



FELLOWSHIP REPORT

Summary of work activities

Larisa Savrasova

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;
- To develop response capacity for effective field investigation and control at national and community level to meet public health threats;

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

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

Pre-fellowship short biography

Before EPIET, Larisa Savrasova worked as an epidemiologist at the Centre for disease prevention and control of Latvia since 2004. Larisa obtained MSc Public Health from Riga Stradiņš University at 2009. She is a second year PhD student at Riga Stradiņš University.

Fellowship assignment: Intervention Epidemiology path (EPIET)

In September 2017, Larisa Savrasova started her EPIET fellowship at the Centre for disease prevention and control of Latvia, under the supervision of Irina Lucenko, but in 2018 EPIET programme supervision was changed. The new supervisor was Elina Dimina who later became the head of Infection disease surveillance and immunisation unit.

Methods

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

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

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

Results

The objectives of these core competency domains were achieved partly through project or activity work and partly through participation in the training modules. Results are presented in accordance with the EPIET core competencies, as set out in the EPIET scientific guide¹.

Fellowship projects

1. Surveillance

Title: Set up enhanced adverse events following immunisation surveillance system and causality assessment mechanisms

Supervisor: Elina Dimina

Latvia conducted regional and national AEFI surveillance, but according to WHO, there is a defined minimum capacity to ensure vaccine safety includes detection of AEFIs, investigation of safety signals, assessment of the causes and final classification of events, as well as vaccine safety communication. To achieve that, there is a need to implement updates in both the surveillance system and legislation and to provide possible AEFI causality assessment. The objective of this project to describe a current situation on surveillance of Adverse events following immunization (AEFI) in order to prepare national recommendations for enhanced surveillance and causality assessment.

Accounting for the WHO recommendation for enhanced adverse events following immunization surveillance, the Ministry of health decided to develop an expert working group, aimed at preparing national recommendations for enhanced AEFI surveillance system. The leader of the working group is a national immunization advisory committee leader. The Centre for the disease prevention and control of Latvia (CDPC) also is involved with secretariat role of the working group.

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

In this stage the working group continues adopting WHO document "Strategy of AEFI surveillance" to the Latvian situation. There is list of objectives of this document and one of them is to provide the evidence for Cabinet to make changes in the definition in some political documents.

According to current legislation all reported AEFI should be investigated by CDPC epidemiologists has the internal regulation on how AEFI investigation should be completed "Procedures by which AEFI should be investigated". The document sets out the criteria based on which visits to medical institutions where suspected vaccine was administered, are carried out.

The next project stage is to implement the WHO recommendations.

Role: Larisa contributed to the project as a part of the working group. She contributed as an epidemiologist and in addition performed secretariat duties for the group. Larisa adopted the translated WHO recommendation text, put together experts' comments, revised and updated the Latvian AEFI reporting and investigation form according to WHO recommendations. She prepared a line list with new or updated AEFI cases to communicate with the State Agency of Medicine. Larisa presented results and recommendations at a local conference.

Title: Invasive pneumococcal disease surveillance data analysis

Supervisor: Elina Dimina

In 2010 in Latvia, invasive pneumococcal disease (IPD) became notifiable for physicians and vaccination of infants with 4 doses of 7-valent pneumococcal conjugate vaccine (PCV7) commenced. In 2012, 10-valent pneumococcal conjugate vaccine (PCV10) (3 doses) vaccination was introduced. We evaluated incidence and serotype distribution of IPD in Latvia and investigated serotypes associated with death from IPD based on surveillance data.

From 2012 to 2018 466 cases of IPD were reported. The highest notified incidence was in 2015 (4.4/100000) fell to 3.9 in 2018. The highest mean annual IPD incidence was in infants (4.8) and in over 65 years (6.0).

PCV10 vaccine were the most prevalent in IPD cases up to 2015 with a decreasing trend from 50% to 19% in 2018. PV23nonPCV13 vaccine serotypes had an increasing trend and rose from 18% to 34%. Non-vaccine serotypes had an increasing trend and rose from 13% to 27%.

Reported total case fatality was 19% (87/466). After adjusting for age, *S.pneumoniae* serotype 3 was associated with death from IPD (adjusted OR 2.3 95%CI 1.25-4.12 p 0.007).

Surveillance data indicate evidence of serotype replacement with increasing trend of serotype 19A and PPV23nonPCV13 and NonVaccine serotypes.

Role: Larisa was a principal investigator of this project. She obtained IPD cases form the electronical surveillance system, completed and cleaned the data base, performed the analyses, presented results, conclusion and recommendations in a poster and oral presentations at international conferences.

Title: Description of invasive pneumococcal disease (IPD) surveillance system

Supervisor: Elina Dimina

The objectives of the IPD surveillance system in Latvia are:

1. Characterization of local trends;
2. Detection of geographic and temporal changes in the prevalence of drug resistant *S.pneumoniae*;
3. Monitoring impact of vaccines on disease;
4. Serotype replacement monitoring

The information IPD notification process was obtained from the Centre for disease prevention and control regional epidemiologists and notification registration group.

There are three paths of IPD cases reporting to the Centre for disease prevention and control of Latvia (CDPC):

- 1) All laboratory confirmed IPD cases should be reported to the CDPC by clinicians.
- 2) All *S.pneumoniae* isolates form normally sterile site should be reported to the CDPC by laboratories.
- 3) *S.pneumoniae* susceptibility to antimicrobial drugs is reporting to the CDPC as a part of the European Antimicrobial Resistance Surveillance System (EARSS). Latvia participates in EARSS since 2004.

Role: Larisa was conducted the interviews with regional CDPC epidemiologists, the notification registration group and obtained information about the route of samples from the laboratories. She wrote a report of the project and presented results and recommendation at the local conference.

2. Outbreak investigations

Title: Salmonellosis outbreak on the wedding party, August 2018

Supervisors: *Elina Dimina, Rita Korotinska*

Following a wedding, three people with gastrointestinal symptoms sought medical aid in the regional hospital emergency department. The outbreak was investigated in order to find the possible source of infection. The food served during the wedding dinner was suspected to be the source of the outbreak

We conducted a retrospective cohort study. The study population was defined as all wedding party participants. We conducted univariable and multivariate analysis to identify food specific association with the disease.

In total 24 cases were reported. All were hospitalized. Contact tracing identified 6 additional cases. Logistic regression demonstrated pork with cheese and mushrooms (aOR 10, p 0,04, 95%CI 1.02-95.6) and grilled chicken wings in honey source (aOR 4.2, 0.03, 95%CI 1.11-16.2) to be independently associated with the disease. Patients' laboratory investigation results detected that all *S.Enteritidis* cultures belong to one type **SENXBa.0002**.

There were recommendations to revise critical points regarding Hazard Analysis Critical Control Point (HACCP) self-control system:

- To introduce journal where kitchen staff with signature approve absents of any gastrointestinal symptoms;
- To mark all cookware for cooked and raw food;
- To enhance cleaning and washing mode

Role: Larisa led the outbreak investigation including case interviews, coordinating and communicating with the national reference laboratory and food and veterinary service laboratory. She developed a questionnaire, performed a cohort study. She wrote an outbreak investigation report.

Title: Acute hepatitis C outbreak at narcology clinic between October - November 2017, Riga, Latvia

Supervisors: *Elina Dimina, Raina Nikiforova*

During December 2017 and January 2018 five acute hepatitis C cases were reported to the Centre for Disease control and prevention of Latvia (CDCP). All cases were epidemiologically linked to one narcology clinic. The investigation was conducted in order to describe the outbreak, identify contact persons, ascertain the extent of the outbreak and to identify the risk factor for transmission.

During the outbreak investigation exposure period and case definitions were defined. All cases were hospitalised, laboratory confirmed and interviewed, letters to the contacts' GPs were sent for tracing. The narcology clinic (NC) activity was observed.

We identified 72 of 92 contacts. From contact tracing, eight more RNS positive HepC cases with possible link to Narcology clinic were identified. Laboratory results identified outbreak association with HepC virus genotypes 1b and 3. Recommendations were provided to the NC to prevent future breaches of infection control.

Role: Larisa contributed to the outbreak investigation. She developed the case definitions, described the cases, developed hypotheses regarding the source of the outbreak, and wrote an outbreak investigation report.

3. Applied epidemiology research

Title: *S.pneumoniae carriage prevalence among children, adults and health care professionals in Latvian hospitals, study protocol*

Supervisor(s): *Elina Dimina*

S.pneumoniae colonisation in Latvian population has not been estimated. There is no data about the characteristics of population level pneumococcal carriage epidemiology which influence the indirect effects of PCV in Latvia.

The aim of the study is to identify the circulating serotypes of *S.pneumoniae* among hospitalized children, adults and health care professionals in Latvia and risk factors (health, demographic and social-economic associated) among study population.

Nine hospitals from all regions of Latvia were selected as sites for the study.

A cross-sectional study will be conducted.

Sample size was calculated using openepi (<http://www.openepi.com/SampleSize/SSPropor.htm>)

Microbiological methods for *S.pneumoniae* identification, serotyping and susceptibility detection was described.

Role: Larisa wrote the study protocol including calculation of the sample size required, communicating to the study sites, preparing all documentation for the ethic committee. She prepared questions for the questionnaire and informed consent form (Latvian, Russian and English).

Title: *Investigation of factors associated with vaccination against diphtheria in Latvian adults' population.*

Supervisor(s): *Elina Dimina*

Latvia has the highest incidence of diphtheria in Europe in last 20 years. We analysed data from the Health Monitoring survey (conducted every other year), to evaluate demographic and health related factors associated with diphtheria vaccination in Latvian adult population

Data obtained from cross-sectional surveys conducted in 2016 and 2018 have been used for the study. Data were stratified by sex, age, place of residence and vaccination statuses against diphtheria. Crude and adjusted odds ratios (OR) were calculated and reasons for vaccination hesitancy were described.

7099 adults participated. Only 49% of the study population had vaccination during the last 10 years Logistic regression results indicated any visits to GP during last year (aOR1.7 95%CI 1.50-1.97 p=0.000), having children in the household (aOR1.3 95%CI 1.09-1.46 p=0.001), age 15-29 (aOR2.5 95%CI 2.11-2.93 p=0.000), age 30-59 (aOR1.8 95%CI 1.28-2.08 p=0.000), sex (aOR1.3 95%CI 1.23-1.51 p=0.000), secondary education level (aOR1.2 95%CI 1.04-1.49 p=0.002), college education level (aOR1.4 95%CI 1.15-1.60 p=0.000), higher or incomplete higher education level (aOR1.7 95%CI 1.41-1.97 p=0.000), two individuals in the household (aOR1.3 95%CI 1.11-1.49 p=0.001), three and more individuals in the household (aOR1.4 95%CI 1.19-1.69 p=0.000), individuals who are fully satisfied of GP provided information about vaccination (aOR3.8 95%CI 2.86-5.01 p=0.000), individuals who are rather satisfied of GP provided information about vaccination (aOR2.6 95%CI 1.97-3.43 p=0.000) had independent associations with vaccination. The commonest reason given for nonvaccination was a "Not informed about necessity to be vaccinated" 23% (864/3637).

The results of this study indicate that vaccination against diphtheria in Latvian adult population was not sufficient, especially in old adults. The data from this study may inform and shape patient education programs conducted in GPs practices for adult vaccinations. There is the need to evaluate and implement general practitioners' communication guidelines on adult patient vaccination.

A manuscript is in preparation.

Role: Larisa performed data analyses and will prepare the manuscript for submission to the peer-reviewed journal.

4. Communication

Publications

One manuscript has been submitted and is currently under review by scientific journal [1], one article is under preparation and will be submitted in September 2019 [2].

Reports

Larisa co-authored one report "Vaccination recommendation for adults" is disseminated in the CDPC website [6].

Conference presentations.

Larisa gave one poster presentation on ESCAIDE 2018 [3], one oral presentation during Riga Stradins university research week on International research conference "Knowledge for use in Practice on Medicine and health care Sciences" [4].

Other presentations

Larisa co-authored one oral presentation during 2nd Euro-Asian summit on pneumococcal infection [5].

Other

5. Teaching and pedagogy

Title: Lectures:

1. Outbreak investigation refresh and examples.
2. Adverse events following immunization surveillance, WHO recommendations

Training objectives: Learning objectives for lecture "Outbreak investigation, refresh and examples":

- To remind the principals of outbreak investigation
- To revise outbreak investigation steps
- To learn outbreak investigation steps through real outbreak investigation prisma

Learning objectives for lecture "Adverse events following immunization surveillance, WHO recommendations"

- To remind global importance of vaccination
- To present current AEFI surveillance scheme with all possible stakeholders involved
- To highlight WHO position regarding AEFI surveillance
- To present the future enhanced AEFI surveillance scheme

Target audience: Epidemiologists from the Centre for disease prevention and control, experts from Food and veterinary service and from Health Inspectorate.

Reflection

There were a one-day meetings of Latvian Association of Preventive Medicine. The lecture has held as a part of educational material during the meetings.

The first (*Outbreak investigation, refresh and examples*) lecture was an overall introduction to communicable disease outbreak investigation. The aim was to refresh outbreak investigation steps and to make the lecture more interesting, I used examples from outbreak investigations I have been working in real life.

The second lecture (*Adverse events following immunization surveillance, WHO recommendations*) was held for the first time. The Centre for disease prevention and control perform AEFI surveillance since 2005 and there was a possibility to explain to the colleagues how surveillance have been conducted, who are the stakeholders, and how and why the Centre is going to enhance AEFI surveillance.

During the development process I adapted the presentations and have reviewed other literature to prepare lectures for the colleagues properly.

Evaluation of the lectures was positive.

6. Other activities

1. Participated at preparing recommendations for adults' vaccination. Final version is available on the Centre for Disease Prevention and Control website.
https://spkc.gov.lv/upload/Metodiskie/vakcinacijaa4landscape_webam.pdf

7. EPIET/EUPHEM modules attended

Nr	Name of the module	Dates	City	Country
1	Introductory course	25 September – 13 October 2017	Spetses	Greece
2	Outbreak investigation module	04-08 December 2017	Berlin	Germany
3	Rapid risk assessments and survey module	14-19 May 2018	Athens	Greece
4	Project review module, 2018	27-31 Augusts 2018	Lisbon	Portugal
	Time series analysis	05-09 November 2018	Brussels	Belgium
5	Multivariable analysis module	16-20 April 2018	Nicosia	Cyprus
6	Vaccinology module	24-28 July 2019	Rome	Italy
7	Project review module, 2019	26-29 Augusts 2019	Prague	Czech Republic

8. Other training

Text

Discussion

Supervisor's conclusions

Larisa Savrasova has managed to combine fellowship requirements with routine work. She managed to implement her new skills in daily work and her new experience was highly appreciated by her colleagues. She also demonstrated good teaching and presentation skills during national level meetings with public health professionals. EPIET program raised her interest on scientific work and she has strong collaboration with Riga Stradins University. Larisa is playing important role in the development process of more targeted national AEFI surveillance system according to the WHO document "Strategy of AEFI surveillance". She presented evaluation of the existing AEFI surveillance system and main results in the high level national seminar organised by WHO. Larisa's work on invasive pneumococcal disease (IPD) surveillance system analysis and data analysis highlighted important weaknesses in collaboration between laboratories, clinical specialists and national surveillance authority as well as imperfection in the flow of samples between settings. That also influenced the national annual program for reference laboratory. She argued her conclusions very well. She also stepped outside her usual field of work and participated two completely different outbreak investigations (Salmonellosis and acute hepatitis C) and did it in strong collaboration with field epidemiologists and senior experts. Another completely different piece of work is analysis of data from the national cross-sectional health survey conducted in 2016 and 2018. Important results regarding self reported vaccination status and risk factors for high hesitancy was found. These results must be published and presented in some national level meetings and used when next campaigns for diphtheria vaccination will be planned. During her EPIET fellowship she demonstrated extremely high capacity and she strengthened her position at The Centre for Disease Prevention and Control.

Coordinator's conclusions

Larisa has worked extremely hard in order to combine her EPIET work with her work in the immunisation department, despite a heavy workload. She has managed to improve her epidemiology skills, including in outbreak management and investigation and technical skills and also develop a protocol for research which will be used in her further doctoral work. Thus, she has addressed all the EPIET competencies and has improved public health in developing guidelines for adult immunisation and for updating investigations for AEFI. Larisa has been a pleasure to work with and I wish her all the success in her career.

Personal conclusions of fellow

This 2-year EPIET programme allowed me to obtain knowledge on different aspects of epidemiology I previously had little experience in. I have learned many new skills through the modules especially through studying practical study questions. During the programme I broad my understanding of the epidemiology of wider range of infectious diseases, of study designs, research methodologies and of outbreak investigation of different infectious diseases. I am proud of contributing to the *S.pneumoniae* carriage study by writing a study protocol and further work during PhD studies. I am very glad to have had the chance to benefit from the programme.

Acknowledgements of fellow

I would like to acknowledge my coordinator Sooria Balasegaram for all the help and constructive comments that helped me improve my knowledge and work practices. I am also very grateful to my supervisor Elina Dimina, to Raina Nikiforova and Rita Korotinska, who helped with specific project advice at my training site, Elena Shmachko and Viktoria Chernisheva for doing a lot of field work during outbreak investigation in regions. I would like to acknowledge the fellows in my cohort and the other cohorts I interacted with.

References

1. L.Savrasova, S.Balasegaram, E.Dimina, I.Zeltina at al. Invasive pneumococcal disease in Latvia in PCV10 vaccination era, 2012-2018. Submitted to Eurosurveillance.
2. L.Savrasova, S.Balasegaram, E.Dimina, D.Grinberga at al. Investigation of risk factors associated with vaccination against diphtheria in Latvian adults' population. Planned to submit to Vaccine
3. L.Savrasova, S.Balasegaram, J.Galajeva Invasive pneumococcal disease in Latvia six years after PCV10 introduction, 2012-2017. In: European Scientific Conference on Applied Infectious Disease Epidemiology, Saint Julian's, Malta, 23 Nov 2018.
4. L.Savrasova, S.Balasegaram, E.Dimina, I.Zeltina at al. Invasive pneumococcal disease in Latvia in PCV10 era, 2012-2018. In: Riga Stradins university International research conference "Knowledge for use in Practice on Medicine and health care Sciences", Riga, Latvia, 2 Apr 2019
5. I.Zeltina, L.Savrasova, S.Balasegaram, E.Dimina, at al. S.pneumonia serotype 3 association with IPD case fatality in Latvia. In: 2nd Euro-Asian summit on pneumococcal infection, Sankt Petersburg, Russia, 24 Aug 2019
6. D.Zavadska, I.Grope, P.Aldins, L.Savrasova, at al. Recommendations for adults' vaccination. In: Centre for Disease prevention and control web-page, https://spkc.gov.lv/upload/Metodiskie/vakcinacijaa4landscape_webam.pdf