D6.10: Report on Short Term Missions 2020 (Y3)

Work Package 6

Responsible Partner: UoS, UK (P23)

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REPORT ON SHORT TERM MISSIONS Y3

Introduction

Short Term Missions (STMs) are small co-funded travel grants which offer and exchange scientific expertise, methodologies, equipment, and facilities to our consortium members. The aim of these missions is to harmonise the existing approaches and methodologies within the One Health EJP (OHEJP).

These STMs drive research forward in a collaborative and non-duplicative fashion to strengthen the scientific capacity within the OHEJP, and to also contribute to the future prevention, preparedness, detection, and response of the EU to foodborne and other emerging threats across human-animal-environmental sectors.

The OHEJP is able to co-fund up to ten STMs each year (each funded 44% by the EU). The Education and Training activities team in Work Package 6 (WP6) are responsible to co-ordinate the call, selections and reporting of the short term missions funded each year.

Short Term Missions 2020 call

The call was launched on 30th May 2019, and a promotional email marketing strategy was used to disseminate the call information to the Scientific Steering Board (SSB), Project Management Team (PMT), Progamme Managers Committee (PMC), Project Leaders, PhD teams, and Communication Contact Persons. The email was visually attractive and incorporated a branded launch infographic and branded text.

The email contained instructions on how to join the 'Call for Short Term Missions 2019' group on the private space of the website, where they could download the guidelines, application form and templates. Readers were asked to forward the email to those in their institute who may find it useful.

The launch of the call was also disseminated on the Education and Training Open Calls page of the website in the form of call flyers containing interactive links to the guidelines and application forms. This page was promoted in the Education and Training activities monthly bulletins, the OHEJP consortium newsletter, and social media channels, Twitter and Linkedin, to increase traffic to the website.

The call was open for three months until 30th August 2019.

Selection of Short Term Missions

The WP6 Team co-ordinated the call and selection of the STMs to take place in 2020 following the validated procedure which involves the following steps:

Applicants completed the STM application form, and were strongly encouraged to compile the following documents with the main application: a detailed work plan, financial budget template, letters of recommendation from the home and hosting institute, Curriculum Vitae, and finally a list of publications (if applicable). After the deadline closed on 30th August 2019, the WP6 Team performed an eligibility check with pre-determined eligibility criteria.
Eligibility criteria included that only scientific staff from, and PhD students based at, the partner institutes of the OHEJP were eligible to apply. STM applications were only considered if they related to the key OHEJP priority areas: One Health Missions- Veterinary, Food, Medical and or Environmental research; skills development missions (e.g. genomics, bioinformatics, big data epidemiology); exchange with researchers, policy makers, and risk managers to complement WP5- Science to Policy translation; risk research; integration of microbiological, risk assessment and surveillance activities; and finally, harmonisation of diagnostics tests, platforms and research. There was no limit for the duration of the STM, as long as the funds requested adhered to the OHEJP budgetary rules, and STMs could take place between Jan and Dec 2020.

Each application and supporting documents were sent to three independent reviewers from within partner institutes, who also completed a signed declaration of confidentiality and a conflict of interest statement. The reviewers were nominated by the SSB.

The WP6 Team compiled and reviewed the scores, detecting and resolving any typographical or administrative errors before submitting to the PMT. The 5 applications submitted were all eligible and of high quality. WP6 suggested a decision to PMT based on the actual comments of reviewers and list of missions recommended for funding. This decision to fund the 5 missions was approved by the PMT.

The final decision was then communicated to the SSB and applicants, and published on the OHEP website on a dedicated webpage for Short Term Missions 2020- https://onehealthejp.eu/short-term-missions-2020/.

Impact of COVID-19

Two of five STMs previously selected for funding still went ahead in 2020 before the COVID-19 travel restrictions were enforced. WP6 monitored the progress of these

missions through the individual reports submitted, and unsurprisingly, the expected outputs of both missions were impacted by the COVID-19 pandemic. The details can be found in the individual reports.

The pandemic also significantly impacted the success of the remaining three missions selected for funding. Two of these three missions were postponed for later in the year, and the last mission was cancelled as the 'new' timing of the training no longer fitted in with the planned work.

Short Term Missions

2. Short Term Mission 1

2.1. Short Term Mission 1 Report

Study of the interactions between STEC and human gut microbiota in the ARtificial COLon (ARCOL) model

Name of applicant	Paola Chiani
Institute of Affiliation/ Contact information	Institute: Istituto Superiore di Sanità Address: Viale Regina Elena 299 00161 Roma
Host institute and names of scientists involved in STM	Université Clermont Auvergne,UMR 454 MEDIS, Microbiologie Environnement Digestif et Santé Stéphanie Blanquet-Diot, PhD, Associate professor Lucie Etienne-Mesmin, PhD, Associate professor
Dates of STM	5th February -12th March 2020
Call Topic	Understand the role played by the human intestinal microbiota upon STEC infection
Research Domain	Dynamics of Microbial populations

Key aims of STM or Workshop	Shiga toxin-producing *E. coli* are zoonotic pathogens, that may cause severe afflictions in humans, including uncomplicated diarrhoea, haemorrhagic colitis, up to the life-threatening haemolytic uraemic syndrome (HUS). The different clinical demonstrations appear to be linked to a number of factors, counting the age of the patient, the host immune status and the interaction of the infecting strains with the intestinal microbiota. Indeed, bacterial species inhabiting the human intestine can interfere with STEC in colonizing the gastrointestinal tract. On the other hand, commensal bacteria may influence the severity of disease and amplify the production and release of the Shiga toxin by offering a susceptible bacterial population for the Stx-phage amplification. The aim of this study was to investigate the interactions between STEC and human intestinal microbiota, using the ARtificial COLon (ARCOL), which simulates the human large intestine functionality. In detail, the aim of the STM was to perform in vitro infection experiments with STEC in presence of a normal human intestinal microbiota using this innovative model in order to understand the role played by the human intestinal microflora upon STEC infection, and to investigate changes occurring in the gut microbiota composition in presence of infecting STEC strains.
Impact and relevance of scientific mission	In this project we used the ARCOL system to investigate the interactions between STEC and commensal bacteria inhabiting the human intestine, upon infection. The hypothesis is that certain microbial species can compete with STEC avoiding their efficient colonization and consequently hindering the progression of the infection towards the most severe clinical manifestations in human patients. The ARCOL is an innovative model which reproduces *in vitro* the characteristics of the luminary environment of the human intestine, including pH, temperature, ileal effluents and anaerobic conditions. For the present study, we selected faecal samples from healthy volunteer donors, one from an infant and the other from an adult, as providing the whole gut micriobiota to the ARCOL system. We developed detailed and specific protocols to set-up the model in order to simulate the intestinal conditions of subjects belonging to the considered age groups. The experiments have been conducted using two different STEC strains, but they opened the way to the possibility to perform further studies selecting other STEC clones whose impact on public health is not completely understood. A better understanding of the variations in the microbiota composition in presence of infecting STEC strains would be of help in unravelling the roles of commensal bacteria as well as in designing strategies for the possible treatment to re-establish the beneficial species and reduce the clinical manifestations in the patients

Moreover, such scientific mission allowed to collect all the relevant data produced and the protocols developed, preparing the way to the reproducibility of these experiments in order to study the dynamics establishing in the host intestine during intestinal infectious diseases caused by enteropathogens other than STEC.

Benefits to OHEJP

The aim of the visit consisted in the study of the zoonotic pathogens STEC, especially in understanding the role played by the human intestinal microbiota upon STEC infection.
The samples produced and collected during this STM will be sequenced and analysed though an enhanced and innovative shotgun metagenomic approach, leading to the identification of a possible unbalance in the taxonomic units of the gut microbiota. This may either be a response of commensal bacteria to the interaction with the STEC strains or a general adaption of the intestinal microbes to the colonization by the pathogen.
The results of this work would provide a good starting point for the execution of future projects, with the main objective of developing non-pharmacological approaches to mitigate the burden of intestinal infections. This is particularly interesting for STEC as the antibiotic treatment is not recommended for the treatment of the infections, which mainly relies on prevention and supportive therapy. All of the results of this STM and of this project in general will be important to complement the knowledge present in the OHEJP on the use of artificial models to study the dynamics of infections with zoonotic pathogens, providing an opportunity for setting up new studies encompassing all the domains and themes of the OHEJP matrix

Summary

Shiga toxin-producing *E. coli* are zoonotic pathogens, causing severe afflictions in humans. Upon STEC infection, the host can present a wide range of symptoms including uncomplicated diarrhoea, haemorrhagic colitis and the life-threatening haemolytic uremic syndrome (HUS). The aim of this work was to investigate the interactions between STEC and human intestinal microbiota, during experimental infection using the ARtificial COLon (ARCOL) model, which simulates the human large intestine functionality.
The realization of this project was possible thanks to the collaboration with collegues from the Université Clermont Auvergne, in Clermont-Ferrand, which developed the model. ARCOL reproduces *in vitro* the characteristics of the luminary environment of the human intestine, including pH, temperature, ileal effluents and anaerobic conditions and can be loaded with human intestinal microbiota. The system allows mimicking a luminal and a mucosal phase, the latter being simulated by filling a segment of the bioreactor with mucin beads. For our experiments, we selected faecal samples from healthy volunteers, an infant (1.5 years old female) and an adult (37 years old male) to act as microbiota donors and used two STEC strains carrying different virulence features (positive or negative for the Locus of Enterocyte Effacement, LEE) and a commensal *E. coli* as infecting strains.

We used three different bioreactors per age group, challenged with a different *E. coli* strain each and collected daily samples from the luminal and mucosal phases up to 8 days post-inoculum. We performed for each sample SCFA analysis and total DNA extraction for the following metagenomic sequencing. Moreover, we analysed every day the composition of the gases from the atmospheric phase.
During the STM all the parameters to simulate the proper conditions for the ARCOL model of the intestine of subjects belonging to the considered age groups were determined and all the samples were collected for the following analyses. Some interesting preliminary results displaying difference between the different experiments could already be observed. We determined that the bioreactor containing the infant microbiota infected with the LEE positive STEC produced a greater volume of gas and that the same intestinal microbiota infected with both commensal *E. coli* and the LEE positive STEC displayed a higher amount of nitrogen in the gas composition. Moreover, the sodium hydroxide (NaOH), used to compensate acid pH, appeared more consumed in both the adult and infant bioreactors containing the LEE+ STEC. Finally, we observed a lesser mucin volume in the bioreactor containing the infant microbiota challenged with the commensal strain. These preliminary results will be complemented with the information on the taxonomic profiling of the gut microbiota obtained through metagenomics upon my return to the home institution and will possibly disclose the dynamics occurring in the intestinal microbiota composition and in the metabolic pathways in the course of infection with STEC. Additional samples have been collected to study the dynamics of the Stx phages populations. Enumeration of the phages will be used to assess whether certain microbiota could act as amplifiers for the Stx-phages.

Technical Report

The different clinical demonstrations that can occur in the human host upon STEC infection, have been proposed to be linked to a number of factors including the STEC strain's features, the age of the patient, the host immune status and the interaction of the infecting strains with the intestinal microbiota. Indeed, commensal bacteria can interfere with the ability of STEC to efficiently colonize the gastro-intestinal tract. Additionally, microbial species of the host microbiota can act as amplifiers of the Stx-converting phage resulting in an augmented ability to produce the toxin and, consequently, in the development of the most severe forms of the infection.
The aim of this work was to investigate changes occurring in the gut microbiota composition and metabolic activity in experimental infections of an artificial colonic model (ARCOL) mimicking the intestinal microbiota of subjects belong to two age groups, infant and adult. The time course of the infections was studied at different times following the challenge with STEC. Part of the study was devoted to assess the capability of intestinal microbial species to acquire and amplify phages carrying the *stx* genes in presence of STEC strains.

The project was based on the use of the ARtificial COLon system (ARCOL) available at the Universitè Clermont Auvergne. ARCOL is a one-stage fermentation system (Applikon, Schiedam, The Netherlands) that integrates the main parameters of the *in vivo* human colonic environment, including pH, temperature, supply of ileal effluents, retention time and anaerobiosis maintained by the sole activity of the resident microbiota, added to the

system through the administration of faecal samples. In detail, each experiment involved faecal specimens collected from two healthy volunteer donors, who had no history of antibiotic or probiotic treatment in the last month before the beginning of the experiment: one was from a female infant 1.5 years old; the other was a male adult 37 years old. As the study was classified as non-interventional, with no additions to normal clinical care, according to the French Health Public Law (CSP Art L 1121-1.1), the protocol did not require approval from an ethics committee.

The hypothesis was that the observed different clinical manifestation occurring in children and adult, upon STEC infection, may due to a different gut microbiota composition between these two age groups. Indeed, a significant shift in the composition of the gut microbial community occurs with the infant transiting to a more solid and varied diet, estimated at around 2.5 years of age. It is commonly accepted that the diversity and functional capabilities of the infant microbiota evolve towards an adult-like configuration, after that age. During the STM the experiments focused on the infant model and use the adult as comparison sample.
We selected three *E. coli* strains among the ISS collection, to be used in the infection experiments, including:

1. ECOR1, a commensal *E. coli* strain (1), in order to provide a control strain with no pathogenetic features;
2. ED1014, STEC strain of O26:H11 serotype, which represents the most prevalent STEC serotype in human infections occurring in Italy. In particular, we considered for this study the STEC O26:H11 strain that caused an outbreak in 2015 in a nursery in the province of Rome (2). Indeed, we already conducted a preliminary study where stool samples from the outbreak cases were subjected to metagenomic analysis, with the aim to investigate the taxonomic composition of the gut microbiota, either in presence or in absence of STEC infection (3).
3. ED0230, STEC strain of O113:H21 serotype that does not possess the locus of enterocyte effacement (LEE), in order to evaluate the capability of a LEE-negative STEC strain to efficiently colonize the intestinal tract, thus investigating possible changes occurring in the gut microbes population.

Each experiment comprised the following step:

- One week was spent for the preparation of the ARCOL system. During this time we set up the system in order to simulate the intestinal conditions of subjects belonging to the considered age groups (infant or adult), with an external compartment simulating the colonic mucosal phase. In detail, the bioreactor was assembled and prepared for the infant model. The preparation included the assembly of the nutrient compartment for the microbiota to be fed, the segment with the mucin beads for the mucosal phase present and the determination of the the chemicals parameters of the bioreactor, which were optimal for the infant model.After this first phase, the faecal sample from infant was introduced in the system.

  During this first week it was very important maintain constant all the parameters through daily check of the nutrient weight, the sodium hydroxide weight, the gas

composition, through gas chromatography analysis, and the volume of expelled gas. Adjustments were made when necessary.
We collected samples for the following analysis prior to inoculation with the challenge strain, directly from the fresh faeces and immediately after inoculation into the bioreactors.

- Following a stabilisation phase, which lasted one week, the three *E. coli* strains were administered into three different bioreactors.

- We collected samples after 3h, 6h. 9h and 12 h from the *E. coli* inoculum. After the first day, we collected samples from each bioreactor daily, only one time point a day, up to 8 days from the inoculum. Samples were collected from both the luminal and mucosal phase and centrifuged. The supernatant was used for the test of the cytopathic effect onto Vero cells monolayers and for SCFA analysis, and the pellet was subjected to DNA extraction for the following metagenomic study. The DNA was extracted using the MO BIO PowerSoil™ DNA Isolation Kit, Qiagen, and stored at -20C°. The DNA was also extracted from fresh faeces, before the introduction in ARCOL, and from the fermentation medium collected at the end of the stabilisation phase, before the *E. coli* inoculum. Gas from the atmospheric phase was also collected and analysed every day.

At the end of the experiments, the bioreactor was cleaned and a HPLC analysis was performed the to test the SCFA present in the supernatant of the bioreactor's content. Additionally, analyses on the gas phase, nutrient consumption and mucin consumption were also carried out.

All the samples were collected and treated during the STM and eventually stored under proper conditions. The supernatants have been filtered and stored at 4°C, while the nucleic acids have been stored at -20°C. All the specimens will be sent to the ISS once the COVID-19 crisis will allowit and subjected to the assays that had been previously planned. In detail, we will perform the cytotossicity assays by inoculating the supernatant of the artificial intestinal content onto Vero cells monolayers to observe and titrate the effect of the free Shiga toxin. On the same samples the presence of free Stx phages will be detected and the phages enumerated. This part of the work will be carried out by the group of Prof. Maria Teresa Muniesa Pérez, Department of Genetics, Microbiology and Statistics (University of Barcelona, Spain). Finally, the extracted DNA will under go to shotgun metagenomic sequencing at ISS for the identification and quantitation of the taxonomic units. On these samples, the connection between the Stx-coding genes and the bacterial species harbouring them will be attempted using a bioinformatic algorithm developed during a previous collaboration between ISS and the University of Utrecht (3).
Such an approach allows the reconstruction of putative draft genomes, obtaining a depth overview of the species composition of the microbiota and of the related virulence traits.

References

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List of dissemination and communication activities

The intention was to present the activities during the STM supported by the OHEJP during the Annual Meeting of the National Reference Laboratories for *E. coli,* (23-24 Septemer 2020 hosted by the ISS institute, Italy). However, the situation of this pandemic led to the meeting being delivered as a virtual event and also saw the reduction of time available for interventions, and so the awardee is still waiting to present the activities of the STM.

Scientific outputs

The major output expected from this project are scientific papers published in peer reviewed journals and communication of the results at workshops and conferences. Additionally, new projects could stem from this piece of work consolidating and possibly expanding the scientific consortium within the OHEJP.

Testimonial

The experience of this STM was very formative for my career. Indeed, the project involved the use of the innovative ARCOL system, which is not present in Italy, and actually is only present in a few institutes in the whole world. As a whole, the concept of this study represents an innovative way to explore the dynamics of microorganisms in the course of infections, particularly for those pathogens, as STEC, for which an animal mode is not available or not ethically feasible. I'm therefore grateful to have had the occasion to visit this excellence centre and to acquire a skill in the use of such model and of such a holistic approach to the study of the STEC-induced disease, which was not previously available at the home institution. Additional value to this experience also consisted in the opportunity to spend time and to share information and knowledge with scientists and lab's staff, who have been working on this model for many years and I'm thankful to them for their willingness in sharing their expertise with me, eventually improving my skills as well as professional, personal and human relationships.

2.2. Short Term Mission 1 Case study

SHORT TERM MISSIONS

Short Term Missions (STMs) are small travel grants with the aim of:

- Sharing scientific expertise, methodologies, equipment and facilities to harmonise the existing approaches and methodologies within the large OHEJP European network
- Driving the research forward in a collaborative and non-duplicative fashion to strengthen both the scientific capacity within the OHEJP
- Contributing to future prevention, preparedness, detection and response of the EU to foodborne and other emerging threats across human-animal-environmental sectors.

Study of the interactions between STEC and human gut microbiota in the ARtificial COLon (ARCOL) model

Theme: Skills Development Missions
Home Institute: Istituto Superiore di Sanità (ISS), Italy
Mission Hosting Institute: Université Clermont Auvergne, France
Duration of mission: 5 weeks

Shiga toxin-producing E. coli (STEC) are zoonotic pathogens, causing severe afflictions in humans. Upon STEC infection, the host can present a wide range of symptoms including uncomplicated diarrhoea, haemorrhagic colitis and the life-threatening haemolytic uremic syndrome.

The aim of this mission was to investigate the interactions between STEC and human intestinal microbiota, during experimental infection using the ARtificial COLon (ARCOL) model, which simulates the human large intestine functionality. During the STM all the parameters to simulate the proper conditions for the ARCOL model of the intestine of subjects belonging to the considered age groups were determined and all the samples were collected for the following analyses.

The realisation of this project was possible thanks to the collaboration with colleagues from the Université Clermont Auvergne, in Clermont-Ferrand who developed the model, and hosted the mission.

...The experience was very formative for my career. It involved the use of the innovative ARCOL system, which is not present in Italy, and only present in a few institutes world wide. I'm grateful to have visited this excellence centre and to acquire a skill in the use of such model and of a holistic approach..."
Paola Chiani, ISS

One Health EJP has received funding from the European Union's Horizon 2020 research and innovation programme under grant agreement No 773830.

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Figure 1: This case study can be found on the OHEJP website: https://onehealthejp.eu/short-term-missions-2020/

This meeting is part of the European Joint Programme One Health EJP.
This project has received funding from the European Union's Horizon 2020 research and innovation programme under Grant Agreement No 773830.

2. Short Term Mission 2

Cross-Domain and Cross-Country Collaboration to Develop Multivariate Syndromic Surveillance

2.1 Short Term Mission 1 Report

Name of applicant	Wiktor Gustafsson
Institute of Affiliation/	Institute: Swedish National Veterinary Institute
Contact information	Address: Statens Veterinärmedicinska Anstalt 75189 Uppsala Sweden
Host institute and names of scientists involved in STM	Norwegian Institute of Public Health: Gry Marysol Grøneng, Gunnar Øyvind Isaksson Rø
Dates of STM	24th February – 6th March 2020
Call Topic	Cross-Domain and Cross-Country Collaboration to Develop Multivariate Syndromic Surveillance
Research Domain	Food borne zoonoses
Key aims of STM or Workshop	• Collaboration and knowledge exchange across countries and domains • One-Health application of syndromic surveillance methods
Impact and relevance of scientific mission	This mission is a collaboration across domains (animal and public health), across countries, and will result in the production of analysis codes that will be shared publicly. In the specific context of automated data monitoring, and detection of early signals of disease occurrence, this mission is an opportunity to advance OH surveillance.
Benefits to OHEJP	NIPH and SVA are leaders of efforts, in public health and animal health respectively, in the implementation of automated data analysis and early detection of unexpected disease trends (syndromic surveillance – SyS). A direct collaboration between these institutes, and exchange of expertise, will allow the development of methods that can extend SyS to One-Health.

Besides allowing this cross-domain sharing of expertise, the collaboration will also ensure that state-of-the-art expertise, within the EU, is gathered to develop a proposed OH syndromic
surveillance system that can, through the OHEJP consortia, be adopted by other European MS.

Summary

During this short-term mission (STM) I visited the Norwegian Institute of Public Health (NIPH). The aim of the STM was collaboration and knowledge exchange between Norway and Sweden in the development of One Health systems for multivariate syndromic surveillance (SyS) of veterinary and public health data combined. Two separate systems are in development in Sweden and Norway by the Swedish National Veterinary Institute (SVA) and the NIPH, respectively. The Swedish system is *explanatory*, aiming to combine several data sources to explain outbreaks and improve the accuracy of detection. Norway, on the other hand, is developing a *predictive* system, which aims to use some source(s) of data to predict the outcome of others. As a test case, both systems are being evaluated on the surveillance and outbreak detection of *Campylobacter* in humans, using data from public health, broiler chicken and weather.

The idea was that the work of this mission would be divided into three phases: (1) presentation and summary of the data and methods available and in development at the two institutes, as well as preliminary results from the countries' respective *Campylobacter* surveillance; (2) a practical phase where I, in communication with the responsible scientists at the NIPH, would test the two systems on each other's data, to compare outputs and evaluate the usefulness of each system in our different contexts; and (3) a conclusion phase, where we would summarise the work done during the STM and plan for the future.

Due to the COVID-19 pandemic, the employees at the NIPH had additional workload which modified the focus of the STM. A significant acheivement was to run Norwegian data through the Swedish surveillance system and evaluate the results. This resulted in a summary document, which provides an overview and comparison of the data and methods currently available in both countries. Further follow up with public health colleagues is planned when possible, to maximise future benefits from the STM.

Technical Report

Tasks Performed

As previously mentioned, the work of this STM became limited in scope since the colleagues at NIPH needed to focus on the ongoing COVID-19 situation. In essence, I was able to perform two distinct tasks:

1. Reviewing and comparing the systems for multivariate SyS in development in the respective countries, as well as the types of data available for analysis in the *Campylobacter* test case, and writing a report on my findings to use when planning future collaboration.
2. Accessing the Norwegian data sources, adapting them to the Swedish context, and running them through our SyS system, to verify that the system can be run on new data and to compare the preliminary results for each country.

There was an initial aim to give NIPH access to the Swedish data as well, but that has been left to the future.

Results

Comparison of Methods and Data

Here follows a summary of the currently existing methods and data in the two respective countries. This summary is copied from the document I produced on-site during the STM. It will be used as a reference in the future to decide on how to proceed with our cooperation.

Methods

The NIPH is developing a system for *predictive* surveillance, i.e. using one or more data streams to predict the outcome of others. They aim to investigate if data from surveillance of chicken and weather can improve the surveillance and increase the accuracy of prediction of future *Campylobacter* case counts in humans. A quasi-Poisson regression model, accounting for seasonality, time trends and holiday, is used in combination with animal cases, rain and temperature data to calculate a prediction of the number of human cases one week ahead. A multivariate energy scoring function will be used to evaluate the quality of predictions.

In contrast, the system in development at SVA is an *explanatory* surveillance system, where several sources of data are weighed together to produce a single prediction for the combined data. A regression model of suitable distribution is fitted to each data stream, and this model is used to, for each time point, calculate a Bayesian likelihood ratio, also called a "value of evidence" (V) which measures the likelihood of the data under the

assumption of an outbreak. To determine V, one needs to define one or several disease profiles that connect to the disease or group of diseases of interest – that is, for each data stream there is a predefined expectation of how the data would behave in event of an outbreak. A large V value speaks in favour of an event that matches the outbreak profile in question, while a smaller value would speak in favour of baseline conditions. A single V for the whole system can be obtained by simply adding together the separate values, or combine them using a multivariate normal distribution based on the covariance between the data streams – the latter assumes a correlation between the variables.

Data

Both systems will initially analyse data of three categories: chicken (broiler), human and weather. Weather data are included alongside the case data from chicken and humans as there are known correlations, and as such weather observations could potentially be used to predict or explain outbreaks.

Norwegian chicken tests are performed on broiler chicken 5-6 days before slaughter. Due to strong seasonal patterns, the tests are only performed in May – October. The data that is sent from the Norwegian Veterinary Institute to NIPH (where the surveillance is performed) is anonymised and aggregated per municipality and week. Data is available from 2006 to 2019.

In Sweden, a monitoring program for *Campylobacter* runs throughout the year, covering 99% of all the slaughter batches. For every slaughter batch, a sample of 10 pooled ceca is tested for *Campylobacter* and the result becomes available to use after 1-5 days of sample collection. The number of submitted samples and number of positives are aggregated per week, along with the number of broilers included in the slaughter batches (batch size) for that week. The batch size can be used as an additional variable to weight the prevalence data stream in model fitting.

As for the human side, the Norwegian data is significantly more detailed than the Swedish; the NIPH has information on each relevant individual GP consultation for each Norwegian municipality, which is then aggregated weekly, while the data reported to SVA by the Public Health Authority (PHAS) are in the form of an already aggregated national case count. Another difference is that the Norwegian case count includes all consultations for gastrointestinal symptoms, while Swedish data are confirmed domestic *Campylobacter* cases only.

The weather observation data are relatively similar for both countries since the Swedish data were intentionally collected by SVA to match what the NIPH already had. Two weather data streams are used currently: temperature and precipitation, which are both

aggregated weekly. Geographically, Norwegian data are collected on a municipal level by the Norwegian Meteorological Institute (NMI), while the Swedish numbers are retrieved from all weather stations of the Swedish Meteorological and Hydrological Institute (SMHI), and then aggregated to a national average to match the human and chicken case data streams. Another difference is that Norway records the total weekly precipitation while an average is used in Sweden.

Running the Swedish System with Norwegian Data

Using Norwegian human, slaughter chicken and weather data provided to me by NIPH and NVI, I was able to set up a surveillance system and produce results using the engine developed at SVA. This involved (1) reformatting the data into a structure which our system was designed to handle, (2) manually reviewing each time series to assign the model suitable distributions and parameters, (3) training baseline models using the majority of the data as a training set, and (4) using the baseline models to try to predict outbreaks in the reaming data (the testing set). While the whole process ran successfully without errors, the results themselves were not very telling as I did not spend a lot of time deciding on proper model definitions. Additionally, there were no known aberration events (outbreaks) on a national level during the timespan covered by the data I was given, which made it impossible to evaluate the system's sensitivity. The fact that it was at all possible to run the system with new data was a desirable result, however, since the main purpose of the task was to investigate exactly that.

Conclusions

Although it would have been preferable that the STM took place under other circumstances, I believe that we made the best out of the situation. The summary document will surely prove useful for both parties in the future, as will the new connections that I formed with people at the NIPH. Since I am new to the OHEJP world it was personally very educational to get the chance to visit another agency, especially one within the public health sector.

List of dissemination and communication activities

Name of the activity:	*One Health EJP Annual Scientific Meeting 2020*		
Date:	*27th-29th May 2020*		
Place:	*Online*		
Specify the Dissemination and Communication activities linked to the One Health EJP project for each of the following categories			
	Yes / No		*Yes / No*
Organisation of a Conference	*No*	***Participation to a Conference***	*Yes*
Organisation of a Workshop	*No*	***Participation to a Workshop***	*No*
Press release	*No*	***Participation to an Event other than a Conference or a Workshop***	*No*
Non-scientific and non-peer-reviewed publication (popularised publication)	*No*	***Video/Film***	*No*
Exhibition	*No*	***Brokerage Event***	*No*
Flyer	*No*	***Pitch Event***	*No*
Training	*No*	***Trade Fair***	*No*
Social Media	*No*	***Participation in activities organized jointly with other H2020 projects***	*No*
Website	*No*	***Other***	*No*
Communication Campaign (e.g. Radio, TV)	*No*		*No*
Specify the estimated number of persons reached, in the context of this dissemination and communication activity), in each of the following categories			
	Number		*Number*
Scientific Community (Higher Education, Research)	***750***	***Media***	*0*
Industry	***0***	***Investors***	*0*
Civil Society	***0***	***Customers***	*0*
General Public	***0***	***Other***	*0*
Policy Makers	***0***		

Scientific outputs

The outputs of this mission, though limited, will contribute towards the goals of Work Package 3 within the OHEJP NOVA project. The development of a multivariate syndromic surveillance engine will continue, and a dashboard will be produced to showcase the surveillance results from the *Campylobacter* test case. An abstract summarising the engine

and the dashboard has been submitted to the OHEJP and was presented as a poster at the Annual Scientific Meeting at the end of May 2020.

Testimonial

I am very grateful to the OHEJP for giving me the opportunity to go on this short-term mission and visit the Norwegian Institute of Public Health. Visiting a new agency in a new country was quite rewarding for me personally, as it gave me the chance to form new connections and exchange thoughts and ideas with new people. My colleagues at the NIPH, despite being busy with work related to COVID-19, were very welcoming and accommodating, and I look forward to working further with them in the future.

When planning this mission in October last year, none of us could have predicted what would happen to the world in 2020. Luckily, we had planned my trip for late February before the coronavirus had hit fully and society locked down, which meant that I could still fulfil the STM. And although the extraordinary situation did affect the outputs, it was a rewarding experience in itself to visit a public health institute at the doorstep of a global pandemic. Once the crisis has passed, I am hopeful that our future cooperation will be strengthened and our goals aligned, so that we can produce syndromic surveillance solutions that will benefit both our countries and the European One-Health programme as a whole.

2.2 Short Term Mission 1 Case Study

SHORT TERM MISSIONS

Short Term Missions (STMs) are small travel grants with the aim of:

- Sharing scientific expertise, methodologies, equipment and facilities to harmonise the existing approaches and methodologies within the large OHEJP European network
- Driving the research forward in a collaborative and non-duplicative fashion to strengthen both the scientific capacity within the OHEJP
- Contributing to future prevention, preparedness, detection and response of the EU to foodborne and other emerging threats across human-animal-environmental sectors.

Cross-Domain and Cross-Country Collaboration to Develop Multivariate Syndromic Surveillance

Name: Skills Development Missions
Home Institute: National Veterinary Institute (SVA), Sweden
Mission Hosting Institute: Norwegian Institute of Public Health (NIPH), Norway
Duration of mission: 2 weeks

The aim of the STM was a collaboration and knowledge exchange between Norway and Sweden in the development of One Health systems for multivariate syndromic surveillance (SyS) of veterinary and public health data combined.

Two separate systems are in development in Sweden and Norway by the SVA and the NIPH, respectively. The Swedish system is explanatory, aiming to combine several data sources to explain outbreaks and improve the accuracy of detection. Norway, on the other hand, is developing a predictive system, which aims to use some source(s) of data to predict the outcome of others.

As a test case, both systems were evaluated on the surveillance and outbreak detection of Campylobacter in humans, using data from public health, broiler chicken and weather.

"...I am very grateful to the OHEJP for this opportunity. It gave me the chance to form new connections, exchange thoughts and ideas with new people. Colleagues were very welcoming: I look forward to working with them in the future. It was a rewarding experience to visit a public health institute at the doorstep of a global pandemic..."
Wiktor Gustafsson, SVA

One Health EJP has received funding from the European Union's Horizon 2020 research and innovation programme under grant agreement No 773830.

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Figure 2: This case study can be found on the OHEJP website: https://onehealthejp.eu/short-term-missions-2020/

3. Short Term Mission 3 (joint mission)

Knowledge exchange and collaboration for improving Syndromic Surveillance of One Health concern

The third STM funded for 2020 was a joint mission, and was awarded to Gry Marysol Groeng and Gunnar Oyvind Ikaksson Ro, at the Norweigan Institute of Public Health (FHI) to visit the Animal Plan Health Agency and Public Health England (UK) for 4 weeks. This joint STM aligns with the following thematic areas: Skills development missions; Exchange with researchers, policy makers, and risk managers to complement Science to Policy translation ; One Health Missions- Veterinary, Medical, Environmental research.
This STM was expected to take place in March 2020, however this coincided with the start of the COVID-19 pandemic and the associated restricted travel restrictions. Therefore this mission has been postponed until it is safe to travel.

4. Short Term Mission 4

Skills development mission in bioinformatics

The fourth STM funded for 2020 was awarded to Dinah Deborah Seligsohn, at the National Veterinary Institute (SVA) to visit the University of Glasgow (UK) for 4 weeks. This STM aligns with the thematic areas, Skills development missions.
This mission was expected to take place in March-April 2020, however this coincided with the start of the COVID-19 pandemic and the associated restricted travel restrictions. Therefore this mission has been postponed until it is safe to travel.

5. Short Term Mission 5

Genetic variability of tick-borne viruses and identification of new antiviral targets

The final STM funded for 2020 was awarded to Camille Migne at ANSES, to visit the University of Nottingham (UK) for 3 months. This STM aligned with the thematic areas Skills development missions and One Health Missions- Veterinary, Medical, Environmental research.
This mission was expected to take place from April to June 2020, however this coincided with the start of the COVID-19 pandemic and the associated restricted travel restrictions. Unfortunately, this mission was cancelled as the 'new' timing of the STM would no longer be suitable. No costs were incurred.

Dissemination of outcomes

The STM reports were submitted to WP6 30 days after completion of the STM. Once the STM reports were submitted, the Communications Teams created visually attractive studies which contained key info and a testimonial. These case studies were uploaded to the website (https://onehealthejp.eu/short-term-missions-2020/), and were promoted through the Education and Training monthly bulletins and OHEJP newsletters.

On the website page above, a link to this deliverable report will be signposted, and uploaded onto our website under 'Public Deliverables' after submission so readers can read the full detailed report of each mission. This report will also be indexed in all communications produced by the OHEJP commuications team around the Education and Training activity deliverables.

An additional deliverable report will also be produced at the end of the OHEJP to follow up and report on the outcomes of all the STMs funded in the OHEJP programme.