions of fellow

EPIET has been a very enriching experience professionally and personally. I did not have much experience in public health in a European institution setting. EPIET gave me the opportunity to be working in one of the best institutions in the world, with internationally recognized experts. PHE has taught me many aspects of what I consider the "gold standard" of the epidemiology in public health. Now I feel ready to work as an epidemiologist in high level institutions. EPIET has been a big professional and career leap for me.

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