



## FELLOWSHIP REPORT

### Summary of work activities

David Hendrickx

Intervention Epidemiology path (EPIET)

Cohort 2016

## 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;

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*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

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

## Pre-fellowship short biography

David Hendrickx started his public health career in 2007 when he joined the Institute of Tropical Medicine in Antwerp, Belgium. There he was responsible for the coordination of an international network on the control of neglected tropical diseases, and developed a proficiency in the public health application of qualitative research methodologies. In 2012, he joined the Telethon Kids Institute in Perth, Australia, to undertake a PhD project on the prevention and control of skin infections in remote Aboriginal communities. David applied for a fellowship with the EPIET programme to gain expertise in applied epidemiological methods and their application to the surveillance and control of infectious diseases.

## Fellowship assignment: Intervention Epidemiology path (EPIET)

In September 2016, David Hendrickx started his EPIET fellowship with the unit of Epidemiology and Health Monitoring at the State Health Office of Baden-Württemberg in Stuttgart, Germany, under the supervision of Dr. Christiane Wagner-Wiening and Dr. Günter Pfaff. This report summarizes the work performed during this 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<sup>1</sup>.

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<sup>1</sup> 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>

# Fellowship projects

## 1. Surveillance

Supervisor(s): Dr. Günter Pfaff, Tarik Derrough

***Title: Identification of alternative sources of information for active case finding of congenital rubella syndrome (CRS). A study to support documenting the elimination of CRS in selected EU Member States.***

The completeness of European national congenital rubella syndrome (CRS) surveillance data does not meet WHO-recommended standards for rubella elimination verification. Supplemental CRS burden assessment methods are required to enable more accurate case reporting. With the aim of developing a generic protocol for retrospective CRS case identification in EU/EEA countries, we performed an extensive literature review of CRS burden assessment methods.

We used the PubMed search engine to retrieve peer-reviewed articles reporting on CRS burden assessments using case counts or incidence calculations published up to April 2017. We excluded seroprevalence studies and those based solely on routine surveillance data. We summarised study characteristics and CRS burden assessment methodologies, including prospective vs retrospective study type, study population, inclusion criteria, case definitions and data sources used.

We identified 771 articles reporting CRS burden assessments, published between July 1964 and March 2017. Thirty-six papers remained after applying exclusion criteria, 26 (72%) of which were of retrospective design. Twelve (33%) studies explicitly reported using WHO or EU case definitions. Data sources documented in retrospective studies were maternity and tertiary hospital records (n=10), laboratory registers (n=3), birth records (n=1), birth defect registries (n=2), pregnancy termination records (n=2), surveys (n=7), surveillance data (n=10), insurance and health system data (n=1), literature review (n=4), and immunisation programmes (n=1). Nine (35%) studies used a combination of data sources. Where evaluated (n=4), retrospective studies reported higher sensitivity compared to routine surveillance data.

We suggest that countries measure CRS burden by reviewing maternal and tertiary care records, and supplement this core assessment using optional methods tailored to the country. We developed an adaptable, generic protocol for retrospective burden assessment that will support verification of rubella elimination in EU/EEA countries.

***Role:*** This was a joint project, undertaken in collaboration with Alastair Donachie (EPIET C2016). Both fellows contributed equally to the structured literature review and the writing and development of the generic burden assessment protocol.

Supervisor(s): Dr. Christiane Wagner-Wiening

***Title: The epidemiology of tuberculosis in Baden-Württemberg 2012-2017. A retrospective analysis of tuberculosis surveillance data.***

Following a period of strong overall decline, the incidence of TB notifications in Germany has been on the increase since 2012. This trend has been associated with migration patterns and increasing numbers of immigrants and asylum seekers who originate from high TB prevalence countries, including countries with high rates of TB drug resistance. The state of Baden-Württemberg has also seen a significant increase in TB notifications since 2012. An in-depth analysis of this trend was required to provide insight in the recent epidemiology of tuberculosis and assist in identifying key areas for public health policy.

A retrospective descriptive analysis was carried out of all TB notifications in Baden-Württemberg from 2012 to 2017 (Source: SurvNet@RKI V.3). Temporal and demographic trends were documented on the basis of TB notification counts and incidences. Clinical and laboratory characteristics of all notified cases were described, including typing data and drug resistance patterns.

A total of 3.701 cases of tuberculosis (TB) were notified in Baden-Württemberg between January 2012 and December 2017, or a cumulative incidence of 34,5 notified TB cases per 100.000 inhabitants. The incidence of male cases (46,0 / 100.000) was twice as high as that of female cases (23,2 / 100.000). Geographically, the highest incidence was reported in the districts of Heidelberg (93,5 / 100.000) and Karlsruhe (56,9 / 100.000), where key refugee shelter and processing facilities are located. TB incidence in foreign nationals (21,12 per 100.000 inhabitants) was twice as high as that in German nationals (10,32 per 100.000 inhabitants). There was a sharp increase in the annual proportion of TB cases identified through active case finding from 2015 (12,9% in 2014, compared to 30,4% to 32,8% in the following years), largely driven by active screening of migrants.

Pulmonary TB was diagnosed in 73,7% of all notified TB cases as the main affected organ (n=2.727; incidence 25,4 per 100.000). Of these, 70,4% (1.921; incidence 17,9) were cases of open pulmonary TB. A total of 52 TB deaths were notified between 2012 and 2017, corresponding to an overall mortality rate of 0,48 deaths per 100.000 population. Drug resistance testing data was available for 2.854 TB cases, of which 2,1% were found to be multi-drug resistant TB (MDR-TB). The proportion of MDR-TB cases was higher for foreign-born patients compared to those born in Germany (2,8% vs 0,6%), particularly in patients born in the Newly Independent States of the former Soviet Union (NIS), where 12,0% (n=22) of tested cases were identified as MDR-TB.

Rising TB case numbers in migrants and a high proportion of infectious pulmonary TB show that tuberculosis remains a relevant public health issue in Baden-Württemberg with an increasing burden in persons originated from high prevalence countries. A focus on the early identification of TB cases, ensuring complete and successful therapy, maintaining high levels of data completeness, and timely and accurate notification of treatment outcomes are essential in order to maintain effective TB control in Baden-Württemberg.

**Role:** David Hendrickx was the principal investigator. He wrote the protocol, extracted the data from the surveillance database, cleaned the data, performed the data analysis and wrote the report.

Supervisor(s): Dr. Christiane Wagner-Wiening

***Title: High burden of tuberculosis amongst unaccompanied minor asylum seekers in southwestern Germany.***

Annually reported tuberculosis (TB) cases amongst foreign-born minors in southwest Germany have increased from 5 in 2012 to 69 in 2016, a trend driven by unaccompanied minor asylum seekers (UMAS). We describe the epidemiological and clinical features of TB in this population.

We performed a retrospective analysis of TB notification data in Baden-Württemberg, Germany, November 2015 to March 2017. Numerators consisted of notified TB cases aged 7 to 17, born out-side Germany. Incidence rates were calculated using state-level migration data and were reported per 1.000 UMAS arrived in this 17-month period.

Ninety-eight TB cases were notified (18,6/1.000). Median age was 16; 84% were male. 61 (62%) of diagnoses were made during asylum seeker screening procedures, 27,5% after symptomatic presentation, 6% during contact investigations. Pulmonary TB was identified in 81,6%, among which secondary infection sites were reported in 10,1%. 54 (55%) of cases were hospitalised. Treatment was completed in 34,7% of cases. Mycobacterium tuberculosis was identified by culture or PCR in 36,7% of cases. Laboratory diagnosis and drug resistance status were available for 89,8% and 55,1% of cases. Five cases were resistant for at least one first-line antibiotic (3 from Eritrea, 2 from Somalia), of which 1 was multi-resistant and 3 were poly-resistant. Highest TB notification incidences were recorded amongst those born in Ethiopia (62,5/1000), Somalia (55,8/1000) and Eritrea (29,2/1.000). Incidence rates were higher among females (57,3/1000) than males (16,6/1.000).

Intensive case follow-up and close coordination between health authorities, physicians and the youth welfare service are essential for TB diagnosis and treatment in this vulnerable population. The results underline the importance of a timely, comprehensive health assessment for UMAS, especially in migrants from highly endemic countries.

**Role:** David Hendrickx was the principal investigator. He carried out the analysis of surveillance and migration data and summarised the findings in a report.

Supervisor(s): Dr. Christiane Wagner-Wiening

***Title: Enhanced surveillance of carbapenem resistant pathogens in Baden-Württemberg, Germany.***

Following reports of the increasing incidence of Carbapenem-resistant pathogens throughout Europe, the mandatory notification of Carbapenem-resistant Enterobacter and Acinetobacter cases came into effect in Germany in May 2016. However, a descriptive analysis of surveillance data for Baden-Württemberg one year after this introduction showed deficiencies in the notification data, severely limiting their use for surveillance purposes and for informing public health policy.

To address this issue, an enhanced surveillance protocol and corresponding data collection form for carbapenem-resistant Enterobacter and Acinetobacter cases in Baden-Württemberg was developed with the aim of implementing a prospective cohort study. The study will be implemented outside of the scope of the EPIET fellowship. Its outcomes will allow for a comprehensive description of the epidemiology of carbapenem-resistant pathogens in Baden-Württemberg, which will enable the development of recommendations for improving their surveillance, prevention and control.

**Role:** David Hendrickx was the principal investigator. He carried out the descriptive analysis of surveillance data, wrote the protocol for enhanced surveillance, developed the corresponding data collection form, and prepared and submitted the required ethics documents.

Supervisor(s): Dr. Christiane Wagner-Wiening

**Title: *Arbovirus preparedness in Baden-Württemberg.***

*Aedes albopictus*, a competent vector for arboviruses including dengue, chikungunya and zika, is becoming more and more established in southwestern Germany, including Baden-Württemberg. This trend increases the likelihood of the occurrence of autochthonous transmission of arboviruses following the return of domestic travellers from countries that are endemic for arboviral diseases. Outbreaks of dengue and chikungunya have recently been observed in Italy and France, illustrating the need for preparedness in Europe, particularly in areas such as Baden-Württemberg where pockets of *Ae. albopictus* populations have been established.

In this context, and in collaboration with the Robert Koch Institute, a set of guidelines and resources that local health offices can refer to when investigating cases of dengue, chikungunya or zika has been developed. The resources include a background information document about *Ae. albopictus* and its potential role in autochthonous transmission or arboviruses in the German context, a choropleth map of Germany indicating the climatic favourability for the occurrence and establishment of *Ae. albopictus* populations at the district level, a flow chart and supplemental information to assist in decision making processes around epidemiological and laboratory investigations and possible control measures, and case investigation forms.

The resources are currently being trialled in Baden-Württemberg and will be reviewed in late 2018 in preparation of their wider implementation in Germany from 2019.

**Role:** David Hendrickx participated in the national working group that set out to develop the described resources. He prepared a literature review on *Ae. albopictus* and its potential role in autochthonous arboviral transmission in the European context.

## 2. Outbreak investigations

Supervisor(s): Dr. Christiane Wanger-Wiening, Dr. Martin Dörner

**Title: *An international outbreak of foodborne botulism associated with the consumption of dried roach (*Rutilus rutilus*), Germany and Spain, November-December 2016.***

Early November 2016, two cases of foodborne botulism were notified almost simultaneously in two German states. We describe the epidemiological and laboratory investigations that followed.

Cases were persons hospitalized in the EU with clinical symptoms of foodborne botulism, 1/10/2016 through 31/12/2016. Local health authorities collected information on food consumption. Food safety authorities collected food samples and initiated traceback investigations. Serum, stool and food samples were tested by mouse bioassay (MBA) and/or PCR for the detection of botulinum neurotoxin (BoNT) or bont genes, confirmed by a reference laboratory. German authorities issued international warnings through European alert networks.

Four additional cases were identified: two in Germany, two in Spain. All six were of Russian/Kazakh background. Age ranged from 37 to 55 years. Two were female. Two cases tested positive for BoNT/E (in serum), four for bont/E (in stool). Two cases were laboratory unconfirmed. All were hospitalised (1 to 21 days), four required ventilation, two received antitoxin, all recovered. All cases had consumed salt-cured, dried roach (*Rutilus rutilus*), purchased at five different retail locations. Presence of bont/E (PCR) was confirmed in two household fish samples. BoNT/E was confirmed (MBA) in one household and two retail fish samples. Traceback investigations identified the distributor of the implicated roach products in Europe. Precise product and batch numbers could not be determined due to missing labels at retail, prompting a multi-product EU-wide recall.

This is the first international outbreak of foodborne botulism in the EU. Dried roach was identified as the source of infection. Although additional cases were likely prevented by the recall, continued monitoring is required. Existing stringent food traceability and production standards for counter-sale fish products require enforcement.

**Role:** David Hendrickx compiled outbreak investigation information available through the RASFF and EPIS-FWD platforms. He collated data on public health measures and trace back investigations, and followed up with relevant health, food safety and laboratory partners as required. David prepared a detailed account of the epidemiological and laboratory investigations and its outcomes, which he summarised in the format of journal paper for submission to EuroSurveillance.

Supervisor(s): Dr. Christiane Wagner-Wiening, Dr. Marieke van der Werf

***Title: A European cluster of MDR-TB cases amongst immigrants originating from the Horn of Africa***

In September 2016, several patients from Somalia were identified with multidrug-resistant tuberculosis (MDR-TB), in which the pathogen showed a rare and characteristic resistance profile (capreomycin-resistant, amikacin-susceptible MDR-TB). Other cases with the same resistance profile have been reported in patients originating from the Horn of Africa in other member states of the European Union (EU) and Switzerland. The assignment of all these cases to a molecular cluster using whole genome sequencing (WGS) led to an epidemiological investigation of the cluster cases that were identified in Germany.

The aim of the investigation was to identify the MDR-TB cluster cases and to elucidate their epidemiological links to try and identify the transmission event. Specific objectives were: i) the identification of all cases in Germany that belong to the MDR-TB cluster; ii) the description of their demographic and clinical characteristics; iii) the identification of possible sites of infection and the detection of possible subsequent infections and diseases. These investigations were part of a wider initiative to investigate the cluster cases in all affected European countries. This was coordinated by the ECDC and facilitated the exchange of information between all involved countries.

Up to June 2017, 17 MDR-TB cluster cases were identified in Germany: 15 WGS-confirmed cases, one probable case, one exclusively epidemiologically-linked case. Fifteen of the 17 patients were classified as infectious due to pulmonary disease and bacteriological evidence of respiratory TB agents. Sixteen patients were from Somalia, one patient from Eritrea. The median age was 17 years. It was considered unlikely that transmission had occurred in Germany. Exposure most likely occurred at the country of origin or along the migration route to Germany. As of October 1st, 2017, when the outbreak report was completed, a total of 21 cluster cases had been identified, of which 19 confirmed by the WGS. Twenty positive contact cases were identified using Interferon gamma-release assay (IGRA), although none had active disease.

Public health vigilance is required, given that additional cluster cases might still remain to be identified. Close follow-up of cases and their contacts is ongoing. TB screening of migrants in Germany should be maintained. The identification of new TB cases that share a drug resistance profile and geographical characteristics with documented cluster cases should prompt WGS investigation to establish cluster status.

***Role:*** David Hendrickx contributed to the collection and descriptive analysis of epidemiological data on the German MDR-TB cluster cases. His role included the preparation of a data collection form that was used by the ECDC to collect relevant clinical, laboratory and migration route data of all the cluster cases in the affected countries. David participated in the German (coordinated by RKI) and European (coordinated by ECDC) workgroups that followed up on the cluster investigations and served to compile investigation outcomes and exchange information between involved partners.

Supervisor(s): Prof. Marianne van der Sande, Prof. Marleen Boelaert, Dr. Veerle Vanlerberghe, Berthe Miwanda, Prof. Jean-Jacques Muyembe

***Title: The cholera epidemic in the Democratic Republic of the Congo. An analysis of national syndromic and laboratory surveillance data, 2008-17.***

An unprecedented countrywide cholera outbreak was reported in the Democratic Republic of the Congo (DRC) in 2017. With the aim of informing targeted prevention and control interventions, we sought to elucidate the dynamics of cholera spread in DRC that culminated in the present outbreak and to identify high-risk areas/groups.

We used national cholera syndromic surveillance and reference laboratory data collected from January 2008 to November 2017, and data extracted from 2015-17 Médecins Sans Frontières (MSF) cholera treatment centre admission registers to describe trends in reported cases, case fatalities and serotyping data; map annual cumulative incidences by health zone; and summarise the characteristics of major outbreaks. We calculated relative risks (RR) and compared case fatality (CF) in provinces, age groups and weeks of admission throughout a selection of outbreaks.

In the study timeframe, 270.852 cholera cases and 5.231 deaths (1,9% CF) were reported. Eighty-two percent of cases were reported in cholera endemic provinces. Of 9.510 suspect case specimens submitted to the reference laboratory, 31% were laboratory confirmed. Inaba was the most commonly identified serotype (90,3%), followed by Ogawa (9,5%) and Hikojima (0,2%). We identified the occurrence of nine major outbreaks, three of which occurred in non-endemic provinces. Incidence mapping and trends in reported cases by province revealed three distinct mechanisms in the spread of cholera in DRC: (i) significant increases in the number of cases in cholera-endemic areas in eastern DRC (2011 and 2015); (ii) recurrent outbreaks progressing downstream along the Congo River (2011-2012 and 2015-2017), and (iii) spread along Congo River branches to areas that had been cholera-free for over a decade (2017).

CF in cholera non-endemic provinces was three-fold higher (2.079/46.640; CF 4.3%) than in endemic provinces (3.152/224.212; CF 1.4%; RR 3,17, 95%CI 3,00-3,35). Cases aged  $\geq 5$  years had higher CF (4.331/204.483; CF 2,1%) than those  $< 5$  years (911/66.008; CF 1,4%; RR 1,52, 95%CI 1,42-1,64). Among treatment centre patients, CF increased from 2,6% (109/4.201) in  $< 20$  year olds to 3,8% (99/2.609; RR 1,46, 95%CI 1,12-1,91) in 20-49 year olds, and 4,3% (32/752; RR 1,64, 95%CI 1,11-2,41) in  $\geq 50$  year olds. During the 2015-17 outbreaks, CF of treatment centre patients decreased throughout an outbreak from 5,1% (week 1) to 4,4% (week 5; RR 0,86, 95%CI 0,52-1,45) and 0,7% (week 10; RR 0,14 95%CI 0,04-0,45).

There remains an important cholera outbreak potential in DRC. Our analysis of cholera spread mechanisms over time and place provides insights in when and where to focus cholera prevention and control efforts in order to avoid more widespread outbreaks from occurring. The higher CF in non-endemic provinces and in the first weeks of an outbreak possibly reflect lower levels of natural immunity and limited access to treatment and water and sanitation services. Targeted use of cholera vaccine, soon after the occurrence of initial cases in non-endemic areas, may decrease CF.

**Role:** David Hendrickx was one of two principal investigators (joint international mission with Brecht Ingelbeen, EPIET C2016). Both fellows equally contributed to the whole project, including: the collection, cleaning and analysis of the data; preparing an internal report to summarise our findings for local partners (DRC Ministry of Health, the National Institute of Biomedical Research, MSF, and the Institute of Tropical Medicine (Belgium)); writing up our findings in the format of a journal paper and submitting it to Emerging Infectious Diseases.

### 3. Applied epidemiology research

Supervisor(s): Dr. Christiane Wagner-Wiening, Dr. Marieke van der Werf

**Title:** *The role of entry-screening procedures in the identification of multidrug-resistant Mycobacterium tuberculosis cluster cases amongst patients arriving in Europe from the Horn of Africa, 2016-17.*

A cluster of 36 multidrug-resistant tuberculosis (MDR-TB) cases among migrants was identified in 2016-17 in eight European countries. We aimed to determine in how far country migrant entry TB screening procedures contributed to the identification of cluster cases to inform public health policy.

We conducted a survey amongst countries known to be affected by the MDR-TB cluster to describe their migrant entry TB screening procedure, to identify the screening status (screened vs not-screened) of cluster cases, and to document the occasion of their diagnosis. Where cluster cases were not identified at screening, we sought to clarify why.

Six of eight countries responded. Entry TB screening procedures varied by country. Screening information was received for 32 out of 36 cluster cases (89%). A total of twenty-seven cases (84%; age range 15 to 25 years) had been screened, all either in Germany (19) or Switzerland (8), where screening is mandatory. Cluster cases in France (1), Italy (2) and Finland (1) did not undergo entry screening. A cluster case in Sweden was diagnosed before entry screening. Amongst screened cases, 13 (48%) were diagnosed as a result of the screening, 12 (44%) later, when they became symptomatic, and 2 (7%) as part of contact tracing investigations. Unscreened cluster cases (5) were diagnosed when TB symptoms developed and medical care was sought.

Systematic entry screening programmes, where mandatory, contributed to MDR-TB cluster case identification for migrants with active disease. Essential, however, is ensuring barrier-free access to host-country health systems after arrival and ensuring health care workers' awareness of TB in persons from countries with a high incidence.

**Role:** David Hendrickx participated in the ECDC-coordinated working group established to follow up on the MDR-TB cluster investigations and assisted in collating and summarising the information on country TB screening practices and the number of cluster cases that were, or were not, identified as a result. David contributed to a research letter summarising the findings of the investigation, which was published in Clinical Microbiology and Infection.

Supervisor(s): Dr. Christiane Wagner-Wiening

**Title:** *Prospective cohort study on infant pertussis and household vaccination practices in Baden-Württemberg, 2016 – 2017.*

In 2016, a total of 3.067 cases of pertussis were reported in Baden-Württemberg (BW); more than twice as many as in the preceding year (1.397 cases). The highest incidence of pertussis was reported amongst infants (130 cases / 100.000 inhabitants), who cannot be fully vaccinated until the age of 1 year. Cocooning strategies therefore remain

an important infant pertussis prevention measure. We performed a prospective cohort study to document infant pertussis cases notified in BW, and to describe the vaccination status and practices of their close household contacts, with the aim of deriving preventive measures.

The study population consisted of all infant pertussis cases notified in BW between April 2017 and April 2018, and their mothers. A structured data collection form was used to document clinical characteristics of cases. A questionnaire was administered to mothers of study cases, which included items on socio-demographic characteristics, pertussis knowledge, vaccination practices, and vaccination recommendations received from healthcare practitioners before, during and after pregnancy. Relative risks were calculated for disease severity in infant pertussis cases (more severe vs less severe) by sex, age group, immunization status of the case, and immunization status of household contacts.

Thirty-seven infant pertussis cases were included in the study. The majority (73,0%) were male (n=27). Median age was 3 months. Sixteen (43,2%) cases had not received any vaccinations prior to disease onset, and ten (27,0%) had received only one. Most cases (81,1%) were hospitalized. No fatalities were recorded. Coughing fits (86,5%) and stridor (43,2%) were the most commonly documented clinical signs. The most common complications were apnoea (n=3), pneumonia (n=2) and hypoxia (n=2). Infants under the age of two months were found to have a higher risk of severe disease compared to older infants (RR=4,13; CI 1,55-11,04; p<0,01).

Of the 29 mothers that completed the questionnaire, 16 (55,2%) indicated that they were familiar with pertussis prior to their infant child's illness. Seventeen (58,6%) respondents indicated that they did not know how pertussis infection occurs, and 13 (44,8%) said that they did not know how it could be prevented. Five respondents (17,2%) replied correctly to all seven multiple choice questions on pertussis knowledge. Twelve out of 29 respondents (41,4%) indicated they did not know that they could protect their infant child from pertussis through their own vaccination.

Eight mothers (27,5%) and eight fathers (27,5%) were up-to-date with their pertussis vaccination. All siblings were vaccinated at least once prior to disease onset in the notified infant pertussis case. Three (10,3%) mothers reported being informed by a health practitioner about the risk of infant pertussis by a healthcare provider prior to their pregnancy. Pertussis vaccination recommendations by healthcare practitioners for the prevention of infant pertussis were equally rare. Amongst those mothers who were recommended to be vaccinated after their pregnancy, 75% (n=3) followed the recommendation.

The low proportion of mothers that received pertussis vaccination recommendations before, during and after pregnancy from health care practitioners is a notable finding and suggests that health professionals could be more pro-active in this regard. The necessity of this is underlined by the increased severity of disease amongst infants under the age of 2 months who are too young to be vaccinated, and the apparent lack of knowledge amongst mothers concerning the importance of their vaccination status in preventing pertussis in their infant child.

**Role:** David Hendrickx was the principal investigator. He carried out the descriptive analysis of surveillance data, developed the study protocol and corresponding data collection forms, prepared and submitted the required ethics documents, compiled and cleaned the survey data, analysed the survey data, and prepared a report summarizing the outcomes of the study.

## 4. Communication

### Publications

#### Manuscripts, unpublished at time of writing:

1. Hendrickx D, Contzen M, Wagner-Wiening C, Janke KH, Hernando-Jiménez P, Massing S, Pichler J, Stark K, Burckhardt F, Schönberger K, Jurke A, Thole S, Stetter L, Varela C, Carbó R, Pacual del Pobil M, Nieto M, Zamora MJ, Sisó A, Valdezate S, Dorner B, Frank C, Dorner M. *An outbreak of BoNT/E botulism in Germany and Spain associated with the consumption of dried roach (Rutilus rutilus), November-December 2016.* (Final draft - to be submitted to Eurosurveillance)
2. Ingelbeen B\*, Hendrickx D\*, Miwanda B, Van der Sande M, Vochten H, Mossoko M, Nyakio JP, Vanlerberghe V, Lunguya O, Jacobs J, Boelaert M, Kebela BI, Bompangue D, Muyembe JJ. *Recurrent cholera outbreaks in the Democratic Republic of the Congo, 2008-17. Emerging Infectious Diseases.* (\* joint first authorship – publication submitted to Emerging Infectious Diseases)

#### Publications published in peer-reviewed journals:

1. Helbling P, Kröger S, Haas W, Brusin S, Cirillo DM, Groenheit R, Guthmann JP, Soini H, Hendrickx D, van der Werf MJ. Screening of migrants for tuberculosis identifies patients with multidrug-resistant tuberculosis but is not sufficient. *Clinical Microbiology and Infection* (2018), <https://doi.org/10.1016/j.cmi.2018.03.015>
2. Walker TM, Merker M, Knoblauch AM, Helbling P, Schoch OD, van der Werf MJ, Kranzer K, Fiebig L, Kröger S, Haas W, Hoffmann H, Indra A, Egli A, Cirillo DM, Robert J, Rogers TR, Groenheit R, Mengshoel AT, Mathys V, Haanperä M, Soolingen DV, Niemann S, Böttger EC, Keller PM; MDR-TB Cluster Consortium<sup>^</sup>. A cluster of multidrug-resistant Mycobacterium tuberculosis among patients arriving in Europe from the Horn of Africa: a molecular epidemiological study. *Lancet Infect Dis.* 2018 Apr;18(4):431-440. (^ member of MDR-TB Cluster Consortium)

### Reports

1. L'épidémiologie de choléra entre 2008 et 2017 en République Démocratique du Congo (RDC) : endémicité aux grands lacs et épidémies de plusieurs années aux bords du fleuve Congo. Une description de dix ans d'épidémies de choléra en RDC. (co-authored with Brecht Ingelbeen; report to DRC Ministry of Health, DRC National Institute for Biomedical Research, Médecins Sans Frontières, Institute of Tropical Medicine; December 2017)
2. Tuberculosis in Baden-Württemberg, 2012 – 2017. An analysis of routine surveillance data. (August 2018)
3. A literature review on the *Aedes albopictus* and its potential role in autochthonous transmission of arboviruses in Germany (internal report for the arbovirus working group; March 2018)

### Conference presentations

1. Hendrickx D & Wagner-Wiening C. High burden of tuberculosis amongst unaccompanied minor asylum seekers in southwestern Germany. (poster presentation, ESCAIDE, November 2017, presented by Dr. Günter Pfaff on behalf of David Hendrickx)
2. Hendrickx D, Contzen M, Wagner-Wiening C, Varela Martinez C, Dorner B, Frank C, Dorner M. An international outbreak of foodborne botulism associated with the consumption of dried roach (*Rutilus rutilus*), Germany and Spain, November-December 2016. (oral presentation, ESCAIDE, November 2017, presented by Dr. Günter Pfaff on behalf of David Hendrickx)
3. Hendrickx D\*, Ingelbeen B\*, Miwanda B, van der Sande M, Mossoko M, Vanlerberghe V, Lunguya O, Jacobs J, Boelaert M, Kebela BI, Bompangue D, Muyembe JJ. The geographical spread of the cholera epidemic in the Democratic Republic of the Congo. An analysis of national syndromic and laboratory surveillance data, 2008-17. (accepted for an oral presentation, ESCAIDE, November 2018) (\* contributed equally, David Hendrickx is presenting author)
4. Donachie A\*, Hendrickx D\*, Sdona E, Pfaff G, Derrough T. Assessing the burden of congenital rubella syndrome in Europe: A review of methods towards verifying elimination. (accepted for a poster presentation, ESCAIDE, November 2018) (\* contributed equally, David Hendrickx is presenting author)

## Other presentations

1. An update on the MDR-TB cluster amongst unaccompanied minor Somalian asylum seekers in Baden-Württemberg (Bund-Länder-Arbeitsgruppe "Surveillance", Robert Koch Institute, September 2016)
2. An outbreak of foodborne botulism in Germany and Spain associated with the consumption of salt-cured roach. Update on investigation findings. (PAE weekly meeting, February 2017)
3. Projektvorstellung: Erhebung von Daten zu Keuchhusten bei Säuglingen und zum Infektions- und Immunstatus der im Haushalt lebenden Familienangehörigen und weiteren Haushaltskontakten, Baden-Württemberg, 2017-18. (PAE 'Jour Fixe', Robert Koch Institute, May 2018)
4. An international outbreak of foodborne botulism associated with the consumption of dried roach (*Rutilus rutilus*), Germany and Spain, November-December 2016. (EPIET Project Review Module, August 2017)
5. Cholera epidemiology in DR Congo, 2008-17. (Joint presentation with Brecht Ingelbeen; Institute of Tropical Medicine, Antwerp, Belgium; December 2017)
6. An update on the infant pertussis study: Aims, data collected, expected outcomes. (IfSG Dienstbesprechung, LGA, December 2017)
7. Outcomes of a cholera outbreak investigation mission in DR Congo, October 2017 (PAE 'Jour Fixe', Robert Koch Institute, March 2018)
8. Epidemiologie der Cholera in der Demokratischen Republik Kongo 2008-17. Eine Analyse der nationalen Surveillance Daten im Rahmen der Unterstützung einer Ausbruchsuntersuchung (IfSG Dienstbesprechung, LGA, May 2018)

## Other

1. Contributions to the LGA's weekly infectious disease bulletin:
  - Summary on the MDR-TB situation in Somalia to contextualise an MDR-TB cluster amongst unaccompanied minor Somalian asylum seekers in Baden-Württemberg (September 2016)
  - Short report on 2017 tick borne encephalitis notification data (June 2017)
2. Contributed to an article describing the increasing number of pertussis cases reported amongst infants in Baden-Württemberg (annual LGA report, March 2017)
3. Short report on the status and significance of carbapenem-resistant pathogens in Baden-Württemberg for state authorities (June 2017)
4. Contributed to a press release on influenza in Baden-Württemberg and vaccination recommendations (September 2017)
5. An article summarising the findings of an analysis of tuberculosis notification data amongst unaccompanied minor asylum seekers in Baden-Württemberg (annual LGA report, March 2018)
6. Retrospective surveillance and enhanced case-finding of congenital rubella syndrome cases using additional data sources. A generic protocol. (co-authored with Alastair Donachie (C2016), ECDC, July 2018)

## 5. Teaching and pedagogy

### Title: QGIS – an introduction to geographical information systems

This half-day training session was organised by the German Centre for Infectious Disease Research (GCIDR) and took place at the Robert Koch Institute in Berlin on the 17<sup>th</sup> of May 2017. I was asked to co-facilitate this session, which was led by Lutz Ehlikes (PAE/EPIET C2015) and also involved Raskit Lachmann (PAE/EPIET C2015) as a co-facilitator. The aim of the training session was to provide a hands-on introduction to GIS technologies and their application to infectious disease epidemiology. The target audience was experienced infectious disease researchers with little to no previous experience with GIS technologies in general and QGIS software in particular. A general introductory presentation was followed by a practical exercise in which participants used QGIS to create a series of maps on the basis of an imported disease surveillance dataset. My role in this session was to provide assistance during the exercise and clarify QGIS functionality to participants as required. The session was well-received and evaluated by means of a brief post-session survey by the GCIDR.

### Reflection

I thought the session was well organised and well received by participants. Co-facilitating the session and interacting with its participants gave me confidence in explaining GIS concepts and QGIS functions to learners, especially since I was relatively new to QGIS myself at the time. Preparation is key for hands-on training sessions that require participants to use software to work through practical exercises, as was demonstrated in a positive way by Lutz who ensured all software was up-to-date and all exercise data files were easy to use and manipulate. The exercise was also designed to be highly relevant to the participants and of immediate practical use to the participants, such as by demonstrating how to import disease notification data from the German surveillance system into QGIS. Lutz, as main

facilitator, therefore set a good example for me to follow next time I find myself in a position to facilitate a QGIS training session.

## **Title: Qualitative & Mixed Methods for Public Health**

This was a half-day session organised as part of the 2017 EPIET Project Review Module (August 2017) to provide an overview of the key concepts of qualitative and mixed research methods, and to illustrate their possible applications in a public health context. The training objectives were to enable participants (EPIET and FETP fellows) to: (i) explain key processes of qualitative and mixed methods research; (ii) distinguish barriers between epidemiologists/microbiologists and their qualitative research colleagues; (iii) describe how structured coding can be used to analyse text data; and (iv) articulate challenges and benefits of incorporating qualitative methods in public health investigations.

The session was co-organised and co-facilitated by myself and Lisa Hansen (EPIET coordinator). I gave a presentation on qualitative data collection methods and mixed methods study designs. I also facilitated the group exercise that we had planned for the final part of the session.

At the end of the session, we had a short discussion during which we requested some direct feedback from participants about the session. We also encouraged participants to provide feedback through the online EPIET module evaluation survey on EVA. Feedback was positive, although several participants indicated that they would have appreciated more time for the exercise. Participants indicated that they thought the session was relevant to the fellowship, and suggested that it could also be offered to future EPIET cohorts.

## **Reflection**

I had previous experience teaching qualitative and mixed methods to an audience of post-graduate level public health students. However, I enjoyed the challenge of adapting the format, content and style of my presentation to the very specific audience of EPIET/EUPHEM/FETP fellows. I think the session as a whole struck a good balance between theory and practice, and was also enriched by presentations by current fellows who shared their own experiences with qualitative and mixed methods studies in the course of their fellowships. This resonated well with the participants and provided specific examples of how these research methods can be applied in the context of field epidemiology. Given the feedback we received, I would certainly make more time for the exercise if we were to repeat this training session.

## **6. EPIET/EUPHEM modules attended**

EPIET Introductory Course – 26 Sep to 14 October 2016 – Spetses, Greece

EPIET Outbreak Investigation Module – 5 to 9 December 2016 – Berlin, Germany

EPIET Multivariable Analysis Module – 13 to 17 March 2017 – Zagreb, Croatia

EPIET Rapid Assessment and Survey Methods Module – 8 to 13 May 2017 – Athens, Greece

EPIET Project Review Module – 28 August to 1 September 2017 – Lisbon, Portugal

EPIET Vaccinology Module – 11 to 15 June 2018 – Cardiff, UK

EPIET Project Review Module – 27 to 31 August 2018 – Lisbon, Portugal

## **7. Other training**

Laboratory Methods for Epidemiologists, organised by the German FETP programme – 20 to 24 February 2017 – Robert Koch Institute, Berlin, Germany

One-week placement with the district health office of Esslingen – 31 January to 6 February 2018 – Esslingen, Germany

## Discussion

### Supervisor's conclusions

Here in Stuttgart at the Landesgesundheitsamt Baden-Württemberg, we have been pleased to host fellows of the EPIET and PAE programmes ever since 2006. It is a rewarding experience to see fellows develop their knowledge, practical skills, and competence in applied infectious disease epidemiology during their period of fellowship.

So, I was very pleased to get the opportunity to supervise David Hendrickx during his EPIET-Training. We received agreement and organisational support of our human resource department and the backing of the State's Ministry of Health.

Coming from a mostly academic background, David has quickly adapted to the work in applied epidemiology. David is a well-organized person coupled with a high level of flexibility and determination. David is very friendly and courteous and contributes to a good working atmosphere in the team. He sees not only the work ahead but also has refined his eye for epidemiological challenges hidden in it. Upon his return from programme modules, it was visible that his work benefitted from newly acquired knowledge, and cases or outbreaks were occasionally approached from a different perspective.

David exceeded our expectations by completing the tasks assigned to him with utmost analytic accuracy and professionalism. His previous academic and practical experience clearly helped him in the course of his work, providing the background for a profound understanding of infectious diseases. David's passion for gaining a deep insight into the public health sector was evident during his work. He proactively approached our team with prepared and well-thought through questions that he asked in order to complement his existing knowledge with background information in order to put new information into context and get an in-depth understanding of the nature of the working field in infectious disease epidemiology.

By posing well-reflected questions, David exhibited high interest and curiosity to get all the information relevant to understand ongoing routine work and running projects.

As David's supervisor, I am pleased that his EPIET-track fellowship will, in short time, reach a successful completion.

### Coordinator's conclusions

Having already experience in the Public Health field, David entered into these two years of training with the clear objective of further developing his competencies in epidemiological surveillance and applied research. I believe he has achieved this goal.

David is a highly capable professional and has demonstrated his abilities as an independent worker throughout the fellowship. Before embarking on any new project, he always seeks out the public health relevance of his studies. His projects on congenital rubella syndrome and the MDR-TB cluster have given him an insight in surveillance at the European level, and his role in the investigation of an international outbreak of foodborne botulism has proven that he can communicate and find agreement with different stakeholders. His work in DR Congo in the context of an ongoing cholera epidemic also underlined his ability to work independently and in different settings. His projects on migrant health have also introduced him to the challenges that come with working in this area, particularly the difficulty of formulating recommendations and dealing with health policy matters in this context. I believe that the experience that David has gained during the EPIET fellowship nicely complements his academic background and makes him a valuable and versatile professional, able to fit into any kind of public health related position.

### Personal conclusions of fellow

The EPIET fellowship has given me the opportunity to broaden my profile as a public health professional and develop a skillset in applied infectious disease epidemiology. Over the two years of the programme, I have been exposed to a wide variety of topics concerning the surveillance, prevention and control of infectious diseases, which has made for an exceptionally insightful experience. Having started the EPIET fellowship with only a basic understanding of intervention epidemiology and its public health applications, I now feel that I have a firm grasp on this applied science and a clear understanding of disease surveillance methods. The exchange with other fellows and the fellowship coordinators, each with their own unique background, has also been an enriching and integral part of the EPIET experience. Therefore, in addition to having developed a skillset, I also feel that the fellowship has provided me with a strong professional network going forward, sustained by the work of the EPIET Alumni Network. I am looking forward to making good use of my EPIET experience by continuing to contribute to the improvement of public health in Europe and beyond.

### Acknowledgements of fellow

My sincere thanks to all my colleagues at the State Public Health Office of Baden-Württemberg for creating a supportive and stimulating professional environment during my EPIET fellowship. I particularly would like to thank my site supervisors, Dr. Christiane Wagner-Wiening and Dr. Günter Pfaff, for providing me with the opportunity to work on such a diverse range of projects, including an international mission. Special thanks also to my frontline coordinator, Dr. Alicia Barrasa, whose great support I was able to count on throughout my fellowship and who helped me keep track of my overall progress. I would like to thank all EPIET coordinators and module organisers for the terrific job they have done throughout the fellowship as teachers and mentors. They embody the unique EPIET spirit that I have had the privilege of experiencing, and which I will carry with me going forward. Finally, a big "Thank You!" to the fabulous team of the Fellowship Faculty Office for all their work and organisation behind the scenes.