



FELLOWSHIP REPORT

Summary of work activities

Susana Monge Corella

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;

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

Susana Monge is a Medical Doctor, with a speciality in Public Health and Preventive Medicine. She holds a Master in Public Health, a Master in International Cooperation and Development and a Diploma in Research Methodology in Health Sciences. Susana completed her PhD (University of Alcalá, Madrid, Spain) on the impact of social inequalities on outcomes of HIV infection and, at the same time, she participated in the Poverty-Related Diseases College, gaining experience in research in Africa. She has worked at the Spanish National Centre of Epidemiology and as an Assistant Professor in the University of Alcalá. Immediately prior to her her EPIET fellowship, she was as a field epidemiologist with Médecins Sans Frontières in Chad.

Fellowship assignment: Intervention Epidemiology path (EPIET)

In 15th September 2016, Susana Monge started her EPIET fellowship at the Rijksinstituut voor Volksgezondheid en Milieu (RIVM), Bilthoven, The Netherlands, under the supervision of Susan Hahné. 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 guide¹.

Fellowship projects

1. Surveillance

Surveillance of Measles, Mumps and Rubella in the Netherlands

Supervisor: Irene Veldhuijzen

Measles and rubella are vaccine-preventable diseases that are targeted for elimination. Surveillance of all cases through notification is of paramount importance for early detection of imported cases and secondary transmission in order to implement control measures. Mumps is also vaccine-preventable, but sporadic cases and small clusters are more frequent; surveillance aims to detect clusters of local transmission to limit the spread. Routine surveillance of the three diseases includes coordination with the laboratories for pertinent confirmatory diagnoses and sequencing of strains, regular analysis of cases to identify suspected source of infection, and communication (including in the absence of cases) with stakeholders. Additionally, regular analysis of reported measles and rubella cases is necessary to verify that the Netherlands does not fulfil criteria of endemic transmission. Finally, a Standard Operating Procedure

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

(SOP) was developed to contribute to improved standardization and quality of the system, and which also served as a basis for SOP of surveillance of other diseases.

Role: *Susana routinely reviewed and compiled case information, sharing communication to the early warning meeting. She drafted the SOP [23]. Laboratory reporting requirements for rubella were revised for cases with Fuchs uveitis, to minimise false alerts. She contributed to the WHO Measles and Rubella elimination report, the WHO/UNICEF joint reporting form, and wrote the mumps chapter of the annual Immunization Programme Report [9].*

Feasibility assessment for a prospective surveillance system for invasive pneumococcal infections in all age groups

Supervisor: Mirjam Knol

Invasive pneumococcal disease (IPD) is notifiable in the Netherlands, although only in children born after 2006, and the sensitivity of the system is low. Moreover, since the highest burden of IPD is among older adults, assessment of the overall impact of the vaccination programme should include all age groups. IPD in all age groups is monitored by a laboratory-based sentinel system based at the National Reference Laboratory on Bacterial Meningitis (NRLBM), covering 25% of the population. However, this latter system lacks clinical and vaccination data, which is collected retrospectively every 3-5 years. Increasing the timeliness would be desirable to facilitate, for example, detecting increases in resistance rates or alerts of emerging serotypes, especially those causing increases in empyema or meningitis presentation, severity and mortality. The goal of this project was to evaluate the feasibility of implementing a surveillance system that covered all ages and collected clinical, vaccination and bacteriological information prospectively, as cases are notified. We reviewed the literature, established the objectives and desirable attributes of the system, and conducted structured interviews with stakeholders and experts. Different scenarios with their costs were drawn and the design with the best scientific and operational feasibility was selected. The proposed system has not been implemented in The Netherlands, but this study provides a basis for its design should the system be adopted.

Role: *Susana wrote the study protocol, reviewed literature and drafted the system characteristics. She developed the structured interview guide and conducted the interviews together with the supervisor. She prepared materials for discussion, reports [11] and briefings for policy-makers [24].*

Optimization of Campylobacter Surveillance in the Netherlands

Supervisor(s): Eelco Franz, Annelot Schoffelen and Roan Pijnacker

Campylobacter surveillance is currently based in a sentinel network of ~15 laboratories who submit weekly information. This system is appreciated to be slow and expensive, with an annual cost of ~€40,000. Moreover, to estimate resistance rates a sample of the isolates received at the RIVM reference laboratory is tested *ex-professo*. ISIS-AR is a surveillance system created to monitor antimicrobial resistance in the Netherlands. It receives data on all resistance tests carried out at around three quarters of all laboratories. Because it is an extended practice to test for resistance *Campylobacter* before establishing antibiotic treatment, ISIS-AR could be an alternative data source for surveillance. Substituting the current system by one based on ISIS-AR would be more efficient, have higher representativeness, provide a good estimate of the resistance rates nationally and at a reduced cost. In this study, we compared both surveillance systems and, based on the finding that not all laboratories seemed to perform universal resistance testing of *Campylobacter*, designed a sentinel surveillance based on ISIS-AR, with three criteria for laboratories selection: (1) regular reporting to ISIS; (2) universal confirmation by culture of *Campylobacter* infections and; (3) universal resistance testing. A survey was set up among ISIS-participating laboratories to verify inclusion criteria and ask for consent to participate. The survey is still running but a significant number of laboratories are available to be included. The best way to estimate the denominator for this sentinel system is currently under discussion. The new system is expected to be piloted by the beginning of 2019. This project could also serve as a concept as well for other pathogens for which ISIS-AR could be an alternative or additional source for surveillance.

Role: *Susana elaborated a study on the overlap between the two systems, proposed the new system design and a roadmap for implementation [12]. She developed the questionnaire for the ISIS-AMR laboratories survey.*

2. Outbreak investigations

An outbreak of Salmonella Agbeni with unknown source

Supervisor: Lapo Mughini-Gras

On 11th August 2017, a case of *S. Agbeni* was reported to the national surveillance system through the salmonella laboratory surveillance network. Over the following months, a few additional cases were notified, prompting the initiation of an outbreak investigation at the beginning of 2018. The aim was to determine if there was a unique source for the cases, and to identify any action to prevent further cases. New cases were interviewed using a

standard trawling questionnaire from January 2018 onwards. Laboratory investigations were undertaken using whole genome sequencing and compared to strains causing previous outbreaks in other countries. Between 11th August 2017 and 26th February 2018, 19 cases of *S. Agbeni* were reported, of mild severity. 42% of the cases were over 65 years. The attack rate was very low, with a peak at 5 cases per week, and the duration of the outbreak suggested a persistent source. Cases were scattered through the country, affecting 9 out of the 25 GGD regions. It was not possible to identify a common exposure among the three patients notified in January-February 2018. Food items implicated in previous *S. Agbeni* outbreaks were not reported by the cases, and no new cases were notified after February 2018. The outbreak is over and the likely source (possibly a food item with long shelf life) could not be identified. No recommendations could be issued following this investigation.

Role: *Susana compiled all the available information, analysed it descriptively and wrote the outbreak report [13].*

Possible food-related HAV outbreak in the Netherlands

Supervisor: Ingrid Friesema

On 26th February 2018, the reference laboratory for hepatitis A virus (HAV) obtained sequencing results from a cluster of four patients with confirmed HAV infection, which was identical to strains from two cases in two different regions in the Netherlands from the preceding week. The strain was genotype IA, originating from Latin America. Cases had no epidemiological link and disclosed no risk factors. Preliminary screening of case information suggested a food source, and an investigation was started with the objective of identifying the source and implementing control measures. 10 confirmed cases from 7 different regions were identified with onset of symptoms between 25/01 and 07/02. We selected controls, matched by age, from respondents to the periodic food habits survey in the same epidemiological weeks as the likely exposure period of the cases, and undertook a case-control study. The case questionnaire focused on products likely imported from the countries of origin of the outbreak strain (according to the Food Safety Authority). Several suspected food items were identified, but epidemiological evidence was insufficient to support a probable source. Our investigation narrowed the list of food items as potential sources of this outbreak, although no definitive source could be identified. As no further cases had been reported, it was presumed that the source was no longer present. No specific recommendations or preventive measures could be adopted as a result of this investigation.

Role: *Susana was the main investigator. She was involved in initial communication and coordination between municipal health services and national agencies, communication to the weekly alerts meeting and to the ECDC epidemic intelligence system. She developed the case definition, undertook case finding, developed the case questionnaires and coordinated the collection of information, entered and analysed data. She prepared reports for outbreak team meetings and participated in risk assessment. She wrote the outbreak report [14].*

3. Applied epidemiology research

Effectiveness of the DTPa-HBV-IPV/Hib vaccine against invasive *Haemophilus influenzae* type b disease in the Netherlands (2003–2016)

Supervisor: Mirjam Knol

In 2016, an increase in invasive *Haemophilus influenzae* serotype b (Hib) disease was observed in the Netherlands among children younger than 5 years. This coincided with the introduction of the hexavalent diphtheria, tetanus, and acellular pertussis-hepatitis B virus-inactivated polio virus/Hib vaccine (DTPa-HBV-IPV/Hib) from 2011 onwards, replacing the pentavalent DTPa-IPV/Hib. We aimed to estimate the effectiveness of the hexavalent vaccine and to compare it with previously used vaccines, to assess whether this increase could be explained by decreasing effectiveness. We did a case-control study including cases among children under 5 with confirmed Hib infection reported to the Netherlands Reference Laboratory for Bacterial Meningitis (NRLBM), diagnosed between Jan 1, 2003, and Dec 31, 2016. Ten controls from the national vaccination register (*Praeventis*) were selected for each case, matched by date of birth. Vaccination status was ascertained by use of *Praeventis*. We included 159 cases and 1590 controls; 91 (57%) of 159 cases had been vaccinated, compared with 1408 (89%) of 1590 controls. The overall vaccine effectiveness was 92.8% (95% CI 88.7–95.4), with no differences between the year of disease onset. There were no differences by type of vaccine: vaccine effectiveness of the pentavalent and other vaccines was 91.8% (95% CI 86.1–95.1) versus 94.0% (89.0–96.8) for the hexavalent vaccine (OR 0.72, 95% CI 0.36–1.45; $p=0.3591$). Vaccine effectiveness was highest in children aged 1–2 years at disease onset (97.1–99.0%) and was lowest in children aged 3–4 years at disease onset (60.7–82.3%; $p<0.01$). Our results support the current vaccination programme, since Hib vaccine effectiveness has not decreased over time or by the introduction of the hexavalent DTPa-HBV-IPV/Hib vaccine. Vaccine effectiveness was high, but waned with age. Evidence supports the incorporation of the hexavalent vaccine against diphtheria, tetanus, acellular pertussis, inactivated polio virus, and *Haemophilus influenzae* serotype b as part of optimised immunisation schedules.

Role: *Susana wrote the study protocol, analysed the data, wrote the manuscript with input from co-authors [2], and prepared an oral presentation for the conference of the European Meningococcal and *Haemophilus* Disease*

Society (delivered my M.Knol) [15], a poster presentation for ESCAIDE [18], an internal RIVM seminar [22] and a press release [25]. She also collaborated in the Hib chapter of the annual report of the vaccination program [10].

Clinical characterization of cases of *Haemophilus influenzae b* in the Netherlands (2005-2013)

Supervisor: Mirjam Knol

In this nation-wide study in the Netherlands (2005–2013), we described clinical presentation, predisposing factors, disease course, and outcomes of invasive infections caused by Hib, overall and by vaccination status, to better understand the influence of immunization on clinical presentation and disease severity. This information is currently not known in contexts with high vaccination coverage such as the Netherlands. We included 51 cases of invasive disease caused by *Haemophilus influenzae* serotype b reported to the Netherlands Reference Laboratory for Bacterial Meningitis between 2005 and 2013, in cohorts eligible for vaccination (born \geq 1993). Patient records were retrospectively reviewed and vaccination status was obtained from the vaccination register (*Praeventis*). Vaccinated (n = 41) and non-vaccinated (n = 10) cases were similar regarding presentation as meningitis (68.8% vs 90.0%; p = 0.25), predisposing factors (29.3% vs 20.0%; p = 0.76), admission to intensive care unit or death (22.0% vs 10.0%; p = 1.00), or sequelae (21.6% vs 10.0%; p = 0.81). We concluded that in a context with high vaccination coverage, invasive Hib disease still occurs in sufficiently vaccinated and otherwise healthy children and can have severe consequences including fatality and long-term sequelae. However, the low number of cases indicate that invasive Hib disease has become extremely infrequent, underpinning the value of vaccination programs against Hib in the Netherlands.

Role: *Susana analysed the data, wrote the manuscript with input from co-authors [1] and presented a poster at ESCAIDE [18].*

Sero-prevalence of *Campylobacter* and associated risk factors in The Netherlands

Supervisors: Lapo Mughini Gras and Ingrid Friesema

Campylobacter is a major causative agent of bacterial gastroenteritis worldwide. However, most infections are asymptomatic or result in self-limiting episodes of gastrointestinal illness that do not prompt clinical consultation or laboratory investigation. Clinical cases underrepresent the true burden of infection, and may not capture the risk factors for exposure to *Campylobacter*, limiting our understanding of its epidemiology. We aimed to estimate population-level exposure to *Campylobacter* and its associated risk factors through a seroepidemiological survey carried out in the Netherlands in 2006-2007. From 1559 respondents with anti-*Campylobacter* antibodies determination, seroincidence was estimated at 1.61 infections/person-year (95%CI: 1.58–1.64). Exposure to *Campylobacter* in the Netherlands in 2006-2007 was much higher than clinical infection rates. It was higher in females, older ages, those with non-Dutch background and low socioeconomic status, and who reported traveling outside Europe, and eating undercooked meat. Our results show that although clinical cases of *Campylobacter* are more frequent in children, exposure increases throughout life; the development of a certain immunity likely protects adults from disease. Other identified risk factors are similar to those previously described. Our results are broadly similar to those from a decade earlier (1996- 1997), indicating that the infection pressure of *Campylobacter* has not decreased. Updated estimations of the seroincidence will allow to further monitor population-level exposure to *Campylobacter* and to evaluate the impact of interventions.

Role: *Susana analysed the data, wrote the manuscript with input from co-authors [3] and prepared an oral presentation for the International Workshop on *Campylobacter* (delivered by L.Mughini-Gras) [16] and a poster presentation for ESCAIDE [17].*

Presentation of enterovirus E-6 in time, space and phylogeny in The Netherlands: a joint analysis of clinical and environmental surveillance data

Supervisors: Kim Benschop, Erwin Duizer, Jacco Wallinga and Roan Pijnacker

In the Netherlands, ECHOvirus type 6 (E6) is identified through clinical and environmental enterovirus surveillance (CEVS and EEVS). In this study, we aimed to identify E6 transmission clusters and to assess the role of EEVS in surveillance and early warning of E6. We included all E6 strains from CEVS and EEVS from 2007 through 2016. CEVS samples were from patients with enterovirus-like illness and EEVS samples from sewage water. E6 was identified in 157 of 3,506 CEVS clinical episodes, and 92 of 1,067 EEVS samples. Eight phylogenetic clusters were identified; 5 included both CEVS and EEVS strains. Among these, identification in EEVS did not consistently precede CEVS. One phylogenetic cluster was dominant until 2014, but genetic diversity increased thereafter. We identified transmission clusters using a combined pairwise distance in time, place and phylogeny dimensions. Of 14 identified transmission clusters, 6 included both EEVS and CEVS; in only 2 of them, EEVS identification preceded CEVS identification. Algorithms using combined time-place-phylogeny data and are increasingly being used at RIVM. This was one of the test applications of this method and we have shown its added value, since they allowed identification of clusters not detected by a single variable analysis. EEVS identified strains circulating in the population, pointing to its value to

characterise strains causing clinical infections in human populations, and its added value for surveillance of non-polio enteroviruses. However, EEVS samples did not systematically precede clinical case surveillance, limiting EEVS usefulness for early warning in a context where E6 is endemic. Its added value may be higher in the case of non-endemic enteroviruses or in contexts where clinical surveillance is less developed.

Role: *Susana coordinated the working group, defined the study objectives, analysed the data together with Kim Benschop and Loes Soetens, wrote the manuscript [4] with input from co-authors and presented a poster at ESCAIDE [20].*

Genetic variability of *Sarcoptes scabiei* and its potential for outbreak investigations

Supervisor: Ewout Fanoy

Incidence of scabies in the Netherlands increased from 0.6/1.000 in 2012 to 1.7/1.000 in 2016, according to the sentinel system of General Practitioners' consultations. Many municipal public health services become involved in management of scabies outbreaks, mostly affecting elderly citizens in institutions, asylum seekers and students, demanding considerable resources. Despite control measures, cases can reappear long after treatment of the affected group. It is relevant to characterize the disease dynamic driving the increase in sporadic cases and outbreaks, and specifically, to understand whether successive outbreaks can be attributed to persistence of the mite or to new introductions. This would point at failure of the current control algorithms to effectively eliminate mites from outbreak settings. On the other hand, it would be useful to understand whether transmission cycles in university students and elderly belong to separate chains of transmission or are connected. One of the techniques that can help clarify these aspects is molecular typing. While there have been previous studies using sequencing and typing methods to study ecology of *S.scabiei*, it is not clear whether molecular typing methods can be incorporated into scabies control activities, specifically in outbreak investigations. This is relevant for source tracing, detection of additional cases in transmission chains, and to evaluate the effect of interventions. The results from this project, if successful, will be directly applicable to prevention and control of scabies at the population level. Funding for this project was approved and is being currently implemented.

Role: *Susana collected data on cases of scabies in the Utrecht region and performed a background epidemiological analysis. She led the development of a study proposal and its submission for funding [27].*

Evaluating the use of Emergency Medical Dispatch (EMD) data for infectious disease surveillance in the Netherlands

Supervisor: Liselotte van Asten and Wim van der Hoek

Surveillance of severe cases of influenza infection is fundamental to determine the severity of circulating strains, their pressure on healthcare services and the groups most at risk of severe outcomes. Surveillance of severe influenza infections is lacking in the Netherlands. We have explored the usefulness of syndromic surveillance based on ambulance dispatch data to capture the severe end of the ILI spectrum, as well as its ability to reflect the activity of influenza and other respiratory viruses. We analysed data from 4 ambulance dispatch centres covering 25% of the population in the Netherlands. ILI incidence was obtained from the sentinel General Practitioners' based surveillance system. Virus reports were obtained from the weekly sentinel laboratories surveillance system. We found a high background incidence of respiratory complaints motivating ambulance calls that could not be attributed to either ILI, influenza or other respiratory viruses. Although a statistically significant association between respiratory syndromes and ILI, influenza A, and other respiratory viruses was observed, the magnitude of the effects was modest or low. Syndromes in ambulance calls developed between 1 and 3 weeks later than ILI or Influenza A laboratory reports. These results demonstrate the potential of ambulance dispatch centres data for situational awareness, but its value for early warning of the annual influenza epidemic or to detect small-scale variations in severity seems more limited.

Role: *Susana analysed the data and wrote two manuscripts with input from co-authors, one has been submitted for publication and the second one is in draft and will be submitted shortly [5,6].*

Updating the disease burden and associated cost-of-illnesses of *Cryptosporidium* spp. and *Giardia* in the Netherlands

Supervisors: Marie-Josée Mangen, Titia Kortbeek, Roan Pijnacker

Burden of disease (BoD) is increasingly used for setting priorities. Many of the parameters needed to estimate the Disability Adjusted Life Years (DALYs) are not known, or subject to great uncertainty. As new evidence becomes available, the estimates need to be updated. Previous *Cryptosporidium* and *Giardia* BoD and costs estimations accounted only for the acute episode, but disregarded long-term manifestations. We updated the models used for BoD of *Cryptosporidium* and *Giardia*, incorporating recently generated evidence. In the Netherlands in 2017, we estimated that *Cryptosporidium* caused 137 DALYs (95% Uncertainty Interval: 54 - 255) and €19.2 million (95%UI:

7.2 – 36.2) in costs. Results for *Giardia* are provisional. The majority of the BoD was attributable to disability ($\approx 80\%$ of DALYs) and the most important cost was productivity losses ($\approx 90\%$). Long-term manifestations contributed close to 10% of the total DALYs and costs for *Cryptosporidium*. This may be an underestimation, as we were conservative in our assumptions. More accurate estimations can better inform decisions around the appropriate scale of efforts directed to the surveillance, prevention and control. Based on our estimations, *Cryptosporidium* needs to be considered a priority organism with respect to public health surveillance, even in a country like the Netherlands with high hygiene and sanitation standards.

Role: Susana reviewed literature, extracted the data, moderated the expert panels, designed the models with help from Marie-Josée Mangen, and wrote two manuscripts, one for *Cryptosporidium spp* (submitted) and another one for *Giardia* (in draft) [7,8].

Epidemiology and risk factors for sporadic *Fusarium keratitis* in the Netherlands: retrospective descriptive study

Supervisor: Barbara Schimmer

Microbial keratitis (corneal infection) is a rare but serious condition that may lead to permanent vision loss. Contact lens (CL) use is the most important risk factor for non-bacterial pathogens like fungi -such as *Fusarium*- and parasites – such as *Acanthamoeba spp*- in countries with temperate climates. In September 2015, an increase of *Fusarium keratitis* was observed in the Netherlands, which had continued up to 2018. The alert was issued from the Centre of Expertise in Mycology Radboudumc/CWZ. Among all cases detected in the last 10 years, of those with known CL use, more than 95% were CL users. Similar increases have been communicated in other countries such as the UK and Germany. We set up a retrospective case-control study to generate hypotheses about risk factors for sporadic keratitis caused by *Fusarium spp*. and *Acanthamoeba spp*. in the Netherlands, from 2009 to 2018. A working group was formed with epidemiologists, ophthalmologists, microbiologists and CL specialists in order to design the study. Cases are to be identified by cornea specialists from all hospitals in the country and a sample of community controls will be recruited via social media. The study is planned to be launched in mid-November.

Role: Susana participated in the study design, wrote the study protocol [28] and coordinated the development and piloting of the study questionnaire. She implemented the controls questionnaire online and collaborated in the development of study documents and materials.

4. Communication

Publications

1. Monge S, Mollema L, de Melker H, Sanders E, van der Ende A, Knol M. Clinical characterization of invasive disease caused by Haemophilus Influenzae serotype b in a high vaccination coverage setting. J Pediatric Infect Dis Soc. 2018 Mar 22. doi: 10.1093/jpids/piy020.
2. Monge S, Hahné S, de Melker H, Sanders E, van der Ende A, Knol M. Effectiveness of DTPa-HBV-IPV/Hib vaccine against invasive Haemophilus influenzae type b disease in the Netherlands (2003-2016): a case-control study. Lancet Infect Dis. 2018 Jul;18(7):749-757.
3. Monge S, Teunis P, Friesema I, Franz E, Ang W, van Pelt W, Mughini-Gras L. Immune response-eliciting exposure to Campylobacter vastly exceeds the incidence of clinically overt campylobacteriosis but is associated with similar risk factors: A nationwide serosurvey in the Netherlands. J Infect. 2018 Sep;77(3):171-177.
4. Monge S, Benschop K, Soetens L, Pijnacker R, Hahné S, Wallinga J, Duizer E. Echovirus type 6 transmission clusters and the role of environmental surveillance in early warning, the Netherlands, 2007 to 2016. Euro Surveill. 2018;23(45):pii=1800288.
5. Susana Monge, Janneke Duijster, Geert Jan Kommer, Jan van de Kassteele, Gé A. Donker, Thomas Krafft, Paul Engelen, Jens P. Valk, Jan de Waard, Jan de Nooij, Wim van der Hoek, Liselotte van Asten. Use of ambulance dispatch calls for surveillance of severe acute respiratory infections. Submitted for publication.
6. Susana Monge, Roan Pijnacker, Wilfrid van Pelt, Eelco Franz, Laetitia M. Kortbeek, Marie-Josée J. Mangen. Accounting for long-term manifestations of *Cryptosporidium spp* infection in burden of disease and cost-of-illness estimations, the Netherlands (2013-2017). Submitted for publication.
7. Susana Monge, Janneke Duijster, Geert Jan Kommer, Jan van de Kassteele, Gé A. Donker, Thomas Krafft, Paul Engelen, Jens P. Valk, Jan de Waard, Jan de Nooij, Wim van der Hoek, Liselotte van Asten. Ambulance dispatch calls attributable to influenza A and other respiratory viruses in the Netherlands (2014-2016). Manuscript in preparation.
8. Susana Monge, Roan Pijnacker, Wilfrid van Pelt, Eelco Franz, Laetitia M. Kortbeek, Marie-Josée J. Mangen. Accounting for long-term manifestations of *Giardia* infection in burden of disease and cost-of-illness estimations, the Netherlands (2013-2017). Manuscript in preparation.

Reports

9. S. Monge, S. Gouma, N. Rots, C.A.C.M. van Els, P. Kaaijk, W.L.M. Ruijs, R. van Binnendijk, I.K. Veldhuijzen. "Mumps". In: RIVM Report. National Immunisation Programme in the Netherlands Surveillance and developments in 2016-2017. Bilthoven, The Netherlands. 2017.
10. M.J. Knol, A. van der Ende, S. Monge, H.E. de Melker. "Haemophilus influenzae disease". In: RIVM Report. National Immunisation Programme in the Netherlands Surveillance and developments in 2016-2017. Bilthoven, The Netherlands. 2017.
11. Susana Monge and Mirjam Knol (RIVM). Feasibility assessment of setting-up a prospective surveillance system for invasive pneumococcal infections in The Netherlands [Internal report]. 22nd May 2017.
12. Susana Monge. Comparison of Campylobacter reports from LSI and ISIS databases. 21st March 2018 [Internal report].
13. Salmonella Agbeni outbreak report. The Netherlands, 02/03/18 [Internal report].
14. Possible food-related HAV outbreak in the Netherlands. Final Report, 30th April 2018 [Internal report].

Conference presentations

15. Oral presentation at the 14th Congress of the European Meningococcal and Haemophilus Disease Society. Sept 18-21, 2017. Prague (Czech Republic). S. Monge, S. Hahné, H. de Melker, E. Sanders, A. van der Ende, M. Knol. "Vaccine effectiveness against Haemophilus Influenzae serotype b following introduction of Hepatitis B containing vaccine in the Netherlands". Presented by Mirjam Knol on behalf of Susana Monge.
16. Oral presentation at the 19th International Workshop on Campylobacter, Helicobacter and Related Organisms. September, 10-14, 2017. Nantes (France). S. Monge, P. Teunis, I. Friesma, E. Franz, W. van Pelt, L. Mughini-Gras. "Infection pressure by Campylobacter and associated risk factors: a seroepidemiological study in the Netherlands". Presented by Lapo Mughini-Gras on behalf of Susana Monge.
17. Accepted as oral presentation at the 2019 International Society for Disease Surveillance (ISDS) Annual Conference. January 30 to February 2, 2019. San Diego, California. Susana Monge, Janneke Duijster, Geert Jan Kommer, Jan van de Kasstele, Gé A. Donker, Thomas Krafft, Paul Engelen, Jens P. Valk, Jan de Waard, Jan de Nooij, Wim van der Hoek, Liselotte van Asten. Use of ambulance dispatch calls for surveillance of severe acute respiratory infections?
18. Poster presentation at ESCAIDE 2017. November, 6-8, 2017. Stockholm (Sweden). S. Monge, P. Teunis, I. Friesma, E. Franz, W. van Pelt, L. Mughini-Gras. Exposure to Campylobacter and associated risk factors: a comparison of three approaches for analyzing serological data from population-based studies.
19. Poster presentation at ESCAIDE 2017. November, 6-8, 2017. Stockholm (Sweden). S. Monge, S. Hahné, H. de Melker, E. Sanders, A. van der Ende, M. Knol. Vaccine effectiveness against Haemophilus Influenzae serotype b following introduction of Hepatitis B containing vaccine in the Netherlands.
20. Poster presentation at ESCAIDE 2017. November, 6-8, 2017. Stockholm (Sweden). S. Monge, L. Mollema, H. de Melker, E. Sanders, A. van der Ende, M. Knol. Clinical features of invasive disease caused by Haemophilus influenzae serotype b in a high vaccination coverage setting.
21. Poster presentation at ESCAIDE 2018. November, 21-23, 2018. Saint Julian's (Malta). Monge S, Benschop K, Soetens L, Pijnacker R, Hahné S, Wallinga J, Duizer E. ECHOvirus type 6 transmission clusters in the Netherlands and the role of environmental surveillance in early warning.

Other presentations

22. Oral presentation (30 min) at the Internal Seminars of EPI – RIVM (Refereer). "Timing of cART initiation in Male and Female Migrants Living with HIV in Western Europe: an observational cohort study (1997 - 2013)".
23. Oral presentation (30 min) at the Internal Seminars of EPI – RIVM (Refereer). "Effectiveness of DTPa-HBV-IPV/Hib vaccine against invasive Haemophilus influenzae type b disease in the Netherlands (2003-2016)".
24. Oral presentation and discussion (30 min) at the DOD - Dinsdag Ochtend Discussie (Tuesday Morning's Discussion). "Keratitis by *Fusarium* and *Acanthamoeba* in the Netherlands: a retrospective study".

Other

25. Standard Operating Procedure: Surveillance of Measles, Mumps and Rubella by the RVP-EPI [Internal working document]. Lead authors: Irene Veldhuijzen, Susana Monge. 18/01/2017.
26. Justification of the need of a prospective surveillance system for invasive pneumococcal disease covering all ages in the Netherlands [Document for policy makers]
27. Nog steeds hoge effectiviteit van vaccin tegen Hib-ziekte / Continued high effectiveness of vaccines against Hib disease [Press release].
28. EPIET/EUPHEM seminars - concept sheet [Internal document]
29. Wintermans B, Monge S, Pattipeilohy J, van den Hazel A, Trompenaars MC, Braks M, Fanoy E. Genetic variability of *Sarcoptes scabiei* and its potential for outbreak investigations. Format C1b programmabudget: Ontwikkelpoject. [Project proposal for an internal funding call]

30. Retrospective study of epidemiology and risk factors of keratitis by *Fusarium* and *Acanthamoeba* in the Netherlands (FUSACA study) [Study protocol].
31. Susana Monge, Mirjam Knol, Susan Hahné. *Haemophilus influenzae* type b in the Netherlands, 2016 [Draft Case Study]

5. Teaching and pedagogy

Outbreak investigation module of the Master in Infection Control at Netherlands School of Public & Occupational Health - NSPOH

This Master is part of the programme for Medical Doctors that are specializing in Infection Control, and they need to follow it during the first phase of their training. Many of them are working during their traineeship at the Municipal Public Health Services. Alongside with them, independent participants can join in for specific modules. In total is a group of around 15 people. The objective of the outbreak investigation module is for participants to understand how general epidemiological methods are applied in the context of an outbreak investigation, as well as specific methods used in such investigations, and to be able to adapt and apply these tools to particular situations. For the 2016/2017 edition of the Master, Susana delivered a lecture on "Methodology of investigating outbreaks and epidemiological curves" and facilitated the case study "Giardiasis in Bergen" (7th February, 6h). For the 2017/2018 edition she delivered two sessions, one with a theoretical lecture on "Study designs for outbreak investigation" and the case study "Epidemic of trichinosis in France" (6th February, 6h), and another one with a theoretical session on "Confounding and effect modification" and the case study "Oysters and alcohol" (6th March, 6h). Formal evaluation of all the sessions, as carried out by the NSPOH, was satisfactory.

Reflection: The materials for these sessions were already prepared and standardised. However, because the audience is already familiar with basic epidemiological concepts, some more examples were added to try to make it more interactive. This was positively evaluated and I felt it helped to keep the group engaged, but my own lack of experience in outbreak investigations made it difficult to illustrate more concepts with real-life examples. For the case studies, it was very positive to allow the group to discuss and the tone of the discussions were very constructive and cooperative. However, as a facilitator, I found it challenging to keep the balance between allowing the group to arrive to their own conclusions based on their judgement and guiding them in the correct direction. I felt it was a great learning experience for the participants and for myself.

Vaccine-preventable diseases at the Leiden University

This was a lecture (22nd May 2018, 2h) part of a communicable diseases module that was optional within the Bachelor in Global Health of Leiden University (The Hague). The audience were around 10 students from this Bachelor, with some background on health sciences. The objective for the session was to familiarize participants with some of the diseases that are preventable through vaccination as well as to introduce some epidemiological concepts specific to this group of diseases. During the session, we covered different objectives in VPD control, from eradication to elimination and control, and used selected examples to illustrate selected general principles in VPD epidemiology.

Reflection: The group was mostly engaged and had a lot of questions; while going through the lecture, I realized that it was difficult for them to follow at some points because of the density of information. Because we stopped for questions and discussions, it was not possible to finish the material. Given the junior audience, I realize it would have been preferable to further reduce the amount of information and spend more time in going through the examples and allowing for even more interaction and discussion.

EPIET seminars

RIVM hosts annually between four or five EPIET/EUPHEM fellows, two to four EPIET/EUPHEM supervisors, one EPIET coordinator and employs a number of EPIET alumni. This brings great learning opportunities through the exchange of experiences and feed-back. For this reason, Susana proposed the organization of internal EPIET seminars. She explored within the group which aspects would be more interesting to discuss and the best duration and periodicity for these sessions. It was established as 1h-duration seminar every 6 weeks or so, in which fellows would provide updates of their ongoing projects, discuss upcoming opportunities for new projects or outbreaks and then, in rotation, one fellow would present more in depth one of their ongoing projects. A concept sheet was circulated with the invitations to participate [26].

Reflection: EPIET seminars have an added value for the fellows training at RIVM, and this has been informally expressed by the fellows in different occasions. So far it has been a very useful forum to exchange experiences and for team-building, and will hopefully facilitate increasing collaboration between fellows. It is a good training as well for presenting and discussing ongoing projects, and for practicing giving and receiving feed-back.

Development of a case study: Haemophilus influenzae type b in the Netherlands

The project on vaccine effectiveness for Hib was a very good learning opportunity for Susana, and together with her supervisors, they identified that this was an opportunity to develop training materials targeted at EPIET fellows, in particular a case study. They explored with EPIET coordinators the need of such case study and the best focus and aims for it. It was decided that the case study would review some aspects of vaccine preventable diseases epidemiology, study designs and data analysis, using two by two tables, and then move to analysis of confounding and effect modification as new topics to practice. It has been designed to follow theoretical presentations on confounding and effect modification during the introductory course. The draft has been circulated for review.

Reflection: Identifying the learning value of projects during EPIET allows fellows to use their experience to support training others. A case study addressing the common issues of confounding and effect modification by age, would be a good addition to help incoming fellows gain familiarity with these concepts and how to handle confounding and effect modification in epidemiological analysis.

6. EPIET/EUPHEM modules attended

1. Introductory Course, 26 Sep-14 Oct 2016, Spetses, Greece
2. Outbreak Investigation Module, 5-9 Dec 2016, Berlin, Germany
3. Multivariable Analysis Module, 13-17 Mar 2017, Zagreb, Croatia
4. Rapid Assessment and Survey Methods Module, 8-13 May 2017, Athens, Greece
5. Time Series Analysis Module, 20-24 Nov 2017, Bristol, England
6. Vaccinology, 11-15 Jun 2018, Cardiff, Wales
7. Project Review Module, 27-31 Aug 2018, Lisbon, Portugal

7. Other training

RIVM offers continued training of all staff through bi-weekly scientific seminars and epidemiology master classes, which Susana has attended regularly. She also participated in specific scientific events, such as the RIVM vaccine-preventable diseases research day. She followed a self-directed course on "Modern Methods for analysing serology data", for methods she applied in one of her projects. Finally, Susana has regularly attended the weekly alerts meeting, which has provided training on event evaluation and communication.

Susana was also placed at the Municipal Health service in Utrecht for two days a week for three months, where she trained in case management, followed numerous case reports, participated in discussions on control measures, and accompanied field work to respond to an outbreak of scabies in a nursing home.

Formal trainings in which she has participated include:

- On-line ECDC course: Writing and Reviewing Scientific Abstracts: a field epidemiology focus 20/04 – 08/05/2017
- Use R [Gebruik-R]. Course for basic training in use of R software for data analysis (7 hours). 09/02/2018.
- Exp R. Course on advanced training for programming in R software (7 hours). 16/02/2018.
- Vis R. Course on elaborating graphs and maps using R (7 hours). 25/06/2018.
- Rapid Risk Assessment (Pilot course, 5h). 15/11/2018. Followed the course and provided feedback as part of the pilot.

Discussion

Supervisor's conclusions

Susana arrived at RIVM with already many skills in epidemiology and with a very professional and efficient working style. At the start, we were somewhat concerned whether the two-year fellowship at RIVM could add to developing new competencies. Due to Susana's enthusiastic and hard-working approach, however, I think she managed to have a very fruitful fellowship. She developed several new competencies: getting acquainted with a number of new infectious diseases, a number of new analytical skills, a number of new approaches (surveillance, outbreak investigation, burden of disease assessment), and a number of new settings (RIVM and the regional health service). The output of her two-year stay with RIVM is extraordinary, both in terms of quantity and quality, and I would like to thank her for this and for our work meetings which always provided me with some new perspectives.

Coordinator's conclusions

Susana came to the fellowship as a skilled public health professional, and has demonstrated extraordinary productivity in completing diverse projects with many collaborators within RIVM and in the municipal health authority. She has actively pursued opportunities to develop her analytical skills in new areas and has been able to contribute to scientific knowledge via publication and presentation in several venues. Susana has also shown her capacity in project management, both in steering multiple fellowship projects but also managing her long-distance family life while based in the Netherlands. She has demonstrated leadership in organizing a seminar series among EPIET/EUPHEM fellows at RIVM, and commitment to contributing to the learning of others by leading the development of a case study based on her work.

Personal conclusions of fellow

Participating in the EPIET Fellowship placed at RIVM has been a privileged training opportunity. I have had the chance to work in varied areas, from vaccine preventable diseases, to gastrointestinal or respiratory infections, each of them having their own internal logic and ways to apply the common epidemiological methods. This is a rarity, since when working at National Institutes it's more usual to be confined to a specific topic, especially in my case, with my previous research background. Being able to gain experience in so many different areas has given me a much broader understanding of the practice of epidemiology and has been a highlight of the experience.

The projects I have been involved with have put me in contact with new epidemiological methods and new software, which I value greatly as new knowledge and skills. But very importantly, they have put me in contact with a wide range of professionals from whom I have learned to think as an epidemiologist, to make the relevant questions and to find the better answers. I particularly value how much I have learned through my projects in surveillance and through outbreak investigations, areas that were mostly unknown to me before EPIET and that have been positively challenging.

RIVM has been a great training site, and has given me so many learning opportunities that I can't even grasp how much I have evolved professionally in these two years. I have also been really dedicated to the fellowship, and I only hope I leave behind at least half of what I bring home with me. This has been a great training and I leave equipped with a vision, a mind-set, a logic and the methods that I believe will be the stepping stones for my future professional development.

Acknowledgements of fellow

I first and foremost would like to thank my site supervisor Susan Hahné for the fantastic support she has given me throughout my fellowship, both professionally and personally. She has always been ready to share facts and explanations, has always provided valuable feed-back to my work and has dedicated me quantity and quality supervision time. At the personal level, the EPIET fellowship has been a challenging period, living apart from my husband through a pregnancy and the first year of life of our son. The needs for conciliation of work and family life resulted in out-of-the ordinary situations and Susan was always supportive and facilitated solutions. I don't know if I would have been strong enough to finish my fellowship without this.

Very importantly, I want to acknowledge my husband, who supported me happily in this professional step and never doubted that, whatever the challenges, they were worth it; my mother, without whose help this whole house of cards would have collapsed; and last but not least, my son, who stole from me so many hours of sleep, but who has given me so much energy to keep going.

I want to thank all the people at the EPI Centre of RIVM, who made me feel welcome and part of the big team from the first day. Special thanks to my project supervisors, who have given me the opportunity to work in projects that were interesting and with great learning values, shared long discussions and long email threads, and who, in

some cases, became friends in the process. But beyond them, the open-doors general attitude at RIVM has given me access to a wide range of knowledgeable professionals who were always ready to share their time, think along with me, and include me in interesting discussions, and this list could get very long! Thank you all for your generosity.

I thank of course the EPIET fellowship for selecting me and for running this wonderful programme. My two front line coordinators Marion Muehlen and Lisa Hansen, for their oversight of the progress; all the coordinators and facilitators we have had during the modules, who have reshaped my mind in many aspects and have helped me understand epidemiology from a wider angle; and the EPIET office, who were there for all the administrative support. You make a great programme and I hope you can continue giving this opportunity to many generations of future epidemiologists.

And finally, I want to thank my fellow fellows, who have travelled with me in this strange journey and from whom I have also learned a lot throughout module sessions, shared meals, mountain trekkings, cruise trips, beers and dances. It will be a pleasure to cross paths with you again along the way.