FELLOWSHIP REPORT

Summary of work activities

Leonidas Georgalis
Intervention Epidemiology path (EPIET)
Cohort 2014 (2014-2016)

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 the European Union (EU) and European Economic Area (EEA) Member States.

Intervention Epidemiology path (EPIET)

Field epidemiology aims to apply epidemiologic methods in day to day public health field conditions in order to generate new knowledge and scientific evidence for public health decision making. The context is often complex and difficult to control, which challenges study design and interpretation of study results. However, often in Public Health we lack the opportunity to perform controlled trials and we are faced with the need to design observational studies as best as we can. Field epidemiologists use epidemiology as a tool to design, evaluate or improve interventions to protect the health of a population.

The European Programme for Intervention Epidemiology Training (EPIET) was created in 1995. Its purpose is to create a network of highly trained field epidemiologists in the European Union, thereby strengthening the public health epidemiology workforce at Member State and EU/EEA level. Current EPIET alumni are providing expertise in response activities and strengthening capacity for communicable disease surveillance and control inside and beyond the EU. In 2006 EPIET was integrated into the core activities of ECDC.

The objectives of the ECDC Fellowship - EPIET path are:

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This portfolio does not represent a diploma. Fellows receive a certificate acknowledging the 2-year training and listing the theoretical modules attended. Additionally, if all training objectives have been met, they receive a diploma.

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

Fellows develop core competencies in field epidemiology mainly through project or activity work, but also partly through participation in training modules. Outputs are presented in accordance with the EPIET competency domains, as set out in the EPIET scientific guide[1].

Pre-fellowship short biography

Leonidas Georgalis studied Public Health in the Technological Educational Institute of Athens and then he obtained his Master degree in "Public Health and Infectious Disease Epidemiology" at the Medical School of Crete. His experience includes:

- Sexually Transmitted Infections (HPV, Screening, Vaccination)
- Foodborne and waterborne diseases (*Salmonella* spp, *E. coli O157:H7*, *Clostridium perfringens*, etc.)
- Zoonoses (*brucellosis, Q-fever, Rickettsial diseases, tick-borne diseases)*
- Mathematical Modeling and Statistics

Fellowship assignment: Intervention Epidemiology path (EPIET)

In September 2014, Georgalis Leonidas joined EPIET as a EU-track fellow based at the Department of National Institute of Epidemiology, Health Institute of Carlos III, Madrid, Spain, under the supervision of María Victoria Martínez de Aragon. He successfully attended the three weeks Introductory Course (29/09/2014- 17/10/2014) which was held in Spetses island, Greece. This report summarizes the work performed during the fellowship.

Fellowship portfolio

This portfolio presents a summary of all work activities (unless restricted due to confidentiality regulations) conducted by the fellow during the ECDC Fellowship, EPIET path. These activities include various projects, and theoretical training modules.

Projects included epidemiological contributions to public health event detection and investigation (surveillance and outbreaks); applied epidemiology field research; teaching epidemiology; summarising and communicating scientific evidence and activities with a specific epidemiology focus. The outcomes include publications, presentations, posters, reports and teaching materials prepared by the fellow.

This portfolio also includes a reflection from the fellow on the field epidemiology competencies developed during the 2-year training, a reflection from the supervisor on the added value of engaging in the training of the fellow, as well as a reflection by the programme coordinator on the development of the fellow's competencies.

[1] European Centre for Disease Prevention and Control. European public health training programme. Stockholm: ECDC; 2013. Available from: http://ecdc.europa.eu/en/epiet/Documents/Scientific%20guides/EPIET%20Scientific%20Guide_C2016.pdf

Fellowship projects

Surveillance

Comparative Analysis of Molecular Epidemiologic Surveillance of HIV-1 Infection in Two Regions of Spain, 2003-2015

Background: HIV-1 genetic forms have implications for transmission, treatment outcomes, immune response and vaccine design. We analyzed trends in non- B subtypes (Non-Bs) in two regions in Spain in order to explore implications for prevention strategies.

Methods: Between 2003-2015, we collected all HIV-1 subtyping data from Galicia and Basque Country regions. Representativeness of the regional data was assessed by comparison with the National HIV Surveillance System. In each region and for each subtype, we described country of origin of the patients, transmission route and their changes over time.

Results: Genetic forms from 3051 HIV-1 infections were analyzed and found representative in terms of age, sex, year of diagnosis, transmission route and country of origin. We detected an increase in Non-Bs from 14.7% and 15.0% in 2003, to 37.3% and 42.4% in 2015 in Galicia and Basque Country, respectively. Half of Non-Bs infections occurred in Spanish individuals; the most frequent Non-Bs were subtype F1 (27%), subtype C (14.3%) and CRF02_AG (12.3%). The latter was more frequent in Basque Country ($p<0.001$) and associated with individuals of Sub-Saharan African origin. Since 2010, a decrease in subtype G and BG recombinants in Galicia has been associated with the decrease in injection drug users ($p=0.001$). Subtype F increased 22% in Galicia since 2010 and 18% in Basque Country since 2014, related to two transmission clusters among men who have sex with men ($p<0.001$%).

Conclusions: Non-Bs HIV-1 infections are increasing in these regions over time. Increasing HIV variability has implications for transmissibility and prevention strategies. Moreover, genetic form surveillance provides information on the strains in circulation in a given region and time, and could be used to tailor prevention measures and treatment strategies.

Role and outputs: Co-investigator

Analysed surveillance data, performed data cleaning and data analysis

Supervisor: Elena Delgado, María Teresa Cuevas, Miguel Thomson & Lucía Pérez

Further activities: We are planning to submit a manuscript to a peer-reviewed journal in the near future

Competencies developed:
By being involved in this surveillance project I became aware of the importance of molecular epidemiology, especially in a disease with high importance for controlling transmissibility and to apply prevention and treatment strategies.

Time-Series Analysis of Pneumococcal disease in Spain, 2004-2013

Background: The infection due to *streptococcus pneumoniae* (neuomococcus) continues to be an important cause of morbidity and mortality globally, causing a great variety of illness. This study aims to describe and understand the seasonal characteristics of pneumococcal disease in Spain, 2004-2013, by using time series analysis.

Methods: The study population consisted of all the patients presenting in Spain, 1 January 2004 – 31 December 2013, with pneumococcal disease that required hospital admission. A time series analysis of pneumococcal cases will be conducted by total population in Spain. The components of a Time Series (trend, cycle, seasonality) will be described and analyzed. Also, we will try to forecast the hospitalizations of pneumococcal disease during the year 2014.

Results: During the study period (2004-2013) a total of 201,880 hospitalised patients were identified. A SARIMA [arima (1,1,1) sarima (0,1,0,52)] model was used to fit the observed data and forecast the expected cases in the year 2014. We saw an increasing trend of hospitalised cases until week 52 of 2008 and then a similar decrease until the end of 2013. There is a clear seasonal pattern every winter, with almost 50% of the cases arise during this period every year (p-value<0.001). We found an autocorrelation of one week in our data. The one step ahead forecast for the year 2014 revealed a decreasing trend, similar to the year 2013. Minimum expected cases for the year 2014 predicted in week 35 (70 cases) and the maximum expected cases predicted in week 6 (357 cases).

Conclusions: We observed a decreasing trend of pneumococcal infection is Spain since year 2009. This may be because of the extensive use of PCV7 vaccine in year 2009 and the corresponding introduction of PCV13 in 2010. We recommend further surveillance of pneumococcal disease.

Role and outputs: Principal investigator

Wrote the protocol, analysed hospitalisation data, performed data cleaning and data analysis

Supervisor: Macarena Estepa Garrido

Competencies developed:
By being involved in this surveillance project it was the first time exposed to Time Series Analysis (TSA). Also, I managed to handle large data bases and bolster my knowledge in STATA.

Investigate the association of Pneumococcal disease with Influenza illness in Spain, 2004-2013

Background: On 27 April 2009, Spain reported the first laboratory confirmed case of the influenza pandemic (H1N1) 2009 infection in Europe. Unlike typical seasonal flu patterns, the new virus caused high levels of summer infections in the northern hemisphere, and then even higher levels of activity during cooler months in this part of the world. The Spanish Influenza Surveillance System (SISS) was established in 1996 and since then it was integrated in European Influenza Surveillance Network (former European Influenza Surveillance Scheme) This study aims to describe the time series of pneumococcal disease in Spain and to compare it with the time series of influenza illness, 2004-2013

Methods: The study population consisted of all the patients presenting in Spain, 1 January 2004 – 31 December 2013, with pneumococcal disease or influenza that required hospital admission. A time series analysis of pneumococcal and influenza cases will be conducted by total population in Spain. The components of a Time Series (trend, cycle, seasonality) will be described and analyzed. Also, we will try to forecast the hospitalizations cases of influenza disease for the year 2014.

Results: During the study period (2004-2013) a total of 525,456 hospitalised influenza patients were identified comparing to 210,880 cases of pneumococcal disease. Influenza cases follow the same

pattern as the pneumococcal cases with two weeks of lag. The two series are highly correlated. There is a constant increasing trend for both series since 2004 with a huge peak of influenza cases in the week 46 of 2009, which is explained from the influenza pandemic. We forecast a decreasing trend for both series for the year 2014, with a mean number of expected cases to reach 555 and 167 cases for influenza and pneumonia disease, respectively

Conclusions: We showed that pneumococcal disease and influenza illness in Spain follow the same seasonal pattern with influenza having a lag of two weeks. The peak of the cases in week 46 of 2009 if totally explained by the influenza pandemic. Decreasing trends were predicted for the year 2014.

Role and outputs: Principal investigator

Wrote the protocol, analysed hospitalisation data, performed data cleaning and data analysis

Supervisor: Macarena Estepa Garrido

Competencies developed:

By being involved in this surveillance project I became aware of the importance of the association of Pneumococcal disease with Influenza illness, that sometimes these two can be indistinguishable. Furthermore, I studied the time cycle of both illnesses and it became clear the benefit of vaccination.

Conducting a research study and prevalence of resistance to anti-retroviral and non-B HIV-1 subtypes and Circulating Recombinant *Forms (CRFs) in the Basque Country, 2015.*

This project was part of the Annual Report on HIV-1 Biology and variability in Basque Country, Spain, 2015. **In collaboration with Horacio Gil Gil (EUPHEM cohort 2014)**

Background: Since 2001, has been held an ongoing study on resistance to antiretroviral in HIV-1 infected patients, as well as a study of molecular epidemiological surveillance of genetic forms of HIV-1 that are circulating in the region of Basque Country. The **aim** of the study is: i)Determine the circulation of resistant strains and genetic forms of HIV-1 in the Basque country, to which, all new cases of infection were analyzed, either primary, recent or new infection diagnoses ii) provide information to the health care system that can adapt treatments depending on the detection of resistance iii) study the clusters of transmission, indicative of common infections origin, in relation to the spread of resistance to antiretroviral pathways and genetic forms of HIV-1 iv) genotypic tropism study of R5 and X4 in patients susceptible to treatment with CCR5 antagonists

Methods: Patients included in these studies are both new diagnoses, including acute and recent infections, and patients with chronic infection. All these studies are carried out from plasma or blood samples, depending on the viral load of HIV-1 detected in the patient at the time of the completion of the relevant studies.

Results: From 1st January until 19th November 2015, we received a total of 345 samples from patients infected with HIV-1, corresponding to 297 plasmas and 48 whole blood samples. A total of 107 newly diagnosed patients were included during 2015. The majority (82.2%) were male and the most common route of transmission is the sexual (97.2%). It was observed a predominance of R5 tropism (77.8%), followed by X4 tropism (12.4%) and dual tropism R5 / X4 (9.7%). Considering only the 100 samples amplified again PR-RT diagnosis, 42 (42.0%) grouped into 23 clusters of ≥5 individuals, of which 17 are of subtype B, 1 is of subtype A1, 1 is subtype F, 2 are CRF02_AG, 1 is CRF47_BF and 1 is BC recombinant.

Conclusions: Such studies can provide information about the strain in circulation, resistance to anti-retroviral drugs, presence of cluster of transmission and genotypic tropism to HIV-1 infected patients and can be used to tailor prevention measures and treatment strategies.

Role and outputs: Performed data cleaning and data analysis
Supervisors: Elena Delgado, María Teresa Cuevas, Miguel Thomson & Lucía Pérez

Competencies developed:
By being involved in this surveillance project I had the opportunity to participate in the writing of the **Annual Report** on HIV-1 Biology and variability in Basque Country, Spain, 2015. I saw from the inside how the surveillance system of HIV is working in a Spanish Region and I took the advantage to communicate our findings by writing the report in Spanish.

Severity of hepatitis A presentation overtime, EU/EEA 1997-2013

This project is part of the "European project on severity of Hepatitis A in EU/EEA, 1997-2013". **Here only the Spanish data are presented**

Background: The proportion of symptomatic hepatitis A virus (HAV) infections increases with age, with children below 10 years of age often asymptomatic. Also the severity of hepatitis A symptoms increases with age. The case-fatality ratio is generally low (0.1 to 0.3%) but can be higher (1.8%) in adults over 50 years of age or persons with underlying chronic liver disease (1). Due to these characteristics, hepatitis A is considered a peculiar infection: in countries with free circulation of the virus and high level of transmission, large proportions of infections occur in asymptomatic children below the age of 10 years. The aim of the study is to test whether the severity of hepatitis A presentation increased from 1997 to 2013 in Spain.

Methods: We designed a retrospective cohort study to meet the study objectives. Study population: patients hospitalised in Spain during the period 1997-2013. Patients are identified through the collection of hospital discharge forms and extracted on the basis of the following ICD-9 codes: Hepatitis A without hepatic coma 070.1;Hepatitis A with hepatic coma 070.0. Both patients with hepatitis A as primary or secondary diagnosis will be selected for the study. Patients hospitalised for a single day (no overnight hospitalisation) will be excluded.

Results: In total we found 8,031 hospitalised cases between 1997 and 2013 in Spain, from which 62% were male. Seventy two percent (5757 cases) were primary diagnosis and only 97 cases (6.4%) developed hepatic coma. The most affected age group was the 18-39 years (4,078 cases; 51%), followed by the 0-17 age group (1872 cases; 23%) and the 40-64 age group (1532 cases;19%). We counted 2117 severe cases (26%) from which 21 died inside the hospital. Median hospital length of stay was 5 days (11 days for severe cases and 4 days for non-severe cases). A strong statistical increase in the median age of severe cases was observed through the years, from 23 years old in 1997 to 36 years old in 2011 (p-value<0.001). The proportion of severe cases diagnosed fluctuate during the study period, from 33% in the year 1997 to 20% in 2009 and then back to 31% in the year 2013 (p-value<0.001).

Conclusions: Spain presented a decreasing trend over time regarding the severity of the diagnosed cases although there was an increase in the median age of hospitalised cases. The decreasing trend is probably due to several concurrent factors such as improved hygiene, sanitation, socio-economic conditions and increased availability of vaccines and food-safety measures.

Role and outputs: Co-investigator
Performed data cleaning and data analysis (Still on-going)

Supervisor: Johan Giesecke, Ettore Severi, Carmen Varela Martinez, Elena Vanessa Martinez Sanchez

Competencies developed:
By being involved in this surveillance project I had the opportunity to participate in a very important and interesting work, that its results can affect the policy of Hepatitis A vaccination in Europe in the

near future. Moreover, it was the first time I worked with Hepatitis A and I can say that I earned a lot of knowledge regarding Hepatitis and vaccination.

Further activities: We are planning to submit at least one manuscript to a peer-reviewed journal the following months

Outbreak investigations

Salmonella Enteritidis outbreak investigation in Kalavryta after a school excursion, Greece, April 2016

Background: On 26th of April 2016, the Hellenic Center for Disease Control and Prevention (HCDCP) was informed via the Mandatory Notification System (MNS) about 6 confirmed non-typhoid salmonellosis cases. All cases were students participating in a 3-day school excursion. We investigated to identify the mode and the vehicle of transmission in order to initiate appropriate control measures

Methods: We defined as case every person participated in the excursion and developed symptoms of vomiting and/or diarrhea, between the 21 and 30 of April, 2016. A retrospective cohort study was conducted to test the hypothesis. Univariate analysis was undertaken to calculate the risk ratios for the exposures of interest. Stratified analysis was performed and the Mantel Haenszel Relative Risks (RRMH) were calculated.

Results: In total, 29 out of the 53 participants (55%) developed gastroenteritis symptoms with diarrhea and abdominal pain being the most common (96%). Symptom onset started on the early morning (00:00-06:00) of April 23, peaked in the same day during the interval 06:00-12:00 and finished in the morning of April 25th (06:00-12:00). Participants that consumed pasta with salsa, in the dinner on the 22nd of April, had 3 (95%CI: 1.76-5.53) times the risk to become cases (develop symptoms of Salmonellosis) compared to participants who did not consume pasta with salsa.

Conclusions: There was an outbreak of Salmonella Enteritidis among students participating in a 3-day excursion to Kalavryta; we identified as common source the dinner on the 22nd of April. Although we found significant statistical association between eating pasta with salsa and developing salmonellosis symptoms, we could not verify the vehicle because of the non-isolation of the Salmonella Enteritidis in the suspected meal.

Role and outputs: Principal investigator

Wrote the protocol, analysed outbreak data, developed questionnaire, developed data entry mask, performed data entry, data analysis, report writing.

Supervisor: Kassiani Mellou, Theano Georgakopoulou

Competencies developed:
By participating in this outbreak investigation I realised all the problems that field investigation can produce; especially, communication and time keeping problems. The involved parts was hard to reach and information were scarce. Also, questions included in the questionnaire have to be very precise and clear, in order to obtain the desirable information.

Outbreak Investigation of New Salmonella with 11:z41:enz15 antigenic type in Greece, March-April, 2106

Background: Between 24th of March and 27th of May 2016, eleven *Salmonella* spp. isolates with an unusual antigenic type were identified by the National Reference Laboratory for *Salmonella* and *Shigella* (NRLSS) in Greece. The objective of the study was to:assess the extent of the outbreak, identify the mode and the vehicle of transmission in order to initiate appropriate control measures and to implement preventive measures to avoid similar outbreaks in the future
Methods: A case-case study was designed in order to meet our study objectives. Outbreak cases were compared with salmonellosis cases due to *Salmonella* Enteritidis. The ratio of Case-Case was 1:2 and we did matching by age and region, to eliminate confounding and gain in efficiency.

Results: In total we had 11 cases between 15 March and 30 May, 2016. All cases (5 male and 6 female) were of Greek nationality. Eleven of the cases were children (15 months to 3 years old) and two were adults (28 and 60 years of age). Cases developed diarrhea (one case had bloody diarrhea), vomiting and abdominal cramps except for one case that was asymptomatic. Three household clusters (with two cases each) were identified. Reported cases were scattered in the region of Attica, with the exception of two cases (one in Northern Greece and the other in Central Greece). Univariate analysis of the data showed a statistical significant association with the consumption of tahini (OR: 15; 95%CI: 1.92-134.48). Tahini is a condiment made from toasted ground hulled sesame seeds. We identified as potential risk factor the infection with salmonella spp, at least one time, in the last six months (OR:21.0; 95%CI:1.37-1080.8).

Conclusions: A new salmonella serotype (*11:z41:enz15*) outbreak took place in Greece between 15 of March and 30 of may. Eight of the 11 cases reported tahini consumption within the incubation time. However, cases did not report the consumption of a single type of tahini or of a specific trademark. They reported the consumption of commercial products widely consumed. The study is still ongoing and we are trying to trace back the origin of the sesame.

Role and outputs: Co-investigator (still on-going)

Supervisors: Kassiani Mellou, Theano Georgakopoulou

Competencies developed: The experience and the feeling that you are facing something completely new. Time is your enemy and information is really difficult to find. I realized the importance of a well implemented surveillance system when comes the time for control finding. Setting up a study with little or no information and with no real hypothesis generation is a real challenge.

Analysis of a Salmonella serotype bovismorbificans outbreak signal in Spain, 2016

In collaboration with Horacio Gil Gil (EUPHEM cohort 2014)

Background: From April 2015 to February 2016, the laboratory of Reference and Investigation in Food and Waterborne Bacterial Diseases of the CNM–ISCIII had detected an increase in the number of *Salmonella* serotype Bovismorbificans isolates. The continuous detection of this infrequent serotype suggested an outbreak signal which was further investigated.

Methods: The Reference laboratory performed the molecular characterization of 31 *Salmonella* serotype Bovismorbificans isolates received from the last year in the CNM- ISCIII, using the Pulse Field Gel Electrophoresis (PFGE). As the cases were old, most of the regional epidemiologists didn't want to interview the cases.

Results: A total of 14 cases were identified, from which 8 cases (57%) were females. The 57% of the cases were older than 50 years old. The cases were distributed in 9 provinces and 7 regions, mostly in the northwest part of Spain. The analysis identified 12 different pulse-types being the XbaI.1474 present in 14 isolates obtained from clinical samples. Interestingly, two isolates which were obtained from a pork carcass in Asturias in June 2015, belonged to the same pulse-type. It was not possible to identify the infected animal and apparently, the meat of this animal reached the food chain and caused the cases. Unfortunately, we couldn't continue the outbreak investigation as no new cases were found.

Conclusion: The detection of this pulse-type in an isolate obtained from a pork carcass point out to the pork meat or pork products as the most likely source of the infection. We recommend that pork carcasses should be retained until the microbiology analyses have been completed before they reach the food chain.

Role and outputs: Co-investigator

Develop questionnaire, communicate with experts in all Spanish Regions

Supervisor: Silvia Herrera & Carmen Varela Martinez

Competencies developed: It was an outbreak that finally we couldn't investigate until the end because of the luck of information. Co-operation between the Regions in Spain have to be more close and dissemination of information is the number one rule during an outbreak investigation.

Applied epidemiology research

HIV-1 transmission clusters in Spain: role in the propagation of transmitted resistance mutations and the spread of the infection

In collaboration with Horacio Gil Gil (EUPHEM cohort 2014)

Background: HIV-1 strains which group phylogenetically in transmission clusters (TCs) are disseminating easier than non-TCs strains. Moreover, propagation of transmitted drug resistance (TDR) within some clusters represents a serious public health problem. Here we analyze the role of TCs in the epidemiology of HIV-1 infection within two regions of Spain during the last three years.

Methods: We included in the study 625 HIV-1-infected individuals diagnosed in the regions of Galicia and Basque Country during 2013-2015, whose partial *pol* sequences were obtained through routine drug-resistance testing. Phylogenetic analysis was performed by maximum likelihood in these sequences, including other 7688 sequences from HIV-1 infected individuals from Spain (1999-2012) for assigning and sizing TCs. TCs were defined as those including viruses from four or more individuals grouping in phylogenetic trees with a bootstrap value ≥90%. Odds ratios (OR) for risk factors were calculated amongst individuals which belong or not to TCs.

Results: 55% of the individuals diagnosed during 2013-2015 clustered in 107 TCs (size 4-124 individuals) identified in the phylogenetic analysis. Men were more likely to belong to TCs than women [OR 8.3; 95% confidence interval (CI): 4.6-15], and men having sex with men (MSM), were more likely to belong to TCs than other risk groups such as heterosexuals or injecting-drug users (OR 3.1; 95% CI: 2.2-4.6). Six TCs presented TDR mutations associated with high level resistance.

Conclusions: TCs play an important role in the spread of HIV-1 infection as evident within the two studied Spanish regions. Early detection of TCs and focusing upon effective measures for preventing high risk transmission groups, especially amongst MSM, will reduce HIV-1 infections TCs and the incidence of TDR within these regions.

Role and outputs: Co-investigator

Data cleaning and data analysis

Supervisor: Elena Delgado, María Teresa Cuevas, Miguel Thomson & Lucía Pérez

Competencies developed:

By participating in this project it became clear to me the importance of Transmission Clusters in the spread of HIV-1 infection. Special attention should be paid to high-risk transmission groups and to those helping the propagation of transmitted drug resistance, because of its major public health concern.

Impact of pneumococcal conjugate vaccines on pneumonia related hospitalizations in Spain, 2007-2012

Background: In 2010, the 7-valent (PCV7) pneumococcal vaccine was superseded by the new 13-valent vaccine (PCV13) in Spain. Since 2006 the region of Madrid included these vaccines in the infant vaccination program (coverage >95%), while it remained optional in the rest of the country (coverage <60%). We described and compared the changes in pneumococcal disease hospitalization rates after the change from PCV7 to PCV13 vaccine in Spain.

Methods: We compared Period 1 (2007-2009), when PCV7 was available, with Period 2 (2010-2012) after PCV13 was introduced. We calculated hospitalization rates (HRs) and hospitalization rate ratios (HRRs) for each period by region, age-group and clinical presentation, using Poisson regression. Analysis is restricted to culture-confirmed cases.

Results: Of the 126,950 hospitalizations recorded in the National Registry of Hospitalizations, 76,789 (61%) were males (mean age 74 years). Most common clinical manifestations were: pneumonia (122,395 hospitalizations; 96%), septicemia (5,966 hospitalizations; 5%) and meningitis (2,870 hospitalizations; 2%). In Period 2, pneumonia HR reduction was significant in every age group (p<0.001), while septicemia hospitalizations increased in adults >64 years (HRR: 1.17; 95%CI: 1.09-1.25). Meningitis hospitalizations decreased, mainly in children <5 years (HRR: 0.61; 95%CI: 0.51-0.74). Regions with known high vaccine coverage showed higher reductions in HRR for all clinical presentations. Adults >64 years presented high mortality rates, especially for septicemia (35.0% and 30.0% in Period 1 and Period 2, respectively).

Conclusions: Introduction of PCV13 appeared to reduce pneumococcal-related hospitalizations, especially in children <5 years. We observed a significant decline in pneumococcal HRs, even in regions without an integrated vaccination program. We recommend evaluating the recent introduction of PCV13 into the national infant immunization schedule in early 2016.

Role and outputs: Principal investigator

Protocol writing, data cleaning, data analysis, first author of manuscript

Supervisors: Macarena Garrido Estepa

Competencies developed:

By participating in this project I learned to work with large databases. I expand my knowledge regarding pneumococcal disease and it was my first EPIET manuscript.

Communication

Manuscripts submitted to peer reviewed journals (in review process)

We submitted the draft of the manuscript **"Change of pneumococcal disease related hospitalisations after the commercialization of pneumococcal conjugate vaccines in Spain, 2007-2012"**, to *Epidemiology and Infection (1)*

Conference presentations

2 posters at ESCAIDE 2016 (2, 3)

Other presentations

1 poster presentation at Reunión Monográfica SEISIDA 2016 (4)

Reports

Annual Report on HIV-1 Biology and variability in Basque Country, Spain, 2015 (5) and 2 outbreak reports (6,7)

Other

Rapid Communications: An outbreak of a possibly new *Salmonella enterica* subspecies *enterica* serovar with the antigenic formula 11:z41:e,n,z15, Greece, March to May 2016. ***Eurosurveillance***, Volume 21, Issue 25, 23 June 2016.(8)

Teaching activities

Course on epidemiology applied to microbiology

I organized with Horacio Gil Gil (EUPHEM, cohort 2014) a course of "Epidemiology applied to Microbiology". It took place in the Institute of Health Carlos III, Majadahonda, Madrid, from 11 to 15 of April, 2016. The course was a total of 15hours (3 hours per day). Our target group were Microbiologists working at the Instituto de Salud Carlos III in the department of Microbiology. Content of the course: Parameters used to quantify in Epidemiology (Rate, Ratios, Incidence, Prevalence ,etc.); Design of tables, maps and graphs; Study designs in Epidemiology (Cohort study, Case -control, Cross-sectional); Outbreak Investigation, step by step; Hypothesis testing and 95% Confidence Intervals ; Sampling methods; case studies (real examples/outbreak simulation).

Supervisor: Ana Alastruey and Silvia Herrera

Educational outcome:

By the teaching activity I learned how to interact with other people and how to prepare myself before the lectures. It was amazing that participants were really interested in epidemiology and that I tried to use the feedback I received daily, in order to prepare the class of the following day

Other activities/missions

Rapid needs assessment at Elliniko refugee camps in June 2016, Athens, Greece

During the Rapid Assessment & Survey Methods module in Athens (20-25.06.2016), I had the opportunity to visit one of the refugee camps in Elliniko, Athens. Small flexible groups composed by two epidemiologists and one translator interviewed refuges in order to understand their needs and to inform them about vaccination programs and how to access the available medical centers inside and outside of the camp. This initiative was part of the **Médecins Sans Frontières (MSF)** program.

Background: In early 2016, MSF-Operational Centre Geneva (OCG) launched support activities in the three refugee camps of Elliniko (3,612 individuals of mostly Afghan origin) in the metropolitan area of Athens. MSF-OCG considered different service provision options and planned to conduct a vaccination campaign among refugees hosted in the three camps. We aimed to assess the health (medical/surgical support, chronic diseases) and sanitary needs of the refugees and to estimate the baseline measles/measles-mumps-rubella (MMR) vaccination coverage among under 15 years of age, in order to provide recommendations to the local heath stakeholders.

Methods: On 24 July 2016, we conducted a rapid needs assessment survey among a random sample of refugees residing in the camps in Elliniko. Assuming a prevalence of 50% for health conditions, precision of ±0.07 and a 10% non-response, we estimated a required sample of 205 individuals. The number of participants by camp was proportional to the camp size. In two camps, we used systematic sampling to select tents and in the third camp, we used simple random sampling. We interviewed one randomly selected individual above the age of 15 from each selected tent and collected information on demographics, access to health care, chronic diseases, trauma/injuries, surgery and post-operative care for trauma/injuries, pregnancy in women, availability of non-food items, safety, anxiety, priority needs, future plans and MMR vaccination status of children under 15 years. We calculated weighted proportions using the number of people per tent as weights and adjusted for clustering for the vaccination coverage estimate; a cluster was defined as a single shelter.

Results: We included 214 individuals in the analysis; median age was 27 years (range 15-75); 50% were male. Of interviewed individuals, 44 (23%) reported having at least one chronic disease. Of those, 12 (30%) reported having high blood pressure, 12 (30%) heart and 11 (28%) kidney diseases. Among those with these pathologies, 50%, 68% and 83% reported not taking the appropriate treatment, respectively. Of all respondents, 106 (51%) reported not having adequate access to soap and 157 (59%) to clothe- washing. Regarding safety, 90 (43%) of responders did not feel safe within the

environment of the camp and 80 (38%) had endured an unsafe event since arriving in the camp. Of all respondents, 168 (83%) felt anxious or depressed. Vaccination against measles/MMR was known for 220 of the 348 (63%) children <15 years of age. Among those, 15 (6.8%) were vaccinated based on vaccination records and 168 (76%) based on parental/guardian recall.

Conclusions and recommendations: This assessment indicated low access to proper care for chronic diseases with the majority of respondents reporting not taking appropriate treatment. It also indicated insufficient hygiene conditions in the camps, with limited access to basic hygiene material. Refugees in Elliniko camps need to be provided with sufficient access to chronic disease and psychosocial care and sufficient hygiene material.

EPIET/EUPHEM modules attended

1. Introductory Course in Spetses, Greece (29.9. -17.10.2014)
2. ESCAIDE 2014, Stockholm, Sweden (5.-7.11.2014)
3. Outbreak Module, Berlin, Germany (08 -12.12.2014)
4. MVA Module, Vienna, Austria (23-27.03.2015)
5. Project Review Module, Lisbon (24-28.08.2015)
6. ESCAIDE 2015, Stockholm, Sweden (11-13.11.2015)
7. Time Series Analysis Module, Utrecht, The Netherlands (23-27.11.2015)
8. Vaccinology Module, Paris, France (16-20.04.2016)
9. Rapid assessment & survey methods module, Athens, Greece (20-25.06.2016)
10. Project Review Module, Lisbon (22-26.08.2016)

Others courses attended

I attended some weekly courses at the Institute of Carlos III, which were part of the Master in Public Health:

- Time Series Analysis
- Outbreak Investigation
- Sampling techniques for health research
- Spatial analysis of diseases

Certificates

1. ***Basic Security in the Field II***, United Nations Department of Safety and Security (UNDSS), 15 June 2016
2. ***Advanced Security in the Field***, United Nations Department of Safety and Security (UNDSS), 15 June 2016

Supervisor's conclusions

During his two-year fellowship at Instituto de Salud Carlos III in the Spanish Field Epidemiology Training Programme, Leonidas Georgalis has participated in several projects, including epidemiological surveillance, outbreak investigation, and particularly applied research for which he was for his extremely valuable because of his analytical skills. Leonidas has demonstrated that he is an independent a proactive professional that can develop and identify the adequate methodological approaches to the different studies he worked on. Leonidas' statistical knowledge and his interpersonal skills, contributed significantly to the successful progress and completion of his studies.

Leonidas is a serious and hard-working professional, able to work both independently and as part of a team. We can strongly recommend him for any kind of position related to public health.

Coordinator's conclusions

Leonidas Georgalis has demonstrated his aptitude to efficiently work in different teams, as shown by his participation in his different projects in Spain, both at the National Centre for Epidemiology and the National centre for Microbiology; and his participation in outbreak investigations in Greece.

Leonidas is an independent professional and a proactive fellow able to defend and develop his own ideas as shown by the time series analysis of pneumococcal disease in Spain he performed. And though he had previous background in public health and statistical analysis, he managed to further enhance his capacities.

I believe that Leonidas's interest and development in field epidemiology, and his statistical and interpersonal skills makes him a very good candidate for an epidemiological and public health related work, either at national or international level.

Personal conclusions of fellow

For me EPIET was a dream came true. I had the opportunity to work closely with some very charismatic scientists and persons and take advantage of the knowledge they shared with me. I managed to work with a lot of different projects and topics and I gained in expertise and experience. I can say that I am leaving EPIET as a better scientist and person and the friendships I made will help me to evolve even more as an epidemiologist in the future. Definitely worth the hard work and the effort you have to make these 2 years.

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