



Fellowship summary report 15 August 2016

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Background

Pre-fellowship short bio

Before joining the Field Epidemiology Training Programme, I had been working for Public Health England since August 2006. I predominantly worked for the South East and London Field Epidemiology Services (SEaL FES) team where I had taken on a number of different roles, predominantly focussing on surveillance and outbreak response. I have also had the opportunity to work at a local level (prior to joining SEaL FES) and the national gastro-intestinal team during the Olympics 2012. Additionally I completed my Masters in Epidemiology part-time between 2009 and 2011.

FETP assignment

During FETP I have had the opportunity to work on a number of very different projects across the competencies. I was able to lead on the second largest VTEC outbreak in the UK and carry out an evaluation on the East Java Diphtheria Immunisation programme, combining my surveillance project with an international mission. In addition, my research projects have been very varied and allowed me to work with academia and other governmental bodies as well as PHE colleagues.

Fellowship projects

Outbreak(s)

1. National VTEC E.coli O157 PT8 VT1+2 outbreak

Introduction: In October 2014, Public Health England identified a cluster of Escherichia coli O157 PT8 (VTEC) cases sharing a Multiple Locus Variable-number Tandem Repeat Analysis (MLVA) profile. The aims of the investigation were to describe the extent of the outbreak; the dynamics of the population affected and identify the infection vehicle.

Methods: We conducted a case-control study (2 controls per case) using multivariable logistic regression to calculate adjusted odds ratios (aOR) and 95% confidence intervals (95%CI). Cases were defined as Great British residents with laboratory-confirmed VTEC with the outbreak strain, aged 18 or over. A consumer survey panel randomly recruited controls by emailing their members a survey link. PHE contacted cases first by phone and then email. We excluded cases and controls with history of travel within seven days of onset.

Results: 102 patients, including 89 primary cases, were identified as having the outbreak strain. Dates of onsets ranged between 1-30 October. 65% of cases were female with median age 49 years (range 2-92). We recruited 36 cases and 96 controls. 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 retailer A.

Discussion: This study demonstrates a strong epidemiological association between consumption of pre-packed salad and disease; however no microbiological testing was possible. It is necessary to work closer with industrial bodies ensuring timely trace-back exercises to identify likely sources and to implement control measures.

Tasks undertaken personally:

During this outbreak I was the lead epi investigator. I was initially responsible for putting together the daily situation reports and briefing notes. I developed and sent out the hypothesis generation questionnaire, before developing the protocol and questionnaire for the case control study. I carried out both the descriptive and analytical analysis, presented the results to the outbreak control team and compiled the final outbreak report.

Outputs

This outbreak has been presented as two oral presentations (5 Nations, 2015 and PHE Applied Epidemiology Conference, 2015) as well as two poster presentations (TEPHINET, 2015 and ESCAIDE, 2015).

Additionally it was also presented at the EPIET Outbreak module.

An outbreak report was uploaded onto the outbreak library and the peer review paper for publication has been submitted for review to Epidemiology & Infection.

2. Measles

In January to February 2015 a measles outbreak resulting in 13 confirmed measles cases was associated with three schools in Hounslow, west London. The first case of probable measles was reported to the North West London Health Protection Team (NWL HPT) on 29th January 2015. The case was a 14-year-old male attending a secondary school and resident in Hounslow. An outbreak investigation was commenced four days later when a further four linked cases of measles were confirmed. Epidemiological investigation revealed that the first notified case was not, in fact, the index case; he was a school contact of the index, whose symptom onset was on 16th January. The index case had contracted measles while in holiday in India and had returned to the UK on 6th January. Over the subsequent month a further ten epidemiologically linked cases of measles were notified in children resident in Hounslow, aged between 18-months and 15-years of age, making a total of 15 cases (13 confirmed, two possible). Eight contacts required exclusion from work/school for extended periods as health records suggested that they were unvaccinated against measles. The outbreak investigation identified a need for further efforts to ensure improved coverage of Measles, Mumps and Rubella (MMR) vaccination amongst children and young people in Hounslow.

Tasks undertaken personally:

Attended OCT teleconferences. Put together a line listing and carried out basic descriptive epidemiology and social network trees.

Outputs

An outbreak report of this incident was compiled by the North West London Health Protection Unit.

Surveillance project(s)

1. Evaluation of the diphtheria immunisation programme, East Java, Indonesia

Introduction: In 2012, an outbreak of diphtheria resulted in 941 cases and 37 deaths in the province of East Java, Indonesia. The vaccination coverage of three doses of diphtheria containing vaccine (DTP3) was estimated as 83% across Indonesia. As a result, Indonesia committed to meeting the Global Vaccine Action Plan 2015 target of 90% coverage of DTP3. Despite this, in 2014, the estimated coverage of DTP3 had fallen to 78%. Our evaluation aimed to assess whether data collection was effective in producing accurate vaccination coverage estimates and supported the vaccination programme in East Java. We provided recommendations for the improvement of data collection for the programme

Methods: Semi-structured interviews were undertaken with pre-selected public health professionals at provincial, district and village levels. The immunisation information system was described and evaluated against the following attributes: simplicity, acceptability and representativeness.

Results: Vaccines are administered to children at monthly clinics and recorded by the village midwife. Information is aggregated by midwives and entered onto a web-based immunisation system by district staff. There is no written guidance for this process. The proportion vaccinated is calculated using doses given divided by the expected number of surviving infants born that year. In 2014, 16 (42%) districts reported over 100% coverage of DTP3.

Discussion: We believe that targets are an acceptable motivational tool; however current data recording practices may lead to overestimation of childhood vaccination coverage. We recommend that guidance on data reporting is developed to ensure only appropriate target age-group vaccinations are included in numerator data.

Tasks undertaken personally:

During this study I provided input into the protocol and created a list of questions for which to conduct the interviews. I carried out interviews with district, regional and local staff in East Java and adapted my questions depending on previous answers. Using the information collected from the interviews and using the data available of the immunisation web system I presented an initial summary of findings to staff at the East Java provincial office and I compiled a surveillance evaluation report looking at a number of different attributes.

Outputs

A summary of findings was presented to the East Java Provincial office. A report was produced for the Global Health Fund. It was additionally presented as a poster at the 5 Nations Health Protection Conference, 2016 and the PHE Field Applied Epidemiology Conference, 2016.

Research

1. Effectiveness and immune correlates of protection induced by Live Attenuated Influenza Vaccine (LAIV/Fluenz TetraM) (Flu Immune)

Introduction: Live attenuated influenza vaccine (LAIV) is a quadrivalent, nasally administered vaccine recently introduced to the UK immunisation programme for children. A number of side-effects following LAIV have previously been identified including nasal congestion, weakness and headache. However, information within a school setting is limited. This study aimed to describe adverse effects experienced by schoolchildren within seven days of receiving LAIV.

Methods: A single LAIV vaccination was offered to all healthy students aged 10-16 years in two schools in England in October 2015. Participants were given a daily diary to record adverse effects for seven days post-vaccination.

Symptoms reported as starting before vaccination or after seven days were excluded. If only a start date was provided for a specific symptom, it was assumed that it lasted only that day.

Results: 235 children received LAIV. Of these, 193 (82.1%) completed diaries. Responses differed in the two schools (97.0% from school A vs 62.7% from school B, $p < 0.005$). No serious vaccine-associated adverse events (VAER) were reported. 142 (74%) reported one or more symptoms following vaccination, the most common being blocked nose (64.3%) tiredness (37.2%) and headache (24.1%).

Twenty-one children reported school absence, seeking healthcare or both in the 7 days following vaccination. Follow-up information was obtained on 17; ten reported self-limiting symptoms potentially associated with vaccination.

Discussion: Despite a high number of mild symptoms, no serious VAER were reported. This supports findings from previous studies that, despite mild flu-like symptoms, this is a safe vaccine.

Several participants reported school absence or seeking medical care. Interpretation is limited due to the lack of a control group.

Tasks undertaken personally:

I have carried out the epidemiological support for this study. I have been involved in finalising the protocol and attending the ethics committee, along with helping revise the protocol for the second year of the study. I designed the questionnaires and assisted with the baseline data collection at the two study sites and attended one of the vaccination days explaining the adverse effects diary to participants.

During the flu season I sent out weekly reminders for completion of the weekly questionnaires and dealt with questions from the parents. I also carried out analysis and provided feedback as needed.

I analysed and produced a report on the adverse effects data and collated and cleaned the baseline data and that form the first year of weekly questionnaires. I am in the process of carrying out some analysis on this data which is due to be compiled into a report.

Outputs

A report on the adverse effects following vaccination was circulated amongst the study team and an abstract was submitted for ESCAIDE. Unfortunately the abstract was rejected. A study report after one year will be produced; however there is still one year of the study still to run. It is likely that this study will be published in peer-review journals after the study is complete.

2. Identifying risk factors for diagnostic delay in TB patients and the impact of diagnostic delay on on-going transmission

Introduction: In 2014, tuberculosis (TB) incidence was 12.0 per 100,000 in England, one of the highest in Western Europe. One key action of the Collaborative TB Strategy for England 2015-2020 is to improve access to services and ensure early diagnosis.

The aim of this study is to identify risk factors associated with patients experiencing a delay of >4 months between symptom onset and start of treatment.

Methods: All TB cases notified to the Enhanced TB Surveillance (ETS) System in England, between 2012-2014 were included. Cases with no symptom onset or treatment start date, and those diagnosed post mortem were excluded. Descriptive and univariable analysis was carried out, followed by multivariable logistic regression.

Results: 21,863 TB cases were notified between 2012-2014; 17,046 were included in analysis (78.0%). Analysis demonstrated that men have lower odds of experiencing delays >4 months than females aOR 0.87 (95%CI 0.78-0.96), while time since entry to the UK was linearly correlated. Those entering the UK between 0-1 years aOR 0.58 (95%CI 0.48–0.70) to 5-9 years aOR 0.82 (95%CI 0.70–0.97) ago have lower odds of experiencing delays compared to those born in the UK. Those entering the UK 10+ years ago had no significant difference to the UK born population. No social risk factors were found to be associated with delay.

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Tasks undertaken personally:

I have carried out the whole of this study under the guidance from the TB surveillance team. I have been responsible for putting together the protocol and carrying out the univariate and multivariable analysis. I am now in the process of starting to draft the findings as a peer-review paper.

Outputs

This project is currently being drafted as a peer-reviewed journal paper.

3. Exploring the joint analysis of large routine data with integrated epidemiology and pathogen genomic datasets from outbreaks of GI pathogens

Introduction: Whole Genome Sequencing has increased outbreak detection and added to investigation. In parallel, extensive datasets are collected by industry which would aid the investigation of human disease. This project used expert review of outbreak cases studies to identify 1) priority goals to support the efficient integration of genomics and other datasets in incidents; 2) issues and barriers; 3) learning points from the reviewed outbreaks; and 4) examples that will support the motivation of wider partners to work together to establish data sharing priorities.

Methods: Outbreaks for case studies were selected to cover a range of different criteria, such as complexity, geographies, collaborative work and data issues. These were identified by literature review, review of a national outbreak database and contact with experts. Original investigators were contacted and a data extraction form was used to capture a summary of each outbreak. Lessons learned from each outbreak were collated and presented to an expert workshop.

Results: 15 case studies were identified, and lessons identified in the areas of alternative control methods, genome sequencing, population generic reference data and in 9 other areas.

Discussion: Genomic clusters appear to detect foodborne outbreaks with good specificity and can allow earlier detection if sequencing is rapid and small clusters are investigated. However, obtaining consistent basic case data nationally is a priority. Additionally routine sources of population exposure data may provide a valid alternative or compliment control data. Access needs to be established in advance so it can be obtained quickly in times of an outbreak.

Tasks undertaken personally:

This was a highly collaborative project which involved working with a small group of individuals and often sharing bits of tasks. Following discussions, I was responsible for putting together the methodology of the protocol as to how the different outbreaks should be selected. I assisted with the outbreak selection, including reviewing databases and discussing with key PHE staff. After the outbreaks had been selected, I compiled two of the case studies using available reports and discussions with the outbreak leads and also assisted in adding to a couple of other case studies and reviewing them. Additionally I was involved in the stakeholder day where a summary of our results was presented and issues discussed.

Outputs

1. A report has been produced for the Food Standards Agency.

Scientific communication

- Four posters, one at ESCAIDE 2015, one at TEPHINET 2015, one at 5 Nations 2016 and one at PHE Applied Epidemiology Conference 2016
- Two oral presentations, one at 5 Nations 2015 and one at PHE Applied Epidemiology Conference 2015
- 1 manuscripts drafted (and 1 in the process of being drafted), 1 manuscripts submitted, 0 manuscripts accepted and 0 manuscripts published.

Teaching experience

1. Lab4epi module

Two day FETP module aimed at introducing epidemiologists to common laboratory methods and interpreting the findings. Put together the agenda for the module and invited speakers. Ensured smooth running during the module and participated in a review of the feedback from the module.

2. Introductory course on the epidemiology and surveillance of Infectious Diseases

This is a 5-day training course carried out at Colindale 3 times per year aimed at a mixed audience (around 20 people) including microbiologists, SpRs and PHE staff on basic epidemiology and surveillance. One-hour Outbreak Investigation lecture (February 2015).

3. Reptile-acquired Salmonella lecture, Annual Zoonoses Symposium

Annual symposium looking at Zoonoses held in Cambridge. Audience consists of around 50 people from a mixture of disciplines including vets, microbiologists, EHOs and SpRs). 35 minute lecture on Reptile Acquired Salmonella (March 2015)

4. Reptile-acquired Salmonella lecture, West Midlands West Annual Study Day

Annual Study Day organised by West Midlands West Health Protection Team. Audience consisted of PHE Health Protection team staff, EHOs, SpRs and Local Authority staff. 25-minute lecture on Reptile Acquired Salmonella (March 2015)

5. Gastro-Intestinal Whole Genome Sequencing Case Study

Invited by the Gastrointestinal Surveillance team to participate in a practice run through of the case study prepared for their study day. Participated in a practice run through to the case study and offered feedback on how it could be improved.

International mission(s) [If applicable]

1. Title Evaluation of the diphtheria immunisation programme, East Java, Indonesia

See Surveillance Project

Other

- Carried out in-hours on-call duty doctor duties from Sept 2014 to Oct 2015.
- Attended the daily 9:15 meeting to discuss on-call issues
- Attended monthly duty doctor training and trainee sessions
- Presented my mission to Indonesia at a trainee session and at an EPIET module.

Next steps

- I will be starting with Camden and Islington Public Health Team as a Public Health Intelligence and Information Analyst in Sept/Oct 2016.

References - List of the publications and communications

Manuscripts

1. Sinclair C, Jenkins C, Warburton F, Adak GK, Harris JP. **Investigation of a national outbreak of STEC *Escherichia coli* O157 using online consumer panel control methods - Great Britain, October 2014.** *Epidemiology and Infection*. *Under review*.

Conferences

- Oral Presentations

1. Sinclair C, Harris J, Adak B. **Investigation of a large, complex national outbreak of VTEC *Escherichia coli* O157 PT8 associated with pre-packed salad - Great Britain, October 2014.** PHE Applied Epidemiology Conference; 18-19 March 2015; Warwick University, England 2015.
2. Sinclair C, Harris J, Adak B. **Investigation of a large, complex national outbreak of VTEC *Escherichia coli* O157 PT8 associated with pre-packed salad - Great Britain, October 2014.** 5 Nations Health Protection Conference; 18-20 May 2015; Edinburgh, Scotland 2015.

- Poster Presentations

1. Sinclair C, Harris J, Adak B. **Investigation of a large, complex national outbreak of VTEC *Escherichia coli* O157 PT8 associated with pre-packed salad - Great Britain, October 2014.** TEPHINET, September 2015
2. Sinclair C, Harris J, Adak B. **Investigation of a national outbreak of VTEC *Escherichia coli* O157 using online consumer panel control methods - Great Britain, October 2014.** ESCAIDE, November 2015
3. Sinclair C, Waite T, Hughes G, Bracebridge S. **A systematic evaluation of the diphtheria immunisation programme in East Java, Indonesia, June 2015,** FES Applied Epi Conference 2016
4. Sinclair C, Waite T, Hughes G, Bracebridge S. **A systematic evaluation of the diphtheria immunisation programme in East Java, Indonesia, June 2015,** 5 Nations Health Protection Conference; 9-11 May 2015; Cardiff, Wales 2016