FELLOWSHIP REPORT

Summary of work activities

Alexandra SEPTFONS
Intervention Epidemiology path (EPIET)
Cohort 2015

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.

Stockholm, September 2016

- 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 guide[1].

Pre-fellowship short biography

Alexandra Septfons has a three level degrees in biology and a master of public health.

Before EPIET, she was employed as an epidemiologist in the Foodborne disease, Zoonotic and Vectorborne Disease team at Santé publique France, the national public health agency in Paris, France since 2013. She was currently working in the surveillance of zoonotic infections and arboviruses.

Fellowship assignment: Intervention Epidemiology path (EPIET)

On September 2015, Alexandra Septfons started her EPIET fellowship at the national public health agency in Paris, France, under the supervision of Henriette de Valk. 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

Title: Outbreaks of gastroenteritis in long-term care facilities (LTCF) for the elderly in France, five seasons of surveillance from November 2010 to May 2015.

Outbreaks of acute gastroenteritis (AGE) are frequent in long-term care facilities for elderly (LTCFE). Vulnerability of the residents and high risk of person to person transmission is associated with significant morbidity and mortality representing a considerable health and economic burden.
In 2010, specific surveillance of AGE outbreaks in LTCFE was implemented in order to document the disease burden and to facilitate the rapid implementation of control measures.

A guideline for the detection, investigation and control of outbreaks was provided to the LTCFE.

[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

We implemented the surveillance each year from November to May. An outbreak was defined as at least five cases of AGE within four days among LTCF residents. We analyzed factors associated with the attack rate (AR) by a negative binomial regression.

From 2010 to 2015, a total of 3549 outbreaks were reported causing 88930 cases of illness. The AR among residents ranged from 28% to 32% depending on the year of surveillance. Laboratory testing was performed in 1694 (48%) outbreaks and norovirus was identified in 582 (73%). The median delay in notifying an outbreak decreased from 5 days in 2010-2011 to 4 days in 2014-2015. For each of the recommended control measures the frequency of implementation increased significantly over the years. The AR among residents was lower when control measures were implemented within three days of date of symptom onset of the first case (IRR=0,90; p<0,001).

The surveillance for outbreaks of AGE in LTCFE provides valuable information to determine the burden of disease and contributes to improve the implementation of control measures. Laboratory confirmation could be strengthened to better characterize the circulating viruses.

Role and outputs:

Main investigator. *Alexandra analysed the data and wrote an article (1). Poster presented at ESCAIDE 2016 (2).*

Supervisor(s): Nathalie Jourdan-Da silva

Title: Chikungunya and dengue surveillance in Metropolitan France, 2015

Aedes albopictus, or Asian tiger mosquito, the vector of dengue and chikungunya, has been established in mainland France since 2004, introducing the risk of autochthonous transmission of these vector-borne infections due to the repeated introduction of the viruses by infected travellers returning from endemic regions.

In mainland France, epidemiologic surveillance has been implemented since 2006. At the national level, it is based on mandatory notification (MN) and a network of laboratories. At the regional level, enhanced surveillance is implemented in the districts where the mosquito is established, during its period of activity from 1 May to 30 November.

In 2015, in mainland France, 52 chikungunya cases and 167 dengue cases were notified, and 425 chikungunya cases and 538 dengue cases were identified by the laboratory network. From 1 May to 30 November, 30 chikungunya cases and 131 dengue cases were confirmed in the 22 districts where the vector was established. With the exception of 6 autochthonous dengue cases identified in Languedoc-Roussillon-Midi-Pyrénées, all cases were imported.

Imported chikungunya and dengue cases in mainland France reflect the epidemiology of the diseases in the areas where travellers come from, in particular the French territories of America. Despite the absence of an outbreak of chikungunya and dengue in the French territories of America in 2015, the number of imported cases was still high. With the geographical expansion of *Ae. albopictus* in mainland France, the risk of autochthonous transmission is increasing. In addition, the recent emergence of Zika virus in Latin America and the French territories, in 2015-2016, creates an additional risk of arbovirus infection. It is therefore necessary to regularly inform travellers and healthcare professionals, in order to disseminate prevention messages and to participate in the surveillance system.

Role and outputs:

Co-investigator. *Alexandra participated in running the surveillance system, analysed the surveillance data and co-authored an article on the system and outputs (3).*

Supervisor(s): Marie Claire Paty, Harold Noël

Title: Zika Virus: Setting up a surveillance system in France metropolitan

Zika virus (ZIKV) is an emerging mosquito-borne flavivirus causing most often mild disease. Since 2015 the virus has spread rapidly throughout the Americas including the French territories (FTA). The outbreak has identified new modes of transmission and clinical manifestations, including adverse pregnancy outcomes and congenital malformations and Guillain-Barre Syndrome. In mainland France there is a risk of introduction and transmission of the virus because of the large number of travellers from FTA and the presence of the vector *Ae. Albopictus*. We set up surveillance of Zika infection and its complications in mainland France to rapidly detect cases, prevent local transmission, and ensure clinical follow up of infected pregnant women.

The surveillance included (i) laboratory and physician notification of cases (confirmed by the detection of specific IgM or IgG by plaque-reduction neutralization test or seroconversion or viral nucleic acids by RT-PCR), (ii) notification by the 44 Perinatal Diagnostic Units (PDU) of microcephaly (foetal head circumference <3rd percentile, or < 2 standard deviations in new-borns) and other malformations in foetuses or new borns of women infected or exposed to sexual or mosquito borne transmission.
As of 29 March 2016, 150 ZIKV cases were reported by 20 laboratories, including 6 in pregnant women, one sexually-transmitted case, and one case of meningoencephalitis. 59 (39 %) cases lived in an area where *Ae.albopictus* is established. No Zika-related congenital malformation has been detected.

The risk of local transmission and the severe Zika-related adverse outcomes trigger the need to monitor closely the autochthonous and vertical transmission in mainland France. Vector control measures must be implemented around cases in *Ae.albopictus* infested areas from May to November, when the vector is active.

Role and outputs:

Co-investigator. Alexandra participated in setting up and implementing the surveillance system including writing of the protocol for the surveillance of pregnant women infected by Zika virus and detection of congenital malformations (4). She analysed the surveillance data and wrote an article (5). She presented the system and the results in an oral presentation at ESCAIDE 2016 (6). The results of the surveillance of pregnant women infected by Zika virus and of congenital malformations will be submitted to a peer review journal. She co-authored a manuscript about surveillance of Zika virus infection in the EU/EEA, published in Eurosurveillance (7).

Supervisor(s): *Marie Claire Paty, Harold Noël, Jet De Valk*

Title: Chikungunya, Zika and dengue surveillance in Metropolitan France, 2016

Aedes albopictus, the vector of dengue, chikungunya and zika viruses, has been established in mainland France since 2004, introducing the risk of autochthonous transmission of these vector-borne infections due to the repeated introduction of the viruses by infected travelers returning from endemic regions.

In mainland France, epidemiological surveillance is based at the national level on mandatory notification (MN) and a network of laboratories. At the regional level, enhanced surveillance is implemented in the districts where the mosquito is established, during its period of activity from 1 May to 30 November.

In 2016, in mainland France, 34 chikungunya cases, 184 dengue cases and 781 Zika virus infection cases were notified. The laboratory network identified 415 persons with at least one positive biological result for chikungunya, 723 for dengue and 1 060 for Zika virus infection. From 1 May to 30 November, 18 chikungunya cases, 167 dengue cases, 453 Zika virus infection cases, 1 dengue-Zika coinfection case and 9 flavivirus cases were confirmed in the 30 districts where the vector was established. All cases were imported, except 3 autochthonous sexually transmitted cases of Zika virus infection.

These surveillance data in mainland France reflected the epidemiological situation in the areas where travelers come from. The Zika virus epidemic in the French territories of America had a major impact on the number of imported cases, and more generally on the surveillance. The risk of autochthonous transmission is real in mainland France. It's determined by the geographical expansion of *Ae. albopictus* and the international epidemiological situation of arboviruses. It is therefore necessary to keep informing travellers and healthcare professionals, in order to disseminate prevention messages and to involve them in the surveillance system.

Role and outputs:

Co-investigator. Alexandra participated in running the surveillance system; she analysed the surveillance data and co-authored an article (8).

Supervisor(s): *Marie Claire Paty, Harold Noël*

Competencies developed:

The surveillance project about gastroenteritis in long-term care facilities permitted me to develop more skills in multivariable analysis, and made me more confident to use these analytical methods in my current work.

All the projects around Zika virus infection allowed me to build competencies in the development of a new surveillance system in a context of emerging disease. I learned to work in a stressful situation, in a rapidly changing environment with new knowledge becoming available constantly. I learned to set up a surveillance system rapidly, facing many challenges such as the initial lack of valid laboratory diagnostic methods and the scarce knowledge on routes of transmission and potential complications. I had to follow on a day basis all scientific developments in order to adapt the surveillance system. I spent a lot of time following the literature, which provided a better understanding of the situation. I had to work in close contact with stakeholders from different fields (epidemiologists, microbiologists, entomologists, healthcare professionals, Blood, organ and tissue safety agency, ECDC, WHO, PAHO…). I have become very aware of how surveillance data is used for action and decision making. I also gained my first experience on the aspects related to the ethics including confidentiality, and protection of individuals, in a sensitive context, related to sexual transmission, congenital malformation and possible medical interruption of pregnancy. All the work around arboviruses surveillance (Chikungunya, dengue and Zika), permitted me to be more confident in setting up and running a surveillance system. It enabled me to be more involved in the communication with stakeholders. For instance, I prepared and presented to the Ministry of Health and the regional health authorities an oral presentation of the performance and results of the surveillance system, on the basis of which the surveillance strategy was revised. All these actions permitted me to use the surveillance data in a different way, not just for information but also for action, in order to make it more efficient for the future.

2. Outbreak investigations

Title: Zika Virus: First detected autochthonous cases in two overseas regions (Martinique and French Guiana)

Following the emergence of Zika virus in Brazil in 2015, an epidemiological surveillance system was rapidly implemented in the French overseas Territories of America (FTA), building on previous experience with dengue and chikungunya, and enabled the rapid detection of the first cases of Zika in the FTA.

General practitioners and medical microbiologists were invited to report all clinically suspected cases of Zika. Laboratory investigations were systematically conducted (RT-PCR) for all suspected cases.

On 18 December, the first autochthonous case of Zika virus infection was confirmed by RT-PCR in French Guiana and Martinique, indicating introduction of Zika virus in the FTA. The circulation of Zika virus was then also confirmed in Guadeloupe and Saint-Martin. We reported early findings on 203 confirmed cases of Zika virus infection identified by RT-PCR or sero-neutralisation in Martinique between 24 November 2015 and 20 January 2016. All cases were investigated. Common clinical signs were observed (maculopapular rash, arthralgia, fever, myalgia and conjunctival hyperaemia) among these patients. However the rash, the basis of our case definition, was absent in a significant proportion of patients (16%).

These results are important for the implementation of a suspected case definition, the main tool for epidemiological surveillance, in territories that may be affected by ZIKV emergence, including Europe.

Role and outputs:

Co-investigator. contributed to developing the surveillance outbreak investigation protocol, establishing and reviewing the case definitions and laboratory criteria for confirmation, writing "frequently asked questions" and information for medical doctors. She also, developed the surveillance database (Voozanoo) and creating a linkage to the vector control database. She co-authored a manuscript published in Eurosurveillance (9)

Supervisor(s): *Marie Claire Paty, Harold Noël, Jet De Valk*

Title: Outbreak of leptospirosis in a prison, February 2016, France

The 17 of February, the national reference laboratory of leptospirosis confirmed two cases of leptospirosis in a prison in Fresnes (two prisoners).

We set up an outbreak investigation to identify recent cases in the prison and to determine the source of infection in order to guide control measures. The investigation took place from 24th of February to 1st of March (team of 16 people mobilized).

We reviewed the medical files of the prisoners who visited the infirmary between 11 January and 19 February 2016 (period defined on the basis of the incubation period of the first confirmed cases). A suspected case was a prisoner who visited the infirmary between 11 January 2016 and 19 February 2016 with « fever ≥ 38°C or flu-like syndrome or myalgia or persisting diarrhoea». A suspect case was classified as "possible" if no other cause of illness had been identified. A case was confirmed if the serology (MAT or Elisa IgM) or RT-PCR was positive.

1573 prisoners (1443 men, 130 women) visited the infirmary between 11 January and 19 February (mean age: 37 years). 344 (21,8%) medical files were missing (prisoners released or relocated: n=211, 13,4%; hospitalized: n=1; used by the medical team: n =132, 8,3%). Among the 1 229 medical files available 59 suspected cases were identified (5%), among whom 33 (56%) were classified as possible cases. Among 33 possible cases, 2 were released and one was excluded by the doctor after a new visit. Among the 30 possible cases still in prison, 21 accepted to provide a blood sample and all of them tested negative. A questionnaire enquiring about exposures was completed by the two confirmed cases. Both cases reported frequent contact with rodents. No common place of exposure was identified. Rodent infestation was wide spread.

We concluded that the severe rodent infestation and the frequent contact between prisoners and rodents were the cause of the outbreak. Vaccination was proposed to all prisoners/staff working in close contact with detritus and rodents. An area was dedicated for prisoners where they can remove and clean their clothes after work before returning to their cell. Information leaflets were created to inform prisoners about the risk of diseases transmitted by rodents, about prevention especially in their conditions: limit contact with rodents, and do not throw waste through the windows. Vector control measures were also reinforced in the prison.

Role and outputs:

Co-lead investigator (with the regional team). Alexandra wrote the protocol, coordinated and participated in the investigations in the prison and the writing of an internal report (10)

Supervisor(s): *Jet De Valk, Alexandra Mailles*

Title: Outbreak of leptospirosis among Kayakers, France, 2016

In September 2016, a kayak club on the Vilaine river, Brittany, reported seven kayakers with symptoms compatible with leptospirosis since July 2016. Human and environmental investigations were performed to identify the outbreak source and guide control measures.

We asked kayak clubs, laboratories, hospitals and general practitioners to report cases with symptoms compatible with leptospirosis (fever, myalgia, arthralgia) or positive laboratory results in a 40km area adjacent to the river and requested further information using a standardized questionnaire.
A possible case was a person with symptoms compatible with leptospirosis between 1 June and 31 October 2016 and exposure to the river, and a confirmed case was a possible case with laboratory evidence.
Rodents were trapped near the river and PCR tested for leptospirosis.

Eight confirmed and 6 possible cases were identified with symptom onset between 22 June and 15 September. Three cases were hospitalized. All cases practiced kayaking over a 30 km section of the Vilaine river. No other at-risk exposure was identified. Nine cases reported skin lesions, 50% wore integral swim suits and none were vaccinated.
L. kirschneri was the only species identified in 5 cases. 24% of the 38 trapped animals were positive for leptospirosis DNA, none being *L. kirschneri*.
We documented an unusually dry summer period and an interruption of rodent control campaigns on the stretch of the Vilaine River in 2016
Access to the river was immediately forbidden after detection of the first cases. We informed the health professionals and all kayak clubs about leptospirosis risk and individual prevention measures including vaccination. We recommended enhanced rodent control and active surveillance of cases for the next season to rapidly identify areas of transmission.

Role and outputs:

Co-lead investigator (with the regional team). Alexandra wrote the protocol, supported the regional team in the investigations, and contributed to the writing of an internal report as last author (11). Abstract accepted for ESCAIDE 2017 as an oral presentation (12). Poster presented at the "National Infectious Diseases Day", French conference (13). An article is in preparation (14) to be submitted to Eurosurveillance (last author).

Supervisor(s): Jet De Valk, Alexandra Mailles

Competencies developed:

The investigation of these outbreaks strengthened my capacity to rapidly develop an outbreak investigation protocol, questionnaire, to use the results of a descriptive analysis to recommend control measures and to report results to different target audiences.

During these outbreaks, I did not develop an analytical study. In this context, active case finding and a detailed description of the cases and their exposures enabled us to guide the most urgent control measures. I was able to use analytic methods in my surveillance project on outbreaks in long-term care facilities.I also learned how to initiate additional studies (of the environment, the wildlife) with other disciplines.

Having different roles in different outbreaks helped me to develop professional and social skills required in outbreak management.

3. Applied epidemiological research

Title: Estimation of the Incidence and hospitalisation rates of Lyme borreliosis (LB) in France using the French Hospital Discharge Data System

Lyme borreliosis (LB) is the most common tick-borne infectious disease in North America and in countries with moderate climates in Europe. It was shown that the incidence of this disease has been increasing in several countries in Europe.

We estimated the number of cases hospitalized with a diagnosis of LB between 2005 and 2015, by clinical manifestation, and analyzed the trends in incidence of hospitalized cases. We used the Programme de Médicalisation des Systèmes d'Information (PMSI), a national data base on hospital discharge diagnoses.
We defined a hospital stay for LB, by the following criteria: hospitalisation with (i) a LB specific diagnosis (M01.2 or L90.4); (ii) a A69.2 code in the absence of any other diagnosis, or (iii) a A69.2 code associated with code(s) compatible with LB symptoms (neurological, cardiac, articular and ocular disorders), from 1 January 2005 to 31 December 2015 in mainland France.

Among the 26 520 files extracted, between 2005 and 2015, containing LB codes, 10 630 met the criteria for a LB hospital stay. In total 8 789 cases were hospitalized at least once. The annual number of new cases requiring hospitalisation ranged from 649 in 2005 to 937 in 2011 with a mean of 799 cases per year. The mean number of hospital stays by case was 1.6, ranging from a minimum of 1 to a maximum of 40. The hospitalisation rate was estimated at 1.3 per 100 000 inhabitants per year. This incidence varied between 1.1 per 100 000 (in 2005) and 1.5 per 100 000 (in 2011) with no significant trend.
Reasons for hospitalisation were neurological disorders (n=4 487, 51 %), arthritis (n=1 131, 13 %), cardiac events (n=564, 6 %), ocular disorders (n=154, 2 %) and ACA (n=213, 2 %).
Fifty seven percent of the cases were men and most cases were in the age group of between 0 and 10 years and 40 to 80 years old with a mean age of 46 years (range 1-95).
Among the 4 487 cases hospitalized with neurological disorders potentially linked to LB, 57% were men and the mean age was 45 years old (range 1-94). The age distribution shows a peak in the number of cases in the age group of 0 to 10 years old. The mean annual hospitalisation rate for neuroborreliosis (NB) was estimated at 0.6 cases per 100,000 inhabitants ranging from 0.5 in 2005 to 0.8 in 2009

The hospital discharge database being stable over the years, they permit to describe the epidemiology of LB, follow trends in incidence and geographical spread of Lyme borreliosis. This study provides important information about LB cases hospitalized in France especially in terms of clinical manifestations of the infection, age description, seasonality and spatial distribution.

Role and outputs:

Main investigator. Wrote the protocol, developed the criteria and algorithm, in collaboration with hospital cliniciens, developed the data extraction form, analysed data, an article will be submitted to Eurosurveillance. First author (15)

Supervisor(s): *Elisabeth Couturier, Jet De Valk*

Title: Prevalence and changes in behaviours, attitudes and perceptions for Lyme Borreliosis using the "Baromètre Santé study 2016", France

Lyme borreliosis (LB) is the most common tick-borne infectious disease in North America and in countries with moderate climates in Europe. Each year approximately 30 000 cases are diagnosed in France but we had no information about the prevalence of tick bites, nor on the attitudes and practices of the population related to ticks and LB prevention. We included specific questions on tick bites and LB in the French Health Barometer 2016., Win order to determine the prevalence of tick bites, and to describe behaviours, attitudes and perceptions related to LB and compare these results between regions with high and low incidence of LB.

The French Health Barometer is a survey of a random sample of the general population living in France. In 2016, 15 216 individuals aged 15 to 75 years took part in the study. Data were collected between January 2016 and August 2016. The survey collected information on various health behaviours and attitudes (vaccination, screening practices, sexuality, and vector borne diseases). We classified regions as high moderate and low LB incidence region on the basis of the 2016 incidence rates estimated by the sentinel network of general practitioners.

In 2016, 4% (95%CI: 3,7 – 4,4) of 15-75 years olds have been bitten by a tick in the last 12 months and 21,2% (95%CI:20,4 - 22,0)had been bitten more than a year ago. The proportion of individuals reporting tick-bites was significantly (p<0,001) higher in the region with high LB incidence (39,3%) compared to regions with moderate incidence (30,2%) and low incidence (20,9%). For those who reported being bitten, 20,0% (95%CI: 16,2 – 23,8) had consulted a healthcare worker. Among individuals who considered being exposed to ticks, 5,6% (95%CI: 4,6 – 6,6) often use repellent, 52% (95%CI:50, 0-53, 9) often wear clothes which cover the legs and 36,2% (95%CI 34,4-38,1) are looking for ticks after a walk in the forest .The proportion of individuals who are using these protective measures are significantly higher in high incidence areas. Among the study population, 64,3% (95%CI 63,3-65,4) reported having heard about Lyme disease with a higher proportion in regions with high incidence (79,5%) compared to regions with moderate (71,8%) and low incidence (58,8%) (p<0,001). Among those who have heard about Lyme disease 47,4% (95%CI: 46,2- 48,5) believe that Lyme disease is a serious illness.

This study shows that knowledge on LB and use of protective emeasures was higher but still insufficient in high incidence régions. Communication efforts should also strenghtened in regions with lower incidence, to prevent tick bites locally but also when travelling to higher incidence regions.

Role and outputs:

Main investigator. Analysed data, wrote internal report. Manuscript will be submitted to a peer-reviewed journal. First author. (16).

Supervisor(s): *Elisabeth Couturier, Jet De Valk*

Title: Estimation of the sensitivity of the mandatory notification for chikungunya and dengue, 2014-2015, France

Aedes albopictus, the vector of dengue and chikungunya viruses, has been established in mainland France since 2004. In mainland France, surveillance of laboratory confirmed chikungunya and dengue cases is based, at the national level, on mandatory notification (MN) and a Laboratories Surveillance System (LSS). At the regional level, enhanced surveillance is implemented in the districts where the mosquito is established. From 1 May to 30 November, when the vector is active, all suspected imported cases must be immediately reported without waiting for laboratory confirmation.

Evaluation of the enhanced surveillance showed that the vector control measures implemented around 30% of the suspected cases were unnecessary since the suspicion was not confirmed. In order to improve the efficiency of the system, we are currently assessing the feasibility of a change in strategy, and the impact on the risk of transmission if vector control measures are implemented only after confirmation of the cases. Within the

framework of this assessment, we conducted a study to estimate the sensitivity of mandatory notification for chikungunya and dengue and to determine factors which influence this sensitivity.

The study was conducted for two different years (2014-2015) with the LSS as reference database. We defined an algorithm (based on date of birth, sex and department) to identify common cases (dengue or chikungunya) in each database. We estimated the MN sensitivity by dividing the number of common cases in both databases by the total number of cases identified in the LSS. We determined factors influencing this sensitivity by Poisson regression (adjusted on age and sex). We identified 696 common cases in MN and LSS (454 chikungunya cases and 242 dengue cases) and estimated the overall sensitivity of MN at 17%.

The sensitivity was higher in 2014 compared to 2015 (18% vs 14%, p<0,03), in departments where Aedes albopictus is established (21% versus 15%, p<0,001), and if the biological confirmation was done by a rapid test (PCR/NS1) compared to serology (36% vs 12%, p<0,001). We observed also that the sensitivity of chikungunya MN was higher (19%) in 2014, when a large chikungunya outbreak occurred in the French overseas departments, compared to 2015 (8%) when no outbreak occurred. Moreover, the sensitivity of the MN was estimated at 28% during the period and in the area of enhanced surveillance and 61% for cases confirmed by a rapid test.

We showed that the sensitivity of the MN for chikungunya and dengue is low in France. The MN should be reinforced especially in departments where Aedes albopictus is established. Nevertheless, we showed that the sensitivity is higher during the period of enhanced surveillance and for cases confirmed by a rapid test. These findings suggest a higher compliance with MN of healthcare professionals, especially of acute cases, during the high risk period.

Role and outputs:

Co-investigator. Wrote the protocol, analysed data, wrote an internal report (17).

Supervisor(s): *Bruno Hubert, Marie Claire Paty*

Competencies developed:

The Lyme projects, allowed me to extend my knowledge of vector borne diseases and of estimating the burden of disease from different data sources.

For two projects, I went through all the steps of a research project: from the conception of the research question to writing the report.

With the first project, I learned how to deal with a very large database, with all the challenges we face when developing a data extraction form. I also learned to use new software, SAS. With the project about behaviours, attitudes and perceptions for Lyme Borreliosis, I gained experience in data analysis in surveys taking into account the sampling frame (epidemiological analysis with post-stratification weights). In the context of political controversy around Lyme disease in Europe, these studies will provide valuable data for Santé publique France and will be communicated to all stakeholders. The results on the time-course of Lyme burden are useful in an international context given the concern about increasing incidence.

4. Communication

Publications in peer reviewed journals

Six manuscripts published (1, 3, 5, 7, 8, 9), two as first author.

Manuscripts submitted to peer reviewed journals (in review process)

Three manuscripts in preparation for submission (14, 15, 16)

Conference presentations

One oral presentation (6) and one poster (2) at ESCAIDE 2016
One oral presentation at ESCAIDE 2017 (12).
One commented poster presentation at the national conference of infectious diseases specialists in France (13)

Other presentations

One presentation at IDEA Course for the teaching activities (18)
Several presentations for the Ministry of health about results and strategy of arboviruses surveillance.
Presentation at regional meetings about results of the arboviruses enhanced surveillance 2016.

Reports

Two outbreak reports (10,11)
One internal reports (17)

5. Teaching activities

Title: IDEA Course (International Course of Applied Epidemiology)

From 27 March 2017 to 31 March 2017, I lectured and facilitated in the International Course of Applied Epidemiology (IDEA). This 3-week course is the equivalent of the EPIET introductory course targeting a French audience. I facilitated the second week of the course.

I facilitated 2 case-studies, namely- (i) "Outbreak of Haemorrhagic fever in Africa, 1976" and (ii) "Epidemiology of measles in France ".
I gave one lecture on Ebola virus following the case study "Outbreak of Haemorrhagic fever in Africa, 1976".
I took the Ebola virus outbreak in Guinee between 2013 and 2015 as example to illustrate lessons from outbreak investigations and implementation of a surveillance system. I also gave a lecture about the surveillance system which was implemented in France due to the Ebola outbreak in West Africa (2013-2015).

The learning objectives of the first case study were to be able to understand and implement the different steps of an outbreak investigation.
The learning objectives of the second case study were to be familiar with the purposes and uses of surveillance in public health, the different key surveillance concepts and types of surveillance and be able to use and interpret surveillance data.

One of the major objectives of the second week of the training was to set up a survey.
The learning objectives of the different workshops were to be able to elaborate a protocol with objectives and data analysis plan, elaborate a questionnaire, collect data in the field, analyse the data and communicate the results. I facilitated the workshops, including the field supervision.

Participants included 35 public health students and professionals.

An evaluation was done by the organizers but only few people filled in. However the students addressed their comments directly to the main organizer and they were very positive.

Supervisor(s): *Delphine Antoine*

Educational outcome:

Teaching activities were really new for me. By preparing and delivering these teaching assignments, I realised how difficult it was to explain specific epidemiological concepts and methods in a simple and clear way. I realized that a good preparation is important. I spent a lot of time revising all the epidemiological concepts, to be able to answer questions if needed.
It was the first time I was a "teacher" in front of professionals, and exposed to very experienced and knowledgeable students.
I learned a lot by accompanying students to set up a study with a challenging schedule (one week), from the protocol to the data analysis and last step, the communication.

Other activities

Epidemiologist with MSF OCA, Somali Region-Ethiopia, 2017.

My mission took place in Somali Region, Ethiopia, from the 10th of June until the 8th of July 2017. I was deployed as an Epidemiologist for the emergency response in Doollo Zone, Somali Region, Ethiopia, following the AWD outbreak and malnutrition crisis.

MSF routine activities covered a large area, the main MSF locations were Wardher, Yucub, Danod and Galadi. In all these locations MSF had set up Inpatient Therapeutic Feeding Centres (ITFC) and Ambulatory Therapeutic Feeding Center (ATFC) programs. Furthermore MSF also set up Cholera Treatment Centres (CTC) in these four locations.

The population in this area has suffered from a prolonged drought which provoked a worsening of the living conditions of the people. A lot of people lost many of their animals (main living sustention) so they had to settle in areas nearby towns where they could find support, and this provoked a growth of the Internally Displaced Persons (IDP) camps in the area. The host populations from the towns are suffering also from this drought and their living conditions have also worsened. All these people face many difficulties to access water and food with really poor hygiene conditions.

The purpose of my mission was "Implementation of surveillance system for morbidity and mortality". When I arrived surveillance systems were already implemented for acute watery diarrhoea (AWD), measles, malnutrition and mortality. But in many locations these systems had to be improved and strengthened.

My main activities were (i) Acute Watery Diarrhea surveillance: CTC data collection supervision (ensuring data quality and monitoring for signals), data analysis, epidemiological investigation; (ii) Community based surveillance: Supporting and monitoring the community based surveillance (CBS) activities (ATFC, ITFC, measles, mortality), Analysis of CBS related data, supervision and analyse of the population count in Wardher, Assessment of the mortality, food and water situation in Galadi district (iii) Support the team in the analyses of data for meetings with stakeholders; (iv) Epidemiological summaries of the project.

On-call duty for Santé publique France

Development of an e-training course on arboviruses surveillance and alert for on-call officers (Video and audio presentation)

Training of regional team or new colleagues on arboviruses surveillance and investigation (Chikungunya, Dengue, Zika)

MSF Pre-Deployment course in Bonn, 31 March -5 April 2016

ECDC meeting on "Zika virus infection and review of surveillance and control measures", Paris,20-21 April 2016

Zika Summit, Pasteur Institut, Paris, 25-26 april 2016

7. EPIET/EUPHEM modules attended

1. *Introductory course , 28 th of September to16 th of October 2015, Spetses, Greece*
2. *Outbreak investigation module,7 th to11 th December 2015, Berlin, Germany.*

3. *Multivariable analysis module, 14th to 18 th March 2016, Vienna, Austria.*
4. *Rapid assessment and sampling module, 20th to 26th of June 2016, Athens, Greece.*
5. *Project review module, 22th to 26th August 2016, Lisbon, Portugal.*
6. *Time series analysis module, 7th to 11th November 2016 , Bucarest, Romania.*
7. *Project review module (PRM), 28th August to 1st September 2017 , Lisbon, Portugal*

Supervisor's conclusions

Alexandra is a highly motivated and enthusiastic fellow, extremely eager to learn and to acquire new competencies. Her impressive energy and work capacity enabled her to get the best out of all the learning opportunities that the EPIET programme offers.

Building on her initial experience of arbovirus surveillance she has been able to very rapidly develop a surveillance system for Zika infections in a crisis situation, and adapt it continuously to the rapidly changing circumstances and knew scientific knowledge. She took many initiatives, such as linking up with other disciplines such as obstetricians, to improve the quality and relevance of the collected data, but also information specialists to improve data management. She pushed outbreak investigations further than what is usually done, by for instance, involving and convincing environmental and animal health officials to carry out additional studies to identify the drivers behind two leptospirosis outbreaks. She established a fruitful collaboration with clinicians and social scientists which has been very beneficial for her projects on Lyme borreliosis (disease burden, and behaviors attitudes and perceptions) . The ministry of health, setting up a national plan for prevention and control of Lyme borreliosis had put high expectations on these studies, needing sound data rapidly. Without Alexandra's skills and perseverance, we would not have been able to implement these studies in time. The Ministry acknowledged their appreciation of the quality and timeliness of the results in writing to SpF, and requested us to repeat these studies regularly because of their importance for the national plan.

Alexandra showed during these 2 years that she can rapidly adapt to a changing environment. She can deal very well with stress and external pressure, and she skillfully manages politically sensitive issues. She has shown her leadership skills repeatedly, in particular in stressful situations. She is a highly appreciated team member, always ready to help out colleagues with difficult tasks, and finding creative solutions to problems.

Alexandra has all the skills and competencies to rapidly move to a senior position.

Coordinator's conclusions

Alexandra was already experienced and skilled in surveillance of vector-borne diseases before her fellowship, but wanted to develop her skills in outbreak investigation and the wider public health aspects of field epidemiology.

Working with the site, and with the support of their excellent supervision, she has managed the difficult task of extending and adapting the necessary work of the department to form field assignments that meet the EPIET scientific standards. This has meant that her outputs are not just of good quality but are also much-needed public health investigations for the site, which have been presented and had much interest in a wider European context, for example her presentation in plenary on Zika surveillance in France at the 2016 ESCAIDE.

She has also worked on projects out with her usual surveillance work, for example the burden of disease project for Lyme, her teaching, and the Leptospirosis outbreak investigations.

Alexandra has worked extremely hard in her fellowship and demonstrated excellent skills in the main competencies required. She undertook an overseas mission in difficult circumstances, again improving her skills and providing good surveillance leadership and support.

In addition her level of competency in the English Language has improved to a high level, both written and spoken, and her confidence in presenting and teaching.

I hope that she is given the opportunities to use her improved skills in the future to investigate a wider range of outbreaks and to contribute to surveillance and public health in a more senior capacity.

Personal conclusions of fellow

I was working in an excellent training site which provided me the best learning opportunities and support. This programme has been a very enriching experience both professionally and personally.

I appreciated the modules and the possibility to apply the new skills developed. This programme enabled me to extend my knowledge in infectious diseases especially in vector borne diseases. Moreover, this programme allowed me to strengthen my epidemiological skills especially on the field of applied epidemiological research.

I highly appreciated the possibility to participate in international assignment with MSF which has been really enriching. As MS Track it was not easy to dedicate time for an international mission, but the support of my colleagues permitted me to participate at this mission and so broaden my field epidemiological skills and allowed me to improve my management skills.

During the fellowship, I acquired experience in teaching public health professionals and public health workers. This programme allowed me as well to present my work at the national and international level and so gain confidence in scientific writing and communication.

I really appreciated the opportunity to be part in this international network which helps to strengthen collaborations between countries.

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