



# FELLOWSHIP REPORT

## Summary of work activities Elisavet Mouratidou Intervention Epidemiology path (EPIET) Cohort 2017

# 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;

This portfolio does not represent a diploma. Fellows receive a certificate listing the theoretical modules attended and the 23month training. Additionally, if all training objectives have been met, they receive a diploma.

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- 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.

## **Pre-fellowship short biography**

Elisavet Mouratidou holds a bachelor of science in Nursing and a Master of Science in Community Nursing from the Faculty of Nursing at the National and Kapodistrian University of Athens, Greece. She had an interest in public health and epidemiology and she participated in the programme for the development of the "Basic Syndromic Surveillance Network» for the Olympic Games in Athens 2004. Since 2004 she has been working for the National Public Health Organisation (former Hellenic Centre for Disease Control and Prevention-HCDCP) as a public health professional. Since 2012, she has been working in the office for Airborne Diseases in the Department for Epidemiological Surveillance and Intervention. In September of 2017 she started her EPIET-fellowship as an MS-track fellow.

## Fellowship assignment: Intervention Epidemiology path (EPIET)

On 11/09/2017, Elisavet Mouratidou started her EPIET fellowship at the Greek National Public Health Organisation (former Hellenic Centre for Disease Control and Prevention) in Athens, Greece, under the supervision of Dr. A. Lambrou. Her frontline coordinator was Dr. Alicia Barassa-Blanco. This report summarizes the work performed during this fellowship.

# **Methods**

This portfolio demonstrates the competencies acquired during the ECDC Fellowship, EPIET path, by working on various projects, activities and theoretical training modules.

Projects included epidemiological contributions to public health event detection and investigation (surveillance and outbreaks); applied epidemiology field research; teaching epidemiology; summarising and communicating scientific evidence and activities with a specific epidemiology focus.

The outcomes include publications, presentations, posters, reports and teaching materials prepared by the fellow. The portfolio presents a summary of all work activities conducted by the fellow, unless prohibited due to confidentiality regulations.

# Results

The objectives of these core competency domains were achieved partly through project or activity work and partly through participation in the training modules. Results are presented in accordance with the EPIET core competencies, as set out in the EPIET scientific guide<sup>1</sup>.

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

# **Fellowship projects**

## **1. Surveillance**

# **1.1. Epidemiological Surveillance of seasonal influenza and Active Surveillance of seasonal influenza in Intensive Care Units (ICUs), Greece, 2017-2019**

Influenza is a viral respiratory infection and can cause epidemics and pandemics which have resulted to significant morbidity and mortality and increased costs to health services. Influenza surveillance is a key component in interpreting and responding to the evolving epidemiology of influenza.

Epidemiological surveillance of Seasonal influenza in Greece includes four systems:

1. Sentinel-based surveillance for Influenza Like Illness in primary health care settings

2. Laboratory-based Surveillance with the participation of three major laboratories, which include two National Reference influenza laboratories that perform Real Time PCR influenza testing and genetic characterization for influenza viruses.

3. Severe influenza surveillance system among hospitalized patients

4. Euro-MOMO system. Greece is part of the European monitoring of excess mortality for public health action (EuroMOMO) which objective is to operate coordinated real-time mortality monitoring and analyses.

The national epidemiological surveillance system for seasonal influenza is coordinated by the Office for Airborne Diseases, in the Department for Epidemiological Surveillance and Intervention of the Greek National Public Health Organization. The Office for Airborne Diseases also monitors all laboratory-confirmed influenza cases admitted to Intensive Care Units (ICUs) and/or in-hospital deaths of influenza patients. Each case is actively followed up daily, by a public health professional with the use of a structured questionnaire until the case is discharged from the hospital. The system is comprehensive and covers all hospitals and ICUs in the country.

Data from monitoring severe influenza cases is used in addition with all the available surveillance data to estimate the burden of influenza in order to inform policy makers, prioritize resources and provide evidence-based guidelines.

Regarding influenza season 2017-2018 the total number of clinical and sentinel samples tested in the three major laboratories was 2,956 out of which 504 (17.1%) were positive for influenza. Among the positive samples 145 (28.8%) were influenza type A and 359 (71.2%) were influenza type B. From 125 positive samples of type A that were sub-typed 17 (13.6%) were A(H3N2) and 108 (86.4%) were A(H1N1)pdm09. Influenza activity started to increase around week 52, 2017 (25 December -31 December 2017) the increase picked in week 8, 2018 (19 February-25 February 2018) and then decreased gradually.

At a total there were 107 cases with confirmed influenza hospitalized in Intensive Care Units (ICU's) out of which 42 deaths reported during follow up.

The predominant influenza type in Greece for season 2017-2018 was type B, the circulating strains for type B and subtype A(H1N1)pdm09 that were tested in the National Reference Influenza laboratories were similar to the strains of the seasonal influenza vaccine. The circulating strains for subtype A (H3N2) tested in the Reference laboratories had significant genetic and antigenic variation in comparison with the vaccine strains.

During the next influenza season 2018-2019 the total number of clinical samples tested in the three major laboratories was, 3,756 of which 1,101 (29.2%) were positive for influenza. Among the positive samples 1,087 (98.7%) were influenza type A and 14 (1.3%) were influenza type B. From 927 positive samples of type A that were sub-typed 246 (26.5%) were A(H3N2) and 681 (73.5%) were A(H1N1)pdm09. Influenza activity started to increase around week 52, 2018 (24 December -30 December 2018) the increase picked in week 6, 2019 (04 February-10 February 2019) and then decreased gradually.

At a total there were 374 cases with confirmed influenza hospitalized in Intensive Care Units (ICU's), out of which 154 deaths reported during follow up.

The predominant influenza type in Greece for season 2018-2019 was A(H1N1)pdm09 with some circulation of subtype A(H3N2), the circulating strains for A(H1N1)pdm09 and for type B that were tested in the Reference Laboratories were similar to the strains of the seasonal influenza vaccine. The circulating strains for subtype A H3N2 tested in the Reference Laboratories had also significant genetic and antigenic variation in comparison with the vaccine strains.

**Role:** Elsa was a co-investigator, she participated in active daily follow up of cases admitted to ICU, data collection, data analysis, preparation of weekly reports (1) and annual reports (2,3), producing and delivering presentations (4) regarding weekly influenza updates for the scientific internal meetings of the Greek National Public Health Organisation.

Supervisor(s) :Dr Th Lytras

#### 1.2 Surveillance of Legionnaire's disease in Greece, 2008-2018

Studies on the epidemiology of Legionnaires' disease (LD) in Greece are limited. We aimed to explore the epidemiology of LD in Greece from January 2008 to September 2018 in order to plan prevention activities.

In Greece epidemiological surveillance of Legionnaire's Disease includes the three following systems:

A) The European Legionnaire's Disease Surveillance Network (ELDSNet) for travel-associated cases (TALD).

B) The National Mandatory Notifiable Diseases system

C) Laboratory-based Surveillance System in Sentinel Hospitals

Greece is a member of the ELDSNet European Legionnaires' Disease Surveillance Network coordinated by ECDC. Data are collected by nominated ELDSNet experts in each European country. These notifications are received in PDF forms and used by the Office of Airborne Diseases in order to create new adapted notifications to inform the Regional Public Health authorities in order to conduct environmental investigations. All the case information was maintained in hard copies in paper folders from 2008 until 2018. We decided to create a new electronic data base and enter all the TALD case information from the paper forms in order to analyze them.

Using the 2012 EU/EEA case definition we analyzed all LD cases reported to the National Public Health Organization through the National Mandatory Notifiable Diseases System (NMNDS), the European Legionnaires' disease Surveillance Network (ELDSNet) and notifications by foreign public health authorities from 01/01/2008-30/09/2018. We described all cases and tested for differences in notification rates amongst tourists between calendar years, using the total nights spent by incoming and domestic tourists in Greece as denominator.

During the study period a total of 844 LD cases were reported, of which 795 (94%) confirmed and 49 (6%) probable. Among total cases, 558 (66%) were male and 693 (82%) were over 50 years old (median: 62, range: 6-92). Furthermore, 539 (64%) were travel-associated, 253 (30%) community-acquired, 29 (3%) hospital-acquired and 23 (3%) ship-associated. Among travel-associated cases: 494 (92%) were non-Greek travelers visiting Greece notified through ELDSNet and by foreign countries and 411 (76%) were located in three touristic island prefectures out of thirteen prefectures in Greece. We compared notification rates of travel-associated LD cases in 2017-2018 to 2008-2016 and observed a geographically dispersed increase (1.2/1,000,000 nights of stay versus 0.6/1,000,000, p < 0.001).

We identified an increase in notification rates of LD mainly among non-Greek travelers in 2017-2018 not explained by any changes in the reporting system or large outbreaks and implemented public health measures including awareness activities for hotel managers/owners in the areas with the highest case burden. **Role:** Elsa was the primary-investigator, she created a new database for travel-associated cases reported through ELDSNet, conducted data analysis, created an internal short report (5) and she was actively involved in organising and implementing the awareness activities/workshops for hotel managers/owners. She also prepared an abstract accepted for ESCAIDE 2019 (6). In addition utilizing the data from the analysis she delivered two oral presentations in ELDSNet annual meetings (7,8) and one oral presentation (9) for the 6th meeting of the European Study Group for Legionella Infections (ESGLI).

*Supervisor(s)* : Dr A. Lambrou, Dr Th. Lytras

# **1.3 Pilot study for setting up a surveillance system for hospital-acquired infections** (HAIs) in Intensive Care Units (ICUs)

In Greece there is a national hospital-acquired infections (HAIs) surveillance system in health care units, focused on incidence of Healthcare Associated Blood Stream Infections (HABSIs). In addition, a point prevalence survey of HAIs and Antimicrobial use is performed every two years at national level.

Currently, there is no ICU-specific surveillance system established for the continuous and systematic monitoring of HAIs' in ICUs, including the most important HAIs such as blood stream infections, pneumonia, urinary tract infections and catheter-related infections incidence.

The main objective of this pilot study was to identify strengths and limitations in setting up a new surveillance system for monitoring HAI in ICUs in Greece. The project supervisor was the Head of HAIs and Antimicrobical Resistance Unit and we collaborated with ICUs doctors and nurses in four ICUs in two major cities in Greece.

Between December 10th and December 13rd, 2018 a joint short exchange site visit was organized in order for the EPIET-fellow and the project supervisor to visit Vall d'Hebron University Hospital in Barcelona where there is an established national HAIs surveillance system for ICUs based on the ECDC protocol. The purpose of the visit was to share good practices and also to be exposed to other countries' expertise on HAIs surveillance in ICUs before the launch the pilot study.

We translated and adapted the HAI-Net ICU v.2.2 protocols of ECDC in Greek, prepared a pilot study protocol and created forms for data collection. Data on new cases of blood stream infections and pneumonia as well as data on antimicrobial use and resistance was collected between April 1st until June 30th, 2019.

Furthermore, this project will facilitate the standardisation of definitions, data collection and reporting procedures for hospitals participating in surveillance of healthcare-associated infections in intensive care units in compliance with EU standards.

**Role:** Elsa was the main-investigator, she collaborated with her supervisors and ICU experts, created a protocol for the pilot study (10), adapted the HAI-Net ICU v.2.2 ECDC protocol in Greek, created data collection forms and also adapted instructions for data collection. She participated in a joint site visit with her project supervisor for which she produced a short report internal report and a report for ECDC (11). She also coordinated and participated in the data collection process for three months in two ICUs in hospitals in Athens.

Supervisor(s): Dr F. Kontopidou, Dr A. Lambrou

## 2. Outbreak investigations

#### 2.1 Focus investigation for Malaria in a city in Central Greece, November 2017

Following the report of a malaria case with evidence of domestic transmission to the National Public Health Organization by a doctor in a local hospital, a focus investigation was performed in a city in a Greek Region, from 27-30/11/2017.

The main objectives of the investigation were active malaria case finding, raising awareness of the local population and providing information for malaria to the public. The investigation team conducted door-to-door visits, interviews of suspected cases and environmental investigations in order to assess exposure risks.

The total number of households in that area was 288, of which 10 were abandoned. The residents were out of the house in 182 households and we interviewed the residents in 96 households. In these 96 households we screened 274 individuals for fever or other malaria compatible symptoms and informed them about malaria and the recommended prevention measures. One suspected case was identified and tested for malaria immediately by rapid test (RDT) and a blood sample was taken to be tested in the Malaria Reference Laboratory.

The result of the RDT of this sample was negative. The blood sample was sent to the reference laboratory and was tested negative for malaria by both microscopy and molecular testing (PCR).

The results of the focus investigation contributed to defining an area within a 6-km radius from the cases' residence and worksite as malaria "affected" by decision of a national dedicated multi-sectored working group. Therefore, a series of public health activities in the area was recommended including enhanced surveillance, enhanced laboratory diagnosis capacity, blood safety measures, and enhanced vector surveillance and control. Additionally, communication with the public was organized for raising awareness of the local population on malaria symptoms and the protective measures against mosquitoes.

**Role:** Elsa was a co-investigator, she participated in active case finding, case screening and informing the local population during door-to-door visits. She was part of the team during the environmental investigation and also created an internal report with the findings of the investigation (12).

Supervisor(s): Dr D. Pervanidou, Dr A. Lambrou

# 2.2 Food-borne outbreak of *Salmonella* spp. among child's party attendees in a city in Northern Greece, May 2018

On 22/05/2018, five cases of salmonellosis in a tertiary hospital in a city of Northern Greece were reported to the Foodborne and Waterborne Diseases Unit (of the National Public Health Organization) through the National Mandatory Notifiable Diseases System. All the cases had attended a child's party in a city in Northern Greece. An outbreak investigation was initiated and a retrospective cohort study was conducted among all party attendees.

Data collection was conducted via phone interviews using structured questionnaires. The information collected included demographics, food consumption, hospitalization, symptoms and laboratory results. The adult supervisors responded on behalf of the children attendees.

All 24 party attendees participated in the phone interviews. Among the participants, 13 out of the 24 met the case definition resulting in an attack rate of 54.2%. Twelve (50%) of the participants were aged up to 14 years. Fourteen (58.3%) were female. The results of the univariate analysis indicated that people who had higher risk of developing symptoms were the people who ate cake [RR=1.98 (95% C.I:1.29-3.03)] and also people who ate ham and cheese toast [RR=1.77 (95% C.I: 1.12-2.80)]. After multiple logistic regression, the consumption of cake remained statistically significant. Among the people who ate toast those who ate cake had higher risk of developing symptoms [RR=1.82 (95% C.I:1.16-2.85)].

Stool samples taken from two cases who were hospitalized were positive for *Salmonella* spp. Stools samples taken from the personnel working in the pastry shop were tested negative for *Salmonella* spp.

The results of the outbreak investigation indicated that the consumption of cake at the party was the main risk factor for developing symptoms. The cake was purchased by a local pastry shop, where environmental investigation was performed. Food items used for making the cake were not available for further laboratory testing. The environmental investigation did not find any omission in food handling procedures. The owner was already informed about the outbreak and had been given recommendations by the regional public health authorities.

**Role:** Elsa was a co-investigator, she prepared the questionnaire form and conducted some of the phone interviews. The information was used by the Foodborne and Waterborne Diseases Unit to produce an internal report (13).

Supervisor(s): Ms Th. Sideroglou, Dr K. Mellou, Dr A. Lambrou

# **2.3. Outbreak of gastroenteritis in a group of excursionists in an Evvoia island, July 2018**

On 09/07/2018, sixteen gastroenteritis cases from a tertiary hospital in Athens Greece were reported to the Foodborne and Waterborne Diseases Unit (of the Greek National Public Health Organisation) through the National Mandatory Notifiable Diseases System. All cases had participated in a one-day bus excursion in Evvoia island on the 8<sup>th</sup> of July. An outbreak investigation and retrospective cohort study was conducted among all excursion participants.

Data collection was conducted by phone interviews using structured questionnaires. Environmental investigation was performed and laboratory samples were taken. We performed univariate and multivariable analysis using Poisson regression with robust error variance to determine whether there were statistically significant associations.

Among the 43 people who participated in the excursion, 39 (91%) answered the questionnaire. Twenty four (24) out of the 39 met the case definition (attack rate: 62%). The analysis showed that excursionists who consumed well water served at the restaurant where they had lunch were 1.9 more likely to develop gastroenteritis symptoms (RR=1.88, 95% CI=0.97-3.63). Six stool samples submitted by cases were tested negative for *Salmonella* spp., *Shigella* spp., *Campylobacter* spp. and *Norovirus*.

Environmental samples from the restaurant water systems were positive for coli-form bacteria, aerobic and anaerobic microorganisms.

The retrospective cohort study indicated that the consumption of "water from the well in tavern" was the most likely vehicle of the outbreak.

After the outbreak report the regional public health authorities recommended to the restaurant owner: disinfection of the water systems in the restaurant and prohibited serving water from the well.

**Role:** Elsa was the primary investigator she prepared the questionnaire form, conducted phone interviews for all of the participants, created the database, performed all data entry, analyzed the data and prepared the internal report (14).

Supervisor(s): Dr K. Mellou, Dr A. Lambrou

## 3. Applied epidemiology research

#### 3.1 Influenza vaccine effectiveness against hospitalization with laboratoryconfirmed influenza in Greece: a pooled analysis across five seasons, 2013/14 to 2017/18

Estimating influenza vaccine effectiveness (IVE) across multiple seasons increases the sample size, allowing for subgroup analysis. To our knowledge, no previous study in Greece has reported pooled IVE estimates. We aimed to estimate overall and viral subtype-specific IVE over the last five seasons, both annually and pooled, in order to provide information on vaccine benefits and support uptake.

We used routine surveillance data on hospitalized patients for five influenza seasons, from 2013/14 to 2017/18. Swab samples from inpatients were tested for influenza by RT-PCR in three laboratories, covering the entire country. We used a test-negative study design to estimate IVE; cases were patients with a positive RT-PCR test for influenza, while patients testing negative were classified as controls. Vaccine effectiveness was calculated as one minus the odds ratio (OR) for influenza vaccination, estimated via logistic regression and adjusted for age, sex, hospitalization in intensive care unit (ICU) and calendar time.

We included 2976 patients with influenza as cases, and 4850 patients as controls. Across all seasons, adjusted IVE was 45.6% (95%CI: 28.5% to 58.6%) against all influenza, 67.1% against (H1N1)pdm09 (95%CI:41.9% to 81.4%), 24.8% against A(H3N2) (95% CI:4.1% to 41%) and 46.9% against influenza B (95% CI: 30.6% to 59.4%).

Over the study period, seasonal influenza vaccination has provided substantially higher protection against subtype A (H1N1)pdm09 but lower against A(H3N2), which is consistent with existing evidence. The National Public Health Organization can contribute to systematically monitoring seasonal IVE, providing evidence to promote vaccination, sustain uptake and inform vaccine development.

**Role:** Elsa was the primary investigator, she participated in the data collection, data cleaning and validation, and analysis. For this project Elsa prepared an abstract that was accepted as poster presentation for ESCAIDE 2019 (15) and she is the first author for the manuscript that is under preparation (16).

*Supervisor(s)*: Dr A. Lambrou, Dr Th. Lytras

# **3.2 Effect of early oseltamivir treatment on mortality in critically ill patients with different types of influenza: a multi-season cohort study**

The available evidence on whether neuraminidase inhibitors reduce mortality in patients with influenza is inconclusive and focuses solely on influenza A/H1N1pdm09. We assessed whether early oseltamivir treatment ( $\leq$ 48 hours from symptom onset) decreases mortality compared to late treatment in a large cohort of critically ill patients with influenza of all types.

The study included all adults with laboratory-confirmed influenza hospitalized in intensive care units (ICUs) in Greece over eight seasons (2010-2011 to 2017-2018) and treated with oseltamivir. The association of early oseltamivir with mortality was assessed with log-binomial models, and a competing risks analysis estimating cause-specific and sub-distribution hazards for death and discharge.

Effect estimates were stratified by influenza type and adjusted for multiple covariates. At total 1,330 patients were studied, of whom 622 (46.8%) died in the ICU. Among patients with influenza A(H3N2), early treatment was associated with significantly lower mortality (Relative Risk 0.69, 95% CI 0.49-0.94; sub-distribution Hazard Ratio 0.58, 95% CI 0.37-0.88).

This effect was purely due to an increased cause-specific hazard for discharge, while the cause-specific hazard for death was not increased. Among survivors, the median length of ICU stay was shorter with early treatment by 1.8 days (95% CI 0.5-3.5). No effect on mortality was observed for A(H1N1)pdm09 and influenza B patients.

Severely ill patients with suspected influenza should be promptly treated with oseltamivir, particularly when A(H3N2) is circulating. The efficacy of oseltamivir should not be assumed to be equal against all types of influenza.

**Role:** Elsa was a co- investigator, she participated in data collection, data cleaning, data validation and the review of the manuscript that was published (17).

**Supervisor :** Dr Th. Lytras

# 3.3 Mortality attributable to seasonal influenza in Greece, 2013 to 2017: variation by type/subtype and age, and a possible harvesting effect

Estimating the contribution of influenza to excess mortality in the population presents substantial methodological challenges. In a modeling study we combined environmental, epidemiological and laboratory surveillance data to estimate influenza-attributable mortality in Greece, over four seasons (2013/14 to 2016/17), specifically addressing the lag dimension and the confounding effect of temperature.

Associations of influenza type/subtype-specific incidence proxies and of daily mean temperature with mortality were estimated with a distributed-lag nonlinear model with 30 days of maximum lag, separately by age group (all ages, 15–64 and  $\geq$ 65 years old). Total and weekly deaths attributable to influenza and cold temperatures were calculated.

Overall influenza-attributable mortality was 23.6 deaths per 100,000 population per year (95% confidence interval (CI): 17.8 to 29.2), and varied greatly between seasons, by influenza type/subtype and by age group, with the vast majority occurring in persons aged  $\geq$ 65 years. Most deaths were attributable to A(H3N2), followed by influenza B. During periods of A(H1N1)pdm09 circulation, weekly attributable mortality to this subtype among people  $\geq$ 65 years old increased rapidly at first, but then fell to zero and even negative, suggesting a mortality displacement (harvesting) effect. Mortality attributable to cold temperatures was much higher than that attributable to influenza. Studies of influenza-attributable mortality need to consider distributed-lag effects, stratify by age group and adjust both for circulating influenza virus types/subtypes and daily mean temperatures, in order to produce reliable estimates. Our approach addresses these issues, is readily applicable in the context of influenza surveillance, and can be useful for other countries.

**Role:** Elsa was a co- investigator, she participated in data collection, data cleaning, data validation and the review of the manuscript that was published (18).

**Supervisor**: Dr Th. Lytras

## 4. Communication

#### **Publications**

#### Publications in peer reviewed journals

- Lytras T, Pantavou K, Mouratidou E, Tsiodras S. Mortality attributable to seasonal influenza in Greece, 2013 to 2017: variation by type/subtype and age, and a possible harvesting effect [Internet]. Eurosurveillance. European Centre for Disease Prevention and Control; April 2019. Available from: <u>https://www.eurosurveillance.org/content/10.2807/1560-7917.ES.2019.24.14.1800118#html\_fulltext</u>
- Lytras T, Mouratidou E, Andreopoulou A, Bonovas S, et al. Effect of Early Oseltamivir Treatment on Mortality in Critically III Patients With Different Types of Influenza: A Multiseason Cohort Study [Internet]. OUP Academic. Oxford University Press; February 2019. Available from: https://doi.org/10.1093/cid/ciz101

#### Manuscripts submitted to peer reviewed journals (in review process)

*Under preparation to be submitted:* Influenza vaccine effectiveness against hospitalization with laboratory-confirmed influenza in Greece: a pooled analysis across six seasons, 2013/14 to 2018/19 (16).

### **Reports**

- 1. Greek National Public Health Organisation. Annual epidemiological report on influenza activity in Greece 2018-2019. Athens, Greece, September 2019 (3).
- 2. Epidemiological Surveillance of Legionnaires ' disease in Greece, 2008-2018. Internal report for the Greek National Public Health Organisation. April 2019, Athens, Greece (5).
- 3. Greek National Public Health Organisation. Annual epidemiological report on influenza activity in Greece 2017-2018. Athens, Greece, September 2018 (2).
- 4. Report for the outbreak of gastroenteritis in a group of excursionists, Evvoia Island, July 2018 (14).
- Report for short exchange visit in Vall d'Hebron University Hospital in Barcelona, 10th-13<sup>th</sup> December 2018 (11).
- 6. Report for the Focus investigation for Malaria in a city in Central Greece in November 2017 (12).

### **Conference presentations**

- Mouratidou E, Andreopoulou A, Triantafylou E, Lambrou A, Lytras Th, Georgakopoulou Th. "Epidemiology of Legionnaire's disease in Greece during 2008-2018: focus on foreign travellers". European Scientific Conference on Applied Infectious Disease Epidemiology, 2019 November 27-29, Stockholm, Sweden (accepted as poster presentation, abstract ID: 271).
- 2. Mouratidou E, Lambrou A, Andreopoulou A, Gioula G, Exindari M, Kossyvakis Ath, Mentis A, Georgakopoulou Th, Lytras Th." Influenza vaccine effectiveness against hospitalization with laboratory-confirmed influenza in Greece: a pooled analysis across five seasons, 2013/14 to 2017/18". European Scientific Conference on Applied Infectious Disease Epidemiology, 2019 November 27-29, Stockholm, Sweden (13) (accepted as poster presentation, abstract ID: 269).
- Mouratidou E, Andreopoulou A. "Epidemiology of Legionnaires' disease in Greece". Oral presentation during the 6th meeting of the European Study Group for Legionella Infections (ESGLI). 2019 September 10-12 Athens, Greece.

#### **Other presentations**

- Mouratidou E. "Surveillance of Legionnaires' disease: update on the situation in Greece, 2014-2018". Oral presentation during the 10<sup>th</sup> annual European Legionnaires' Disease Surveillance Network (ELDSNet) meeting under ECDC coordination. 09-10 September 2019 Athens, Greece.
- Mouratidou E. "Update about Influenza activity in Greece for week 3/2019". Oral presentations for the Greek National Public Health Organisation weekly scientific meetings, January 2019, Athens, Greece.
- Mouratidou E. "Surveillance of Legionnaires' disease in Greece, 2008-2017: organising prevention activities". Oral presentation during the 9<sup>th</sup> annual European Legionnaires' Disease Surveillance Network (ELDSNet) meeting under ECDC coordination. 27-28 August, 2018 Lyon France.
- Mouratidou E. "Legionnaires' disease: main characteristics and modes of transmission" Oral presentation during a series of five daily awareness workshops in island regions for hotel managers/owners. May-June 2018 Greece.

## 5. Teaching and pedagogy

# **5.1 Practical training of Post Graduate Public Health Students at the National Public Health Organization (former Hellenic Centre for Disease Control and Prevention), Athens, January 2018**

A 50-hour practical training was organized at the National Public Health Organization (former Hellenic Center for Disease Control and Prevention) in January 2018. The target audience was five postgraduate public health students from the Nursing Faculty of the National and Kapodistrian University of Athens.

The training was organized from 08/01/2018 until 19/01/2018, for three days per week for eight hours per day and two hours on 22/01/2018.

#### Training objectives:

The overall goal was to gain experience in public health. At the end of the practical training the participants were expected to be able to:

- Describe the structures and operations of the National Public Health Organization (former Hellenic Center for Prevention and Disease Control).
- Describe the basic epidemiological surveillance systems in Greece.
- Identify the basic steps of an outbreak investigation.

Teaching methods: Lectures and case study

Evaluation method:

- a) The five finger method
- b) A structured questionnaire

This five finger method was used by the EPIET coordinator Alicia Barassa during the evaluation of the Outbreak Investigation module in Berlin in December 2017.

The structured questionnaire comprised of six questions and responses were collected using a Likert scale (Not at all, Poorly, Somewhat, Very much). In addition, the questionnaire included three open-ended questions about suggestions for improvement and a free field for comments. After the end of the session, the evaluation process was described in detail to the participants who were informed that all responses to the questionnaires were anonymous. The questionnaires were distributed and the participants filled in and handed them over to the facilitator (EPIET-fellow).

**Role:** Elsa organized the practical training and the case study sessions, prepared the training material, delivered lectures/case studies, evaluated the activity and wrote the training activity report.

#### Reflection

The training was evaluated with very positive feedback from all participants. This activity provided the opportunity to learn and combine new methods for evaluation. In the future it would be more beneficial to allocate more time for practical activities, including exercises using statistical programs for epidemiological investigations.

# 5.2 Awareness activities for the prevention of Legionnaires' Diseases among travellers in Greece, May-June 2018

Instructional design/ content: a team from the National Public Health Organization comprised of two public health professionals from the Office for Airborne Diseases and an administrative officer in collaboration with Regional Public Health Authorities and Regional Public Health Laboratories conducted a series of five daily workshops/awareness meetings in five touristic islands in Greece. Each workshop consisted of four 40-minute sessions followed by a 20-minute discussion, so the total duration of each workshop was three hours. The target audience was hotel managers and owners.

The areas where the activities took place were selected based on increased Legionnaire's Disease case burden as it was indicated by the analysis of epidemiological surveillance data.

Training objectives:

- to raise awareness about the risk of legionnaires' disease in hotel settings
- to inform hotel managers about prevention measures regarding the disease.
- **Role:** Elsa with two other colleagues from the Office for Airborne Diseases in the Department for Epidemiological Surveillance and Intervention was actively involved in all phases of organizing the awareness activities, from selection of venues, liaising with the local public health authorities, preparing the agenda and the content of the workshops. Additionally she was a member of the team of Public Health professionals who delivered the awareness lectures on Legionnaires' disease prevention.

#### Reflection

Overall there was an active interest from regional public health authorities and hotel managers. The key to a fruitful cooperation is engaging the local people, both from the regional public health authorities and the private touristic sector as much as possible and considering their opinion. The main issue that has to be considered in similar activities for the future is scheduling the timing of the activities between March-April before the start of the touristic season.

# **5.3 Case study on "West Nile virus outbreak in Greece, 2010", Athens, September 2018**

The European Society for Clinical Virology (ESCV) organized the 21st ESCV Annual Meeting in Athens. A preconference workshop on "Update on West Nile virus infections" was organised by the ESCV, National Public Health Organization (former Hellenic Centre for Disease Control & Prevention) in collaboration with the Hellenic National School of Public Health. The workshop took place on Saturday 22nd of September 2018 from 10am until 5pm at the Hellenic National School of Public Health in Athens and consisted of an introductory part and the case study on West Nile outbreak in Greece, 2010.

The introductory part included presentations on the clinical manifestations of the West Nile disease in humans, laboratory tests applied for the detection of the WNV, surveillance data and public health control actions for WNV infection in humans in Greece and finally a presentation on epidemiological principles and key terms. The duration of the introductory part was 1.5 hours.

The case study was facilitated by EPIET-EUPHEM supervisors: Angeliki Lambrou, Kassiani Mellou, Kyriaki Tryfinopoulou, current fellows: Elisavet Mouratidou, Anastasia Flountzi and EPIET/EUPHEM alumni: Heli Harvala and Maria Tseroni. The twenty seven (27) participants were divided in three groups of eight to ten (8-10) people and each group had two (2) facilitators. The duration of the case study was 3.5 hours. The target audience were virologists, microbiologists, hospital infection nurses and medical doctors.

Training objectives:

The overall goal of this case study was to illustrate the steps of a cross-sectional study to estimate prevalence. By the end of this case study, participants were expected to be able to:

- outline the main steps used for the design of a cross-sectional epidemiological study
- explain the principles of sampling, select a sampling approach suitable for the study objectives
- calculate sample size, calculate sampling weights
- estimate prevalence
- interpret the results of a cross-sectional survey.

For the evaluation, we created a structured questionnaire with eight questions with structured responses using Likert scale (Not at all, Poorly, Somewhat, Definitely). In addition, two open-ended questions about suggestions for improvement and a free field for comments were included. After the end of the case study, the evaluation process was described in detail to the participants, who were informed that all responses to questionnaires were anonymous. The questionnaires were distributed and the participants filled in and handed them over to the facilitators.

**Role:** Elsa was a facilitator for the case study and she also created a structured evaluation questionnaire, and analysed the results of the evaluation. She contibuted in guiding the discusion through open endend questions and helped participants in clarifying the basic concepts of a cross sectional study.

#### Reflection

Preparing for this case study provided an excellent opportunity to review the basic principles of sampling and cross sectional studies. The interaction with professionals from different disciplines helped in exchanging experiences and knowledge. During the case study the participants engaged in active conversation with each other and with the facilitators. After the end of the case study all participants gave a very positive overall feedback.

The use of the case study helped everyone in clarifying basic epidemiological methods using learning by doing approach.

#### 5.4 Case study: "Investigation of Trichinosis outbreak in France".

The case study was part of the "Field Epidemiology and Public Health" Module of the Disaster Medicine and Global Health postgraduate program of the Medical School of the National and Kapodistrian University of Athens. The duration of the case study was two (2) hours. The target audience was 25 postgraduate students.

Training objectives:

At the end of the case study students were expected to be able to:

- Describe the steps of an epidemic investigation
- Develop a case definition in the context of an outbreak investigation
- Construct and interpret an epidemic curve
- Choose an appropriate control group for a case control study
- Calculate and interpret an odds ratio

**Role:** Elsa was a facilitator for the case study. She contributed in maintaining organization and time in the session and in creating an open and safe environment for discussion making sure everyone had an opportunity to participate.

#### Reflection

Preparing for this case study provided an excellent opportunity to refresh the material from the EPIET Introductory course regarding outbreak investigation. This case study also provided the opportunity to exchange experiences and opinions with other health professionals with an interest in Field Epidemiology. In the future it would be useful to add possible case studies regarding disaster scenarios.

# 5.5 Case study: "Epidemiological Surveillance of HIV infection in Spain", Athens, March & May 2019

This case-study was originally designed for the European Program for Intervention Epidemiology Training (EPIET) of the ECDC, by Alicia Barrasa and Yvan Hutin at the Spanish National Centre for Epidemiology for use in the Introductory Course of the EPIET-EUPHEM programme of ECDC. The case study was further translated and adapted in Greek for the purposes of the teaching assignment by the EUPHEM fellow, Dr Anastasia Flountzi. The case study was delivered for the Postgraduate Program in Public Health of the National School for Public Health (NSPH) in Athens, Greece on Thursday, 21<sup>th</sup> March, and on Thursday, 30<sup>th</sup> May 2019, at the National School of Public Health in Athens. The case study was facilitated by the EPIET-EUPHEM Cohort 2017 fellows: Anastasia Flountzi and Elisavet Mouratidou. The target group was postgraduate students who were distributed in two groups of eight (8) and ten (10) participants. The scientific supervisor and head of the HIV Reference Laboratory at the NSPH, Dr Marika Kotsianopoulou, was supervising. The duration of the case study was three (3) hours each day.

#### Training objectives:

The overall goal of this case study was to illustrate the characteristics of different surveillance systems, their implications and the difference between incidence and prevalence. The learning objectives were that at the end of this case study, participants were expected to be able to:

- Describe the characteristics of a surveillance system and explain the implications of these
- Differentiate between incidence and prevalence in disease surveillance, and assess how they are used to inform public health action
- Interpret surveillance information

- Propose public health recommendations on the basis of surveillance information
- Critically evaluate the comparison of reported data from across Europe.

For the evaluation we used a structured questionnaire with eight questions with structured responses using Likert scale (Not at all, Poorly, Somewhat, Definitely). In addition, two open-ended questions about suggestions for improvement and a free field for comments were included. After the end of the case study, the evaluation process was described in detail to the participants who were informed that responses to questionnaires were anonymous. The questionnaires were distributed and the participants filled in and handed them over to the fellows for evaluation.

**Role:** Elsa was a facilitator for this case study and she also created the evaluation form. She contributed enganging the participants in active conversation and she helped the group to focus toward achieving the objectives of the case study.

#### Reflection

Preparing for this case study provided an excellent opportunity for collaboration with the EUPHEM fellow. Overall the feedback from the participants was very positive. It was an excellent opportunity to learn more about engaging people with different backgrounds.

## 6. Other activities

#### 6.1 Surveillance

Active involvement in the routine on-call activities of the Department of Epidemiological Surveillance and Intervention that involved checking data completeness and quality, and performing case investigations for the Mandatory Notifiable Diseases System reports approximately for one week per each month during the two years 2017-2019.

**Role:** Elsa was a Public Health professional on call; she evaluated data completeness and data quality of the notifications, conducted case/cluster investigations and wrote daily internal reports.

# 6.2 Field activities - Contact tracing in the community for Tuberculosis cases in a migrant camp in a Greek island between 05/06/2018-11/06/2018.

The Department of Epidemiological Surveillance and Intervention of the Hellenic Center for Disease Control and Prevention (HCDCP) was notified on 17/5/2018 through the Mandatory Notifiable Diseases System about a confirmed case of drug resistant pulmonary Tuberculosis (TB) in a migrant living in supported housing facility run by a Non- Government Organization in a Greek island.

The HCDCP formed a special working group of experts and developed specific guidelines for the management of the case in collaboration with the local health authorities. At 3/6/2018 a field team was then formed in order to identify the contacts of the case in the community. The field team consisted of an EPIET alumni, an EPIET fellow and a public health professional from PHILOS Project, a specially designed project to address the health-care needs of migrants and refugees.

From June 5<sup>th</sup> to June 11<sup>th</sup> 2018, the field- team consisting of three HCDCP's public health professionals visited the island's local hospital and the camp on a daily basis to collect data in close collaboration with the field coordinator of the camp in order to identify the case's contacts.

The team:

- created data collection form for the interviews
- created a data base to follow up the progress of contact tracing
- conducted interviews with the case's roommates
- collected data on the results of TB screenings of the case's contacts in the hospital
- prepared daily reports on the contact tracing progress

- increased awareness among the local Non Government Organisations about TB symptoms and ways of transmission.

One of the case's roommates was diagnosed with pulmonary tuberculosis and was hospitalized in the same hospital unit in Athens as the index case.

Regarding the case's contacts in the community a total of 28 people were identified. All case contacts were screened with Mantoux test and chest x rays in the local hospital. No other case of active TB was detected among the case's contacts.

**Role:** Elsa was a member of the field team, she prepared data collection forms, contributed in creating the data base and also prepared daily internal activity reports.

#### 6.3 Scientific Committee:

Member of the Scientific Committee for 6th Meeting of the ESCMID Study Group for Legionella Infection that was organized on September 10-12, 2019 in Athens Greece.

The meeting was organized as a conference and covered a wide range of topics related to Legionella and Legionnaires' disease from basic microbial genetics and pathogenesis to applied aspects of detection, control and management. The goal of the meeting was to bring together researchers, professionals and practitioners from various related disciplines. The conference presented the latest scientific developments and knowledge about epidemiology and surveillance; clinical aspects and diagnosis; host-microbe interactions; microbial ecology; outbreaks and case reports; genetics and genomics; prevention and control strategies.

**Role:** Elsa was the liaison between the Greek National Public Health Organisation and the European Study Group for Legionella Infection. She assisted in the selection of a venue for the conference in Athens and recruiting delegates and sponsors for the conference. She participated in abstract reviewing for the conference, the selection of the best oral and poster presentation by students and she moderated one session.

## 7. EPIET/EUPHEM modules attended

- 1. Introductory Course, 24/09/2017-13/10/2017, Spetses, Greece
- 2. Outbreak Investigation Module, 03/12/2017-09/12/2017, Berlin, Germany
- 3. Multivariable Analysis Module, 16/04/2018-20/04/2018, Nicosia, Cyprus
- 4. Rapid Risk Assessment Module, 14/05/2018-19/05/2018, Athens, Greece
- 5. Project Review Module, 27/08/2018-31/08/2018, Lisbon, Portugal
- 6. Time Series Analysis Module, 5-9/11/2018, Brussels, Belgium
- 7. Vaccinology Module, 24/06/2019-28/06/2019, Rome, Italy
- 8. Project Review Module, 26/08/2019-30/08/2019, Prague, Czech Republic.

## 8. Other training

Non applicable.

# **Discussion**

## Supervisor's conclusions

Since 2012, Elisavet has been working as a public health professional in the Department of Epidemiological Surveillance and Intervention at the National Public Health Organization (former Hellenic Center for Disease Control and Prevention) where she was trained as an MS-track fellow. Her commitment to the EPIET programme was evident before and after the start of her fellowship in 2017 and despite having a lot of routine work, she managed to achieve all her EPIET objectives.

Working in the Office for Airborne Diseases, she recognized the need for and took the initiative to create an electronic data base for travel-associated legionnaire's disease (LD) surveillance data. This database is now routinely and conveniently used by the Department in the context of the daily work activities, expediting the time needed for analysis. She continued on to analyze all the national LD surveillance data for a multi-year period, providing the first indications for an increase in the LD notification rates during the recent years. The results of her work prompted her to also initiate and implement public health measures, including successful awareness activities in areas with high disease burden. These activities have been incorporated into the Organization's plans of action for preventing LD. In addition, her pilot study for setting up a new surveillance system for monitoring HAIs in ICUs in Greece will inform the Organization on the strengths and limitations anticipated in setting up such a system which is much needed for the continuous and systematic monitoring of HAIs' in ICUs in a way that is in compliance with EU standards. Elisavet participated and led epidemiological investigations of outbreaks which allowed her to work on her team-building and analytical skills. Her research on influenza vaccine effectiveness for multiple seasons allowed for more precise IVE estimates for subgroup analysis and provided the first country specific pooled IVE estimates. In addition, Elisavet was always eager and enthusiastic to take on teaching activities, for which she prepared the teaching material and approach targeting different audiences, successfully delivered lectures and efficiently facilitated in case studies and workshops.

She demonstrated a positive attitude towards scientific review, and she was always ready to accept constructive criticism. Through the EPIET training and her projects, Elisavet managed to improve her competencies in epidemiology and public health, and advanced her epidemiological, communication, and teaching skills with an area for improvement in her analytical and time management skills.

## **Coordinator's conclusions**

Being already a professional epidemiologist with years of experience working in surveillance at the Greek National Public Health Organisation (former Hellenic Centre for Disease Control and Prevention), Elsa started this fellowship aiming to extend her skills on epidemiological applied research which she has achieved very successfully as shows her participation on the cohort study on the effect of early oseltamivir treatment on mortality in critically ill patients with influenza.

But Elsa has not only expanded her analytical skills, she has contributed greatly to the National system in these two years by setting up a pilot surveillance system for hospital-acquired infections in Intensive Care Units which she will be able to follow up and be part of its future development; and thanks to her work on legionnaires disease surveillance utilizing surveillance data for organizing workshops for hotel managers to raise awareness on prevention of Legionnaires disease among travellers visiting Greece. Overall the workshops were very well received and she will be involved in reorganizing them in 2020. I personally believe that the Greek National Centre has benefited and will continue benefiting from having Elsa amongst its workforce.

## Personal conclusions of fellow

During my EPIET Fellowship as an MS-track fellow I had the opportunity to grow both as a public health professional and as a person. One of my main goals during this fellowship was to implement part of my learning in my routine work and I managed to fulfil that. The diverse variety of projects gave me the opportunity to understand the role of a field epidemiologist and strengthen my competencies.

I got familiarized with different methods of group work and also visited various public health institutes and gained knowledge by interacting with other public health experts from other countries.

I gained valuable experience on how to conduct outbreak investigations, public health research and organize teaching activities. During these two years I worked on improving my communications skills and also my competencies in team building and negotiation. The fellowship also helped me improve my competencies in applied epidemiology especially for routine surveillance and epidemiological studies.

My main challenges are to built up my skills in biostatistics and informatics and be more effective regarding time management. As a person I am very thankful for meeting and networking with all of my co-fellows and all the modules' facilitators who are a great group of talented and motivated public health professionals. In the future I look forward in using all this experience from the fellowship working as a trainer regarding field epidemiology in programmes for public health professionals.

## Acknowledgements of fellow

I am immensely grateful to my site supervisor Dr. Angeliki Lambrou for her infinite support, guidance, motivation and patience. As a site supervisor she went above and beyond and she was always available with constructive advice and helpful feedback for my professional development.

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