FELLOWSHIP REPORT

Summary of work activities

Timothée Dub
Intervention Epidemiology path (EPIET)
Cohort 2017

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 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 listing the theoretical modules attended and the 23-month training. Additionally, if all training objectives have been met, they receive a diploma.

Stockholm, September 2018

- 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.

Pre-fellowship short biography

Prior to EPIET, Timothée Dub was a Public Health medical resident based in Paris. He had been working in several clinical research and epidemiology departments on different topics such as the association between early infectious exposures and childhood lymphomas, Guillain-Barré syndrome and birth defects following Zika virus infection in French Polynesia and natural history of human papillomavirus among HIV-positive women in Thailand.

Fellowship assignment: Intervention Epidemiology path (EPIET)

On 11 September 2017, Timothée Dub started his EPIET fellowship at the National Institute for Health and Welfare (THL), Helsinki, Finland, under the supervision of Dr Outi Lyytikäinen. This report summarizes the work performed during the fellowship.

Methods

This portfolio demonstrates the competencies acquired during the ECDC Fellowship, EPIET path, by working on various projects, activities 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. The portfolio presents a summary of all work activities conducted by the fellow, unless prohibited due to confidentiality regulations.

Results

The objectives of these core competency domains were achieved partly through project or activity work and partly through participation in the training modules. Results are presented in accordance with the EPIET core competencies, as set out in the EPIET scientific guide[1].

Fellowship projects

1. Surveillance

Improving the surveillance of antimicrobial consumption in Finland: Producing a first detailed report of antimicrobial consumption

Antimicrobial resistance is estimated to be responsible, worldwide, for 700 000 deaths per year which might rise to 10 000 000 per year by 2050 unless actions are taken to tackle this issue. As there is evidence that emergence of resistant microbes is partly driven by a human population's exposure to antimicrobial agents, the Finnish national action plan on antimicrobial resistance 2017-2021 includes improving surveillance of antimicrobial use.

The aim of this project was to provide a detailed report of antimicrobial consumption, as a first step towards improved surveillance. We focused on antibacterials for systemic use, antimycotics and antifungals for systemic use and specific antimicrobials used for the treatment of patients infected with multidrug-resistant bacteria. Yearly consumption data was transmitted from the Finnish medicine agency.

[1] European Centre for Disease Prevention and Control. European public health training programme. Stockholm: ECDC; 2013. Available from: http://ecdc.europa.eu/en/publications/Publications/.pdf

We calculated Defined Daily Doses (DDD) per Anatomical Therapeutic Classification (ATC) group per 1000 inhabitants per day both on a national level and per hospital district. We conducted descriptive analysis and analysed the evolution of consumption over time.

From 2010 to 2017, total amount of antibacterials for systemic use consumed in Finland decreased significantly from 21.85 to 17.35 DDD per 1000 inhabitants per day. Nationally, a significant decrease was also observed in all ATC subgroups. The terbinafine group was by far the largest among antifungals and antimycotics for systemic use and in 2017, accounted for 78% of the total use of antifungals and antimycotics. The levels of consumption were heterogeneous between hospital districts, with a two-fold range on antifungals and antimycotics consumption and specific antimicrobials used for the treatment of patients infected with multidrug-resistant bacteria. This first detailed report on antimicrobial consumption on a hospital district level was the first step towards a better understanding of the regional differences regarding antimicrobial use. Hospital districts authorities will be using it to monitor trends in their antimicrobial consumption. Additionally, now that data has been processed; it will be used in several research projects on antimicrobial consumption and emergence of resistance.

Role: Timothée wrote the protocol, managed data obtained from the Finnish medicine agency, conducted analysis of consumption levels and trends nationwide and per hospital districts, wrote an R script in order to produce semi-automated annual reports. Reports were produced for years 2016 and 2017 before the task was transferred to Veronica Cristea (EPIET fellow Cohort 2018) under Timothée's guidance. Additionally, once data had been properly managed and could be used for other purposes, it was used in an ecological study on the association between consumption levels and the increase of antimicrobial resistance which was presented as a poster at ESCAIDE 2018.

Deliverables:

- Dub T, Sarvikivi E, Möttönen T, Voipio T, Ollgren J, Lyytikäinen O. Improving the surveillance of antimicrobial consumption in Finland: Producing a first detailed report of antimicrobial consumption research protocol
- Dub T, Sarvikivi E, Möttönen T, Voipio T, Ollgren J, Lyytikäinen O. Antimicrobial consumption in Finland, 2010-2016.
- Dub T, Sarvikivi E, Möttönen T, Voipio T, Ollgren J, Lyytikäinen O. Antimicrobial consumption in Finland, 2010-2017.

Supervisors: Outi Lyytikäinen, Emmi Sarvikivi

Prevalence, incidence, knowledge of status and associated risk factors of Human Immunodeficiency Virus (HIV), and Hepatitis C (HCV) among Finnish persons who inject drugs(PWID).

In Finland, where the estimated number of people who inject drugs (PWID) was 14 500 – 19 000 in 2005, low threshold service centres operating in 48 municipalities have the following objectives among others: obtain contact with injectors, reduce risk behaviours through information on drug-related diseases and risks and needle exchange, refer PWID to treatment and test them for infectious diseases (HIV, HCV, hepatitis B). PWID specific surveillance of blood borne virus is not implemented in Finland.

The aim of this study was to gather information on HIV and HCV prevalence and associated risk behaviours among PWID in Finland in order to inform the development of a surveillance and prevention programme. The results will be used to help prevent the spread of infectious diseases and increase development of the low threshold service centres.

Role: Timothée wrote the protocol, participated in the development of the questionnaire, created a data entry form accordingly and visited several low threshold service centres across Finland. Recruitment is still ongoing and Timothée will participate to data-analysis and drafting of a manuscript as he will be staying at THL for the end of year 2019, once his fellowship is over.

Deliverables:

- Dub T, Toikkanen S, Liitsola K, Brummer-Korvenkontio H. Prevalence, incidence, knowledge of status and associated risk factors of Human Immunodeficiency Virus (HIV), and Hepatitis C (HCV) among Finnish persons who inject drugs (PWID) protocol.

Supervisors: Henrikki Brummer-Korvenkontio, Salla Toikkanen

Norovirus virological surveillance in Finland, 2014-2017

In Finland, annual incidence of norovirus infections, as monitored by the National Infectious Disease Register (NIDR) ranged between 25 and 50 cases per 100 000 inhabitants per year during 2010-2016. In 2016, out of 89 suspected gastroenteritis outbreaks reported to RYMY, the national food and waterborne outbreak notification system, norovirus was found to be the responsible pathogen in nearly half of them.

Our aim was to evaluate virological surveillance of norovirus in Finland. Characteristics evaluated were: completeness of genotyping in outbreaks and age, sex and regional representativeness of genotyping

Finally, we wanted to compare trends in NIDR notifications and visits linked to gastrointestinal symptoms to Finnish healthcare centres and assess whether the occurrence of norovirus outbreaks reported to RYMY could explain the increased frequency of healthcare centre visits and norovirus diagnosis in the NIDR.

Role: Timothée wrote the protocol, contributed to data-management and is currently proceeding to statistical analysis and the drafting of a report.

Deliverables:

- Dub T, Husko S, al-Hello H, Ollgren J, Rimhanen-Finne R, Lyytikäinen O. Norovirus virological surveillance in Finland, 2014–2017. Surveillance evaluation protocol

Supervisor: Outi Lyytikäinen

2. Outbreak investigations

Clostridium perfringens *gastroenteritis outbreak following a wedding reception in Kuopio, Finland, July 2018.*

An unexpected number of gastroenteritis following a wedding dinner on July 21st 2018 was notified to the Kuopio Environmental Health Unit on July 23rd. An outbreak investigation was conducted in collaboration with the National Institute of Health and Welfare.

A detailed list of food items served was obtained. All the 92 wedding participants were e-mailed a questionnaire on potential symptoms and food items consumed while leftovers from the buffet were tested. A case was defined as a wedding participant who had presented at least one gastro-intestinal symptom, such as diarrhoea, abdominal pain, nausea and vomiting following the event.

Forty-six eligible participants answered the survey, including 36 cases (Attack rate: 78%). Median incubation period was 16.0 hours [Range: 3.0 – 41.0]. Wedding participants who had eaten pork fillet were more likely to meet the case definition (Relative Risk [95% confidence interval]: 3.2 [0.6-17.7], p-value=0.04). *Clostridium perfringens* was detected in the pork fillet in high concentration along with *Staphylococcus aureus* and *Bacillus cereus*. *Clostridium perfringens* was also found in 4 stool samples out of 5 collected and matched the strains obtained from food leftovers.

Our results strongly indicate that the pork fillet served at this wedding was contaminated by *Clostridium perfringens*, probably due to improper cooling of the meat before it was served cold.

Role: In cooperation with Leif Lakoma, infectious diseases specialist, Timothée's role was to conduct data management and statistical analysis as data was being collected by the local infectious diseases unit in Kuopio, put findings in perspective with microbiological investigations conducted in parallel: diagnosis and phylogenic analysis, performed locally and at THL, respectively. Additionally Timothée wrote an outbreak investigation report shared with the Kuopio outbreak investigation team.

Deliverables:

- Dub T, Lakoma L, Kervinen A, Karinen P, Sane J, Lyytikäinen O. *Clostridium perfringens* gastroenteritis outbreak following a wedding reception in Kuopio, Finland, July 2018.

Supervisor: Jussi Sane

Salmonella gastroenteritis outbreak among customers of a snack-bar restaurant in Maalahti, Finland, July 2018.

On July 20th 2018, several cases of gastroenteritis following a meal in a snack-bar restaurant in Maalahti (Ostrobothnia region, Finland) were notified to the West Coast Environmental Health Unit. An outbreak investigation was carried out. The local Health authority led the outbreak investigation, while National institute of Health and Welfare provided assistance with statistical analysis and microbiological analyses.

A case was defined as a customer of the snack-bar restaurant who had had a meal either on 12th, 13th or 14th of July 2018 and presented at least one gastro-intestinal symptom, such as diarrhoea, abdominal pain, nausea and vomiting following exposure.

A total of 130 self-administered questionnaires were distributed to potential customers and 50 responses collected (38% response rate). Nineteen of the 50 respondents fulfilled the case definition (Attack rate: 38%). Median incubation period was 52 hours [interquartile range: 32.0-81.5]. Salmonella Newport was identified in 10 out of 11 stool samples collected from cases. Descriptive analysis showed that exposure had occurred on Friday 13th July. The most common exposures among sick patients were eating meat stew (95%), cucumber (68%), iceberg salad (58%) and tomatoes (58%), however univariate statistical analysis did not show any significant association between food exposures and the outcome,. We were therefore not able to determine which food item would have been the outbreak vehicle, or if cross contamination could have occurred between different food items.

Role: Request for assistance in investigating this outbreak came quite late: Data had already been collected and the local investigation team had difficulties interpreting results of statistical analysis conducted using EpiInfo, hence, Timothée's contribution, here, was limited to performing statistical analysis in order to confirm their findings and produce an outbreak investigation report.

Deliverables:

- Dub T, Huusko S, Rimhanen-Finne R, Sane J, Lyytikäinen O. *Salmonella newport* gastroenteritis outbreak among customers of a snack-bar restaurant in Maalahti, Finland, July 2018.

Supervisor: Ruska Rimhanen-Finne

Measles transmission worst-case scenario

On November 28th 2018, THL was informed of a measles case in a pre-school child returning from a family trip to the Middle East. It occurred in Northern Ostrobothnia, where 2* Measles Mumps Rubella (MMR) coverage approximates 75%, an insufficient level to reach herd immunity. As this child had been attending several social gatherings during the period of communicability, active contact tracing, case-finding and control measures were conducted by local healthcare centres. Two probable secondary cases (siblings of index case) were reported to THL, some time after disease onset.

Using contact tracing and control measures data, we classified contacts in three categories: i. contacts at high-risk: i.e. without history of immunisation and immunoglobulins pre-emptive treatment (n=10), ii. intermediate-risk (n=37), i.e. with only one MMR injection documented, and iii. low-risk (n=88) of transmission. We developed a worst-case transmission scenario for internal use, in order to assess human resource needs over the holiday period.

Role: Timothée created a line listing template in collaboration with Salla Toikkanen. It was used to collect systematic data by local healthcare centres participating in contact tracing and implementation of control measures. Data were transmitted to THL for follow-up. As several contacts refused immunisation or IgG therapy and only two secondary cases were reported to THL long after disease onset, Timothée developed a worst-case transmission scenario for internal use.

Supervisors: Jussi Sane, Mia Kontio

Investigation of an increase of pertussis in Finland 2015-2018: possible artefact due to seroresponse to vaccination?

In Finland, from 2015 to 2018, pertussis incidence increased from three to nine cases per 100 000. A large proportion of cases during this period occurred among 0-4 and 10-14 year olds, age groups eligible for pertussis vaccination in the national immunisation programme. We investigated whether the increase in reported cases was real or could potentially be explained by false positives.

We extracted laboratory-confirmed cases data from the National Infectious Diseases Registry (NIDR) and linked them to individual records from the National Vaccine Register (NVR) which was implemented since 2009. We described microbiological diagnosis methods (MDM) to identify potential false positive cases, i.e. patients diagnosed using IgG serology within a year of immunisation.

During 2015-2018, out of 1467 pertussis cases notified to NIDR, 326 were born from 2009 onwards. Overall, 141/1467 (10%) cases had received pertussis containing vaccine within a year prior to diagnosis confirmed with IgG serology, including 103/326 (32%) cases born since 2009. Additionally, among 0-4 year olds, as many as four in ten cases (94/225) might have been due to serological response following routine immunisation. The proportion of potential false positives remained stable over time, ranging from 12/165 (7%) initially to 46/469 (10%) in 2018.

False positives contributed to the amount of pertussis cases seen in Finland, but cannot entirely account for the recent increase. PCR should be considered as preferred MDM in children aged 0-4 years, likely to have been immunised recently. This recommendation is now being implemented as part of the guidance of the reference centre to the laboratories nationally. Additionally, in the future, clinical data from recently vaccinated cases should be reviewed in order to confirm pertussis diagnosis and improve the quality of the routine surveillance data.

Role: Timothée wrote the protocol, conducted records linkage, proceeded to data management and statistical analyse routine surveillance, made several presentations of this project including a poster presentation at ESCAIDE 2019, on site presentation at the THL NITAG meeting, and drafted a scientific paper submitted during summer 2019.

Deliverables:

- Dub T, Sane J, Mertsola J, Möttönen T, Sundman J, Nohynek H. Increase of pertussis in Finland 2015-2018: Contribution of potential false positives? Poster presentation at ESCAIDE 2019, November 27th-29th 2019, Stockholm, Sweden.

Supervisor: Jussi Sane, Hanna Nohynek

3. Applied epidemiology research

Spatial and temporal distribution of tick borne encephalitis in Finland from 2007 to 2017

Tick-borne encephalitis (TBE) is an endemic infection of public health importance in Finland. To inform prevention, we analysed emerging trends in TBE and investigated the effects of ecological factors.

We obtained data on serologically confirmed TBE domestic cases during 2007-2017 from the National Infectious Diseases Register. Cases with missing place of exposure or sampling date were excluded from the analysis. We collected weather data (minimum, mean and maximum temperatures) from the US National Oceanic and Atmospheric Administration. We obtained yearly number of mammals hunted (moose, red foxes, European and mountain hares, white-tailed, fallow and roe deer) per game management area from the Natural Resources Institute Finland: a proxy for the density of known TBE hosts. We performed time-series analysis using multilevel mixed-effects negative binomial regression with stepwise forward selection and time lags on weather and animal parameters (per 100 units), adding a random effect on game management areas to assess ecological factors' effects on TBE incidence. Statistical significance was considered at 5% level.

From 2007 to 2017, 395 out of 460 cases were reported with known place of exposure and date of sampling. Median yearly number of cases was 28 [IQR: 20-50]. Overall, TBE incidence increased yearly by 15%, with regional variations. Analysis of weather data showed no significant association. Adjusting for minimum temperature and other animal density, our final model showed that TBE incidence was negatively associated with roe-deer density (IRR=0.94 [0.88-1.00]) and positively associated with white-tailed deer density (IRR=1.03 [1.01-1.07]).

Our results suggest that variation in host animal density, including white-tailed deer, should be taken into account when assessing TBE risks, forecasting future trends, and designing interventions.

Role: Timothée wrote the protocol, managed case, weather and hunting data, performed time series analysis, submitted an abstract to ESCAIDE 2018 (preliminary analysis: rejected) and 2019 (final analysis: rejected), made a presentation to a general audience and wrote a manuscript to be submitted to a peer-review journal.

Deliverables:

- Dub T, Sane J, Spatial and temporal distribution of tick borne encephalitis in Finland from 2007 to 2017. Research protocol

- Dub T, Ollgren J, Huusko S, Turtiainen P, Sane J. Trends in the incidence of Tick-borne Encephalitis in Finland, 2007-2017. Abstract submitted to ESCAIDE 2018 and rejected
- Dub T, Ollgren J, Huusko S, Uusitalo R, Siljander M, Sane J. Ecological drivers of Tick-borne Encephalitis epidemiology in Finland, 2007-2017. Abstract submitted to ESCAIDE 2019 and rejected
- Dub T. Ecological drivers of tick-borne encephalitis trends, Finland 2017-2017. Reflective note on an oral presentation to a lay audience at French scientific coffee, April 11th 2019, Helsinki, Finland

Supervisor: Jussi Sane

Ecological study on the association between human antibacterial consumption and incidence of Extended Spectrum β Lactamase-producing Escherichia coli and Clostridium difficile infections in Finland

In Finland, during 2010-2016, incidence of invasive Extended Spectrum β Lactamase-producing *Escherichia coli* (ESBL-*E. coli*) infections significantly increased from 0.48 to 0.85 cases per 1000. *Clostridium difficile* (C. *difficile*) remained stable nationwide, but with major regional variation (0.32-2.10 cases per 1000). As human antibacterial consumption influences emergence of antimicrobial resistance, we investigated whether it was associated with their incidence.

We obtained wholesale data from 2010-2016 on number of packages by products from the Finnish Medicine Agency; and data on ESBL-*E. coli* and *C. difficile* infections from the National Infectious Disease Register. We classified products according to their anatomical therapeutic classification (ATC) and calculated annual Defined Daily Dose (DDD) per day per 1000 inhabitants, nationally and regionally (n=21). We assessed consumption trends over time trough linear regression using years as explanatory and annual antibacterial consumption as dependent variables and looked for correlations between consumption and incidence of ESBL-*E. coli* and *C. difficile* infections.

Nationally, consumption of antibacterials for systemic use (ATC code J01) significantly decreased from 21.9 to 19.1 DDD per day per 1000 inhabitants during 2010-2016 (p-value< 0.05) and in 17 regions out of 21. We found a negative correlation between annual consumption of antibacterials for systemic use, and ESBL *E. coli* incidence: r [$CI_{95\%}$] = -0.48 [-0.61 - -0.32] and no correlation with *C. difficile*: r [$CI_{95\%}$] = 0.00 [-0.19 - 0.18].

Antibacterial consumption was surprisingly negatively correlated to ESBL-*E. coli* infections and did not explain in itself the incidence of *C. difficile*. This was an ecological study in which associations between consumption and incidence were investigated at a regional level. Links between individual-level actual use of antibacterials both, in the community and in-hospital, along with other factors which remain to be identified, and the occurrence of these infections require further investigation.

Role: Timothée extracted data on ESBL-*E. coli* and *C. difficile* infections from the National Infectious Diseases Register and combined it with data obtained from his project on antimicrobial consumption in Finland, conducted statistical analysis and made a poster presentation at ESCAIDE 2018.

Deliverables:

- Dub T, Sarvikivi E, Möttönen T, Voipio T, Ollgren J, Lyytikäinen O. No association between human antibacterial consumption and incidence of Extended Spectrum β Lactamase-producing Escherichia coli and Clostridium difficile infections in Finland: Findings from an ecological study: poster presentation at ESCAIDE 2018, November 21st-23rd 2018, Saint-Julian, Malta

Supervisor: Outi Lyytikäinen

Healthcare workers immunisation recommendations in the Nordic countries

Healthcare workers (HCWs) are at higher risk of both exposure to and transmission of infectious diseases. Two European Union (EU) directives (2010/32/EU and 2000/54/EC) state that employers are responsible for assessing employees' exposure to occupational infectious hazard and for offering immunisation, accordingly. Our aims were to assess: 1) current policy for immunisation of HCWs, and 2) the availability of vaccine coverage data for HCWs, in the Nordic countries.

We surveyed national vaccination experts in Denmark, Finland, Iceland, Norway and Sweden, and Swedish county medical officers, due to decentralized organisation. We used a self-administered structured questionnaire on diseases and HCW categories covered by the recommendation and availability of coverage data. The surveyed experts validated these results.

All national experts (n=7) and 81% (17/21) of the Swedish county medical officers responded. EU member states had transposed the European directives into national law, while Norway and Iceland had similar legislation. There were national immunisation recommendations in Finland, Iceland and Norway, national guidelines in Denmark, and regional recommendations in 15 out of 17 responding Swedish counties. Hepatitis B and pertussis immunisation were recommended in all countries where national guidelines/recommendations existed and in 13 and 5 Swedish counties, respectively. Measles immunisation was recommended in Iceland, Norway and Finland and 14 Swedish counties. No coverage data were available for HCWs at a national or sub-national level except for two Swedish counties and ad-hoc hospital surveys elsewhere.

Recommendations on HCWs immunisation differed across Nordic countries. No country systematically measured uptake of HCW immunisation programmes. This lack of data hampers assessment of the existing recommendations, and any future interventions to improve uptake in this group.

Role: Timothée designed the protocol, wrote the questionnaire and discussed the answers with the surveyed experts. Additionally, he gave an oral presentation at the Nordic Vaccine meeting 2018 and poster presentation at ESCAIDE 2019 and wrote a scientific paper summarising the findings to be submitted to Eurosurveillance as a perspective paper once the review among the interviewees has been completed in September 2019.

Deliverables:

- Dub T, Nohynek H. Healthcare workers vaccination in the Nordic countries: Assessment of the existing recommendations and their implementation. Oral presentation at Nordic Vaccine meeting, 14th-15th June 2018, Helsinki, Finland
- Dub T, Søborg B, Andersen P, Nøkleby H, Lindstrand A, Carlsson R-M, et al. Immunisation of healthcare workers in the Nordic countries: Differences in policy and practice and a lack of surveillance. Poster presentation at ESCAIDE 2019, November 27th-29th 2019, Stockholm, Sweden

Supervisor: Hanna Nohynek

4. Communication

Publications

Manuscripts submitted to peer reviewed journals (in review process)

1. Dub T, Sane J, Mertsola J, Möttönen T, Sundman J, Nohynek H. Increase of pertussis in Finland 2015-2018: possible artifact due to seroresponse to vaccination? Submitted to Eurosurveillance
2. Dub T, Søborg B, Andersen PH, Gudnason T, Nøkleby H, Lindstrand A, Carlsson R-M, Nohynek H. Immunisation of healthcare workers in the Nordic countries: Variation in recommendations and practices and a lack of assessment. Submitted to Eurosurveillance
3. Dub T, Ollgren J, Huusko S, Uusitalo R, Siljander M, Vapalahti O, Sane J. Game animal density, climate and Tick-borne Encephalitis in Finland, 2007-2017: A time-series analysis. Submitted to Emerging Infectious Diseases

Reports

1. Dub T, Sarvikivi E, Möttönen T, Voipio T, Ollgren J, Lyytikäinen O. Antimicrobial consumption in Finland, 2010-2016.
2. Dub T, Sarvikivi E, Möttönen T, Voipio T, Ollgren J, Lyytikäinen O. Antimicrobial consumption in Finland, 2010-2017.
3. Dub T, Lakoma L, Kervinen A, Karinen P, Sane J, Lyytikäinen O. Clostridium perfringens gastroenteritis outbreak following a wedding reception in Kuopio, Finland, July 2018.
4. Dub T, Huusko S, Rimhanen-Finne R, Sane J, Lyytikäinen O. Salmonella gastroenteritis outbreak among customers of a snack-bar restaurant in Maalahti, Finland, July 2018.
5. Dub T, Lakoma L, Sane J, Nohynek H. Pertussis in the Helsinki & Uusimaa hospital district, 2016

Conference presentations

- Dub T, Nohynek H. Healthcare workers vaccination in the Nordic countries: Assessment of the existing recommendations and their implementation. Oral presentation at Nordic Vaccine meeting, 14th-15th June 2018, Helsinki, Finland

- Dub T, Sarvikivi E, Möttönen T, Voipio T, Ollgren J, Lyytikäinen O. No association between human antibacterial consumption and incidence of Extended Spectrum β Lactamase-producing Escherichia coli and Clostridium difficile infections in Finland: Findings from an ecological study: poster presentation at ESCAIDE 2018, November 21st-23rd 2018, Saint-Julian, Malta

- Dub T, Søborg B, Andersen P, Nøkleby H, Lindstrand A, Carlsson R-M, et al. Immunisation of healthcare workers in the Nordic countries: Differences in policy and practice and a lack of surveillance. Poster presentation at ESCAIDE 2019, November 27th-29th 2019, Stockholm, Sweden: **accepted**
- Dub T, Sane J, Mertsola J, Möttönen T, Sundman J, Nohynek H. Increase of pertussis in Finland 2015-2018: Contribution of potential false positives? Poster presentation at ESCAIDE 2019, November 27th-29th 2019, Stockholm, Sweden: **accepted**

Other presentations

1. Dub T. Improving the surveillance of antimicrobial consumption in Finland: Producing a first detailed report of antimicrobial consumption in Finland. Oral presentation at Nordic Mini Project Review 2018, March 5th – 6th 2018, Oslo, Norway

2. Dub T. Spatial and temporal distribution of tick borne encephalitis in Finland from 2007 to 2017. Oral presentation at Nordic Mini Project Review 2018, March 5th – 6th 2018, Oslo, Norway

3. Dub T. Norovirus surveillance project, Finland 2014-2017. Oral presentation at Nordic Mini Project Review 2019, March 11th-12t h 2019, Copenhagen, Denmark

4. Dub T. Ecological drivers of tick-borne encephalitis trends, Finland 2017-2017. Oral presentation at Nordic Mini Project Review 2019, March 11th-12t h 2019, Copenhagen, Denmark

5. Dub T. Ecological drivers of tick-borne encephalitis trends, Finland 2017-2017. Oral presentation to a lay audience at French scientific coffee, April 11th 2019, Helsinki, Finland

6. Dub T, Sane J, Mertsola J, Möttönen T, Sundman J, Nohynek H. Increase of pertussis in Finland 2015-2018: Contribution of potential false positives? Oral presentation at a national workshop on pertussis diagnosis, June 3rd 2019, Turku, Finland

7. Dub T, Sane J, Mertsola J, Möttönen T, Sundman J, Nohynek H. Increase of pertussis in Finland 2015-2018: Contribution of potential false positives? Oral presentation to Finnish National Immunization Technical Advisory Group, June 11th 2019, Helsinki, Finland

8. Dub T. Pertussis trends in Finland 2015-2018: Interpreting surveillance findings in light of the immunisation programme. Oral presentation at EPIET vaccinology module, June 24th-28th 2019, Rome, Italy

Other

1. Dub T, Prattingerová J, van Beek J. Essentials of Infectious Disease Epidemiology School of Health Sciences, university of Tampere, Finland, 22-26 January 2018. Reflective note

2. Dub T, Prattingerová J, van Beek J. Outbreak investigation day Statistics and epidemiology module Global Development and Management in Health Care masters programme Laurea University of Applied Sciences, Vantaa, Finland, 6th April 2018. Reflective note

3. Dub T. Ecological drivers of tick-borne encephalitis trends, Finland 2017-2017, Café scientifique, Institut Français de Finlande, April 11th 2019. Scientific presentation to a lay audience reflective note

4. Dub T, Igloi Z, Reh L, Donachie A. ECDC fellowship 2018 fellow satisfaction survey.

5. Dub T. Outbreak investigation related activites Reflective note 2017-2019.

5. Teaching and pedagogy

Essentials of Infectious Disease Epidemiology

- Training objectives:
    - Surveillance
        - Understand the role of the laboratory in public health surveillance
        - Identify the type of specimen to take along with the role of non-human-samples in Salmonellosis investigation
    - Outbreak investigation
        - Describe the steps in an outbreak investigation
        - Develop a case definition in the context of an outbreak investigation
        - Construct and interpret an epidemic curve and calculate and interpret an attack rate
        - Combine epidemiological and laboratory data to formulate conclusions during an investigation.
    - Methodology
        - Choose a relevant study design depending on the research question, exposure and outcome studied.
        - Compare and contrast case-control and cohort approach in analytical epidemiology
        - Define an appropriate cohort for a cohort study
        - Choose an appropriate control group for a case control study
        - Calculate and interpret relative risks and odds ratio
        - Insights in difficulties in the field during an outbreak situation
- Target audience: University of Tampere, School of Health sciences PhD students

Reflection

Timothée prepared and gave a lecture on study designs and basic statistics used in outbreak investigation, facilitated several case studies in small groups and ran a morning recap briefing in order to establish that learning outcomes from the previous days had been properly achieved by all participants. During this teaching assignment, Timothée learnt how to deliver a lecture and facilitate case-studies interactively by initiating discussions between participants

The similar amount of time spent on practical exercises versus theoretical lectures combination worked very well and allowed students to improve their theoretical knowledge and simultaneously use what they had just learnt.

The screening of the movie "Outbreak" (Wolfgang Petersen, 1995) was a good opportunity for students to point out what they think should or should not have been conducted in a real setting, including the intrication of microbiology and epidemiology, the steps of an outbreak investigation, the implementation of control measures and risk communication to the general public.

Discussion between fellow-facilitators and supervisor pointed out that one of the case study (botulism in Argentina) might have been too easy compared to the other ones conducted during the course. Replacing it with a waterborne outbreak case study was suggested.

Two types of evaluations were conducted: a daily informal wrap-up and discussion with students followed by an extensive debriefing with Ralf Reintjes and Pekka Nuorti (head of the doctoral programme were conducted to gather feedback and discuss how to the training over the next days while a feedback was also organised by the University of Tampere. Six students out of seven answered to this evaluation. On a scale from 1 (disagree) to 5 (agree), they considered that learning objectives of the course were considered as achieved (Mean: 4.3) and that it was properly supported by the case studies and group works (Mean: 4.7). The one week course was given a mean note a 4.0 over 5.0.

Outbreak investigation day- Statistics and epidemiology module

- Training objectives:
    - Describe the steps in an outbreak investigate
    - Develop a case definition in the context of an outbreak investigation
    - Construct and interpret an epidemic curve
    - Choose an appropriate control group for a case control study
    - Calculate and interpret an odds ratio
    - Define an appropriate cohort for a cohort study
    - Calculate and interpret an attack rate
    - Compare and contrast case-control and cohort approach in analytical epidemiology
    - Adapt the steps of an outbreak investigation to a healthcare setting
    - Insights in difficulties in the field during an outbreak situation.
- Target audience: Laurea university of applied sciences, global development and management in healthcare masters programme student

Reflection

Timothée prepared and gave a lecture on study designs and basic statistics used in outbreak investigation and facilitated a case study. This was a good opportunity to adapt a lecture he had already given to a different audience with lower skills in epidemiology and improve Timothée's confidence in facilitating case-studies.

As participants required more practice, more practical examples could have been added, such as calculation of attack rates, relative risks and odds ratios to the lectures. Students and facilitators agreed that a day might have been to short and that it could be interesting if fellows were invited again to cover this part of their epidemiology and statistics module that another time slot is assigned to this topic. This had already been mentioned the previous year when Jana Prattingerová and Janko van Beek (cohort 2016 fellows) had participated to this teaching activity.

The 1-page evaluation form fellows had prepared was returned by 21/22 students. When asked about their level of experience in outbreak investigation, 50% of respondents knew nothing about it or had never performed it, while 35% were aware from some practices. Only two students (9,5%) found the content of the course too advanced, while 19 (90,5%) others felt it was about right Most students (68,4%) felt the mix of lectures and group work was appropriate, but 5 students would have appreciated to spend more time on the case study we had prepared. The learning outcome felt mostly completed for 67% of students and fully completed for 33% of participants. Students were all either probably (30%) or definitively (90%) sure to apply in the future what they had learnt.

Basics of Vaccine Preventable Diseases epidemiology for EUPHEMs

- Training objectives: To acquire knowledge of the main concepts of VPD and vaccine epidemiology
    - Reproductive number
    - Herd immunity
    - Vaccine efficacy versus effectiveness
        - Vaccine effectiveness calculation methods
    - Vaccine coverage
        - Administrative methods
        - Survey methods
    - Vaccine failure
- Target audience: EUPHEM fellows attending Project Review Module 2018

Reflection

Using materials from several lectures he had received during the vaccinology module, Timothée prepared and gave a presentation summarising the essentials of VPD epidemiology including some practical exercises and discussions as to which methods might be the most suitable to assess vaccine efficacy and vaccine coverage depending on the setting. Most EUPHEM fellows from cohort 2017 and 2018 attended, as well as some EPIET fellows from cohort 2018 eager to learn about basics of vaccine epidemiology before they have the vaccinology module next year.

R-mentoring of a junior EPIET fellow

As Timothée's project on antimicrobial consumption involved the generation of annual semi-automated reports, the task to produce the 2018 report was transmitted to Veronica Cristea (EPIET Cohort 2018), hence he took care of giving her initial R-training, teaching her how to proceed to data-management, create functions, proceed to statistical analysis and generate Rmarkdown documents.

Additionally, Timothée reviewed the programming of the analysis of one ecological study on antimicrobial consumption and the increase of antimicrobial resistance Veronica undertook.

Epi and Stat mentoring of a microbiology PhD student

By the end of his second year at THL, Timothée was offered to provide epidemiological and statistical mentoring to a microbiology student from the University of Turku as a capacity building exercise. It involved helping her adapt a study design to her project, teaching her the basics of statistical analysis how to use SPSS in order to perform bivariate and multiple variable analyses and how to present statistical analysis results.

6. Other activities

Cohort-representative activities

As cohort-representative, Timothée's main role was to represent the fellows' opinions and issue on the fellowship. To do so, he attended several teleconferences with ECDC and EAN and went to the Training Site Forum 2018 meeting in Stockholm.

Timothée also participated to the design and conducted statistical analysis of a fellows satisfaction survey conducted in summer 2018 whose results were shared as an oral presentation during PRM 2018 and as a report transmitted to all scientific coordinators and members of the Training Site Forum. The following year, Timothée led the design of an updated version of this survey whose results were presented at PRM2019 and will participate to the drafting of new report.

He also set up a mailing list in order to ensure adequate communication and information sharing within the cohort and was at several times used as an additional communication channel by some scientific coordinators when they wanted to make sure that all fellows had been made aware of timely changes.
Additionally, Timothée participated to the setting-up of an updated buddy-system so that all new fellows from cohort 2018 would be put in relation with a cohort 2017 buddy and a recent alumnus mentor.

Scientific presentation to a general audience

Timothee was invited to give a 30 minutes presentation, including 10 minutes for questioning at an event (café scientifique) are organised every three months by the science and higher education attaché to the French embassy in Finland. The aim of these events, set in French, are to have scientists from different disciplines present works they have conducted in Finland to a general audience of French speakers followed by a one hour wine and cheese buffed for further discussion and networking.

Timothee chose to present his project on Spatial and temporal distribution of tick borne encephalitis in Finland from 2007 to 2017 as the disease is endemic in Finland and gets an important amount of media coverage around the emergence of new focis across the country; it made it a topic people can relate to.

Giving this presentation was a good opportunity to learn how to make a scientific project understandable to a general audience without over-simplifying its content.

7. EPIET/EUPHEM modules attended

1. Introductory course, 25/09/2017 – 13/09/2017 ,Spetses, Greece
2. ESCAIDE 2017, 06/11/2017 – 08/11/2017, Stockholm, Sweden
3. Outbreak Investigation module, 04/12/2017 – 08/12/2017, Berlin, Germany
4. Multiple Variable Analysis module, 16/04/2018 – 20/04/2018, Nicosia, Cyprus
5. Rapid Assessment and Survey methods, 14/05/2018 – 19/05/2018, Athens, Greece
6. Project Review module 1, 27/08/2018 – 31/08/2018, Lisbon, Portugal
7. Time Series Analysis module, 05/11/2018 – 09/11/2018, Brussels, Belgium
8. ESCAIDE 2018, 21/11/2018 – 23/11/2018, Saint-Julian, Malta
9. Vaccinology module, 24/06/2019 – 28/06/2019, Rome, Italy
10. Project Review module 2, 25/08/2019 – 31/08/2019, Prague, Czech Republic
11. ESCAIDE 2019, 27/11/2019 – 29/11/2019, Stockholm, Sweden: **UPCOMING**

8. Other training

1. Nordic Mini Project Review 2018, March 5th – 6th 2018, Oslo, Norway
2. Nordic Vaccine meeting, 14th-15th June 2018, Helsinki, Finland
3. Nordic Mini Project Review 2019, March 11th-12th 2019, Copenhagen, Denmark
4. Writing and Reviewing Scientific Abstracts: a field epidemiology focus (5th edition), e-learning course
5. Behaviour Change Science & Policy symposium: Intervention evaluation & field experiments. Interdisciplinary perspectives on evaluating societal interventions to change behaviour, May 14th-15th 2019 ,Helsinki, Finland
6. User! Conference, July 9th-12th 2019, Toulouse, France
7. EAN workshop: Social media for Public Health Professionals, August 31st – September 1st 2019, Prague, Czech Republic

Discussion

Supervisor's conclusions

Outi Lyytikäinen, Hanna Nohynek, Jussi Sane

During the two-year fellowship at THL Timothée Dub has been involved in a variety of public health activities, including surveillance, outbreak investigations, descriptive and analytical epidemiology and research as well as communication and teaching, as described in the core competencies of the EPIET programme.

The outcome of his work has been excellent, benefitting the department of health security at THL as well as the national and international community. He has contributed to the development of Finnish surveillance systems for antimicrobial consumption, HIV and HCV among persons who inject drugs and norovirus infections. The outbreak investigations he was involved in gave valuable information to improve internal processes at THL and laboratory diagnostics of certain infectious diseases such as pertussis. His research projects increased our knowledge of spatial and temporal distribution of tick-born encephalitis in Finland, associations between human antibacterial consumption

and occurrence of certain bacterial infections, the challenges in pertussis surveillance and impact analysis of the pertussis vaccination programme, and healthcare workers immunization recommendations in the Nordic countries. The two-year experience at THL has increased his confidence in the field of infectious diseases epidemiology, especially in analysing and reporting surveillance data as well as scientific writing and teaching. His participation in the daily work of the department has made it possible for the supervisors to carry out projects that would otherwise have been difficult or impossible to accomplish.

The fellow developed both personally and professionally during the fellowship and solved the given tasks in a highly competent way with a high and increasing degree of independence, but at the same time seeking assistance when necessary.

A positive attitude towards challenges in the field of infectious diseases, and an open mind towards colleagues makes the fellow a very good team player. Based on his personal and professional skills, we can highly recommend Timothée Dub for any kind of public health work.

Coordinator's conclusions

Daniel Thomas

Timothée has been a very active member of the Fellowship. Over the two years Tim has made very good progress in meeting his competencies in field epidemiology, and has benefited from the excellent supervisory support provided by THL. The site has provided a wide range of projects on a variety of important public health topics. This has suited Tim who has proved himself to be flexible, hard-working and innovative. Tim appears to have very much enjoyed the Fellowship, and took on the role of EPIET representative for his cohort. Tim took a bit of time to adapt to the Finnish language and climate but after two years appears to be very much at home. He is a good communicator and recently presented his work to the Finnish French Society.

On a personal note, I have very much enjoyed working with Tim and will miss his recommendations for Finnish film and music as much as our interesting epidemiological discussions. I wish Tim well for the next step in his career.

Personal conclusions of fellow

During my 2 years placement at the department of Health Security of the Finnish Institute for Health and Welfare I have had the opportunity to work on a wide range of projects across the whole EPIET competencies spectrum and on different topics, from antimicrobial resistance to vaccine preventable or vector-borne diseases.

Additionally, I was given a lot of independence in conducting my projects covering the whole spectrum of the expected EPIET competencies. I highly appreciated the high level of expertise of my colleagues and how they were all keen on giving me the possibility to put in practice and turn into competencies what I had learnt in the EPIET modules.

Finally, the fellowship will also have improved my teaching and presentation skills.

I am sure all of this will be of great benefice for my upcoming professional career.

Acknowledgements of fellow

First, I would like to acknowledge all my training supervisors for everything they taught me over the past two years. I would more especially thank Outi Lyytikäinen, my local supervisor for all the support, trust and independence she provided me with and for understanding that my interest in Finnish literature and movies was not my only motivation to come to Finland; Jussi Sane for his mentoring, friendship and all the ad-hoc meetings we had to discuss the future of epidemiology, global health or democracy in Europe; Hanna Nohynek for involving me in vaccine preventable diseases projects and for her guidance; Henrikki Brummer-Korvenkontio for allowing me to work on a deeply interesting PWID project: an adventure to be continued.

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