

Summary of work activities

Petra Klepac
The ECDC Fellowship Programme
Field Epidemiology path (EPIET), 2020 cohort

Background

The ECDC Fellowship Programme is a two-year competency-based training with two paths: the field epidemiology path (EPIET) and the public health microbiology path (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 provide 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.

According to Articles 5 and 9 of ECDC's founding regulation (EC No 851/2004) 'the Centre shall, encourage cooperation between expert and reference laboratories, foster the development of sufficient capacity within the community for the diagnosis, detection, identification and characterisation of infectious agents which may threaten public health' and 'as appropriate, support and coordinate training programmes in order to assist Member States and the Commission to have sufficient numbers of trained specialists, in particular in epidemiological surveillance and field investigations, and to have a capability to define health measures to control disease outbreaks'.

Moreover, Article 47 of the Lisbon Treaty states that 'Member States shall, within the framework of a joint programme, encourage the exchange of young workers.' Therefore, ECDC initiated the two-year EUPHEM training programme in 2008. EUPHEM is closely linked to the European Programme for Intervention Epidemiology Training (EPIET). Both EUPHEM and EPIET are considered 'specialist pathways' of the two-year ECDC fellowship programme for applied disease prevention and control.

This report summarises the work activities undertaken by Petra Klepac, cohort 2020 of the Intervention Epidemiology path (EPIET) at the National Institute of Public Health of Slovenia (in Slovene: Nacionalni inštitut za javno zdravje, NIJZ).

Pre-fellowship short biography

Petra Klepac, an MD with specialisation in public health, has been working as an epidemiologist at the Communicable Diseases Centre at the National Institute of Public Health (Slovene: Nacionalni Inštitut za javno zdravje, NIJZ) of Slovenia. Her main fields of interest are infectious disease epidemiology, surveillance and outbreak investigation. The title of her specialisation assignment was 'Effects of ambient air pollutants on preterm birth and low birth weight: a meta-analysis'. She participated in the after action review (AAR) of 'West Nile virus (WNV) 2018 cAse detection and contRol in Europe (AWARE)' project and contributed to the update of the WNV preparedness plan in Slovenia.

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Methods

This report accompanies a portfolio that demonstrates the competencies acquired during the EPIET fellowship 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 ECDC Fellowship Manual¹.

1. Epidemiological investigations

Outbreak investigations

An outbreak of acute gastroenteritis in primary school Grosuplje, Slovenia, 2021

Supervisors: Veronika Učakar (MD, PhD), Jana Svetičič Marinko (MD), NIPH, Ljubljana, Slovenia

NIJZ defines a norovirus outbreak in an institution, as two epidemiologically linked cases and one confirmed case within an institution. On 11 November 2021, the regional paediatrician informed the NIJZ of at least 20 pupils absent from classes at the dislocated unit (DU) of the primary school Grosuplje, Slovenia, due to diarrhoea and vomiting. We immediately proposed hygiene measures and exclusion of ill persons from classes. We defined cases as pupils or employees at DU with onset of vomiting, diarrhoea, nausea or stomach cramps from 2 November 2021 onwards without confirmed COVID-19 infection during the same time. We conducted a cohort study among pupils and employees defining exposure as a group activity on 9 November 2021, excluding cases with symptoms onset before 9 November and restricting the case definition to outbreak cases with symptom onset during the outbreak peak on 9–11 November. Stool specimen of a case was tested for bacteria, parasites and viruses. Seventy-six cases were identified (attack rate 32%) with symptom onset during 3–13 November, occurring in both employees and pupils of all classes. Fifty-nine percent of pupils and employees responded to questions on the outcome and exposure in a cohort study. Compared to non-participants, participants in the group activity had two times higher risk of developing illness during 9–11 November (relative risk: 2.00, 95% confidence interval 1.11–3.62). Pupils and employees shared a small number of toilets. The specimens collected, tested positive for norovirus. Results suggested initial norovirus introduction into DU from the community. Group activities at DU on 9 November were the probable source of cases occurring during the peak of the outbreak, followed by secondary transmission at DU. Early outbreak notification and cooperation with public health authorities as well as current highly sensitive definition of a norovirus outbreak in an institution are crucial for rapid detection and timely implementation of control measures.

Role of the fellow: Principal investigator. Developed questionnaire, cleaned and analysed data, wrote outbreak report.

Training modules related to assignment/projects

EPIET/EUPHEM Introductory Course: The 10 steps of outbreak investigation were applied. Knowledge of descriptive epidemiology and types of epidemiological studies enabled formulation and confirmation of the hypothesis. Understanding the possibility of bias and confounding contributed to the interpretation of results. Knowledge on statistical inference contributed to the exclusion of chance as a possible explanation of the data.

Outbreak Investigation Module: R code for data cleaning, descriptive, univariate and stratified analysis enabled the estimation of crude and adjusted risk ratios.

Multivariable Analysis Module: Knowledge of the principles of multivariable analysis and the corresponding R code enabled the estimation and interpretation of adjusted odds ratios to exclude possible confounding.

¹ European Centre for Disease Prevention and Control. European public health training programme. Stockholm: ECDC; 2020. Available from: <https://www.ecdc.europa.eu/en/publications-data/ecdc-fellowship-programme-manual-cohort-2021>

Educational outcome

During this outbreak investigation, the fellow developed several competencies. She formulated a case definition, described an outbreak in terms of time, place and person, generated hypotheses about risk factors, conducted analytical epidemiological study, recommended evidence-based control measures and applied basic principles of risk communication. She prepared the final report on the outbreak investigation.

2. Surveillance

Design and implementation of a new surveillance system to monitor weekly excess mortality based on the EuroMOMO methodology to monitor the impact of COVID-19 on all-cause mortality

Supervisors: Mario Fafangel (MD), Irena Klavs (MD, PhD), NIPH, Ljubljana, Slovenia

Excess mortality in a given period is defined as the difference between the observed and expected overall mortality in that period. At the end of October 2020, NIJZ introduced weekly surveillance of excess mortality in Slovenia and joined the European mortality monitoring (EuroMOMO) network. The objectives were timely monitoring of the excess mortality within the comprehensive national COVID-19 surveillance system and assessment of impact of the COVID-19 epidemic on overall mortality in Slovenia. Every week, data on all individual deaths were updated using the electronic Central Registry of Patient Data (CRPD) which is updated daily. The EuroMOMO algorithm was applied to data on deaths from 2015 onwards using R software and excluding data after week 1, 2020 from baseline estimation. Substantial increase in mortality has been defined as a z-score >2. We defined COVID-19 death as a registered death in a person with SARS-CoV-2 infection confirmed within the previous 28 days or after death. Substantial increases were found during weeks 43, 2020 to 3, 2021, weeks 44 to 49, 2021 and weeks 5 to 7, 2022, coinciding with the peaks of reported COVID-19 deaths, and in week 29, 2022, coinciding with the end of a heat wave and a smaller peak in reported COVID-19 deaths. Mortality was the highest among aged the 65-and-above age group. Weekly all-cause mortality surveillance represented a complementary tool for timely assessment of epidemic impact. Timely data on the cause of death were needed to accurately assess impacts of COVID-19 as well as concurrent indirect factors e.g. access to healthcare. The results contributed to the implementation of targeted control measures and awareness of risk in general population.

Role of the fellow: Engaged with stakeholders to ensure access to historical data and weekly updated data, performed data management and analysis, shared knowledge on weekly data management and transfer with colleagues, and wrote the surveillance report for 2020.

Training modules related to assignment/projects

EPIET/EUPHEM Introductory Course: Lectures and case studies on how to develop a surveillance system and how to use the results for action were applied. Basic knowledge on R software was gained through exercises-enabled data analysis using the EuroMOMO algorithm. Interpretation skills gained through case studies were applied in writing of the report.

Time Series Analysis module: Knowledge of analysis of residuals was applied in the assessment of the model fit (i.e. no remaining pattern in the residuals as shown in one of the algorithm outputs).

Educational outcome

During developing and using this surveillance system, the fellow developed several competencies. She identified surveillance data needs to assess risks, setup and run a surveillance system and proposed appropriate public health interventions based on surveillance data (i.e. nonpharmacological interventions and vaccination of vulnerable older groups of population, especially in long-term care facility settings).

3. Applied public health research

3.1 Prevalence of and risk factors for sexually transmitted infection with Chlamydia trachomatis to guide control measures: findings from the Slovenian National Survey of Sexual Lifestyles, Attitudes and Health, 2016–2017

Supervisor: Irena Klavs (MD, PhD), NIPH, Ljubljana, Slovenia

In Slovenia, the annual reported incidence of *Chlamydia trachomatis* (CT) infection during 2014–2018 varied between 11.9 and 16.0 cases per 100 000 population, which was 10 times lower than in other European countries. CT infection prevalence of 4.7% among sexually experienced 18–24-year-olds was estimated in the national survey in 2000. A proportion of CT infections in Slovenia could remain undiagnosed and untreated. One of the objectives of the second Slovenian National Survey of Sexual Lifestyles, Attitudes, and Health, 2016–2017 was to estimate the prevalence of and identify risk factors for CT infection among sexually experienced 18–49-year-olds in Slovenia. Data were collected from a stratified probability sample of the general population.

Respondents were invited to provide urine for testing for CT infection with polymerase chain reaction (PCR). Data were weighted to adjust for the distribution of sex, age, region, and type of community of the general population. We estimated the prevalence of CT infection and used logistic regression to calculate adjusted odds ratios (OR) with accounting for the sample stratification and clustering.

Out of 3 473 eligible individuals, 1 046 sexually experienced respondents with a test result were included. The prevalence of CT infection was 0.5% (95% confidence interval [CI]:0.1–1.9) in men and 1.7% (95% CI: 0.9–3.3) in women. The highest prevalence was among women in the 18–24 age group (5.6%; 95% CI: 2.0–14.4). New sex partner in the previous year was associated with CT infection among women in the 18–49 age group (OR: 8.9; 95% CI: 2.5–31.9). Targeted testing was considered in Slovenia: introduction of annual opportunistic testing for CT for sexually active women <25 years old, and offering testing to older women reporting a new sex partner during the previous year in primary healthcare gynaecology clinics to prevent late sequelae for reproductive health among infected women. By known evidence, impact of widespread young population screening on the reduction of the prevalence of CT infection is not clear.

Role of the fellow: Planned and conducted data analysis, interpreted the data, proposed public health recommendations and published the manuscript in a peer-reviewed journal as the first author [1].

3.2 Research protocol: Slovenian national point prevalence survey of healthcare-associated infections (HAIs) and antimicrobial use in long-term care facilities (LTCFs), 2024

Supervisor: Irena Klavs, (MD, PhD), NIPH, Ljubljana, Slovenia

Estimated annual burden of six main types of HAIs in European hospitals was 501 disability-adjusted life years per 100 000 population. Most LTCFs are homes for the elderly and the residents are considered at risk for an HAI and its adverse outcomes with consequent frequent antimicrobial use. Previous studies in Slovenian LTCFs of limited national representativeness found prevalence of HAIs similar to other EU/EEA countries and frequent empirical and broad-spectrum antibiotic use. The protocol for a national survey in LTCFs in 2024 has been adapted from the ECDC Protocol for point prevalence surveys in European LTCFs to obtain comparable results, using the same inclusion criteria and case definitions. Assuming that 21 629 of beds in Slovenian LTCFs were 100% occupied and adjusting for the design effect estimated for Slovenia by ECDC in previous studies, we calculated that 4 282 residents and 27 LTCF units would need to be included in the survey to estimate an anticipated HAI prevalence of 4% with a 95% confidence interval of 3–5% (1% precision). We will obtain a probability sample from the published list of 134 Slovenian LTCF units ranked by number of beds. Data on HAIs and antimicrobial use as well as defined risk factors, infection prevention and control and antimicrobial stewardship will be collected. Prevalence on the day of the survey will be calculated as percentages of residents with at least one active HAI and/or receiving at least one antimicrobial. Univariate and multivariate logistic regression models of association of any HAI acquired during LTCF stay with risk factors will be constructed. Analyses will be done in STATA software. Possible limitations include limited national representativeness in case of non-response, misclassification of HAIs, data entry errors and underascertainment of causative microorganisms. A pilot study is planned before the national study in one of the LTCFs to check the feasibility and to test the validity of the results.

Role of the fellow: Drafted the protocol.

Training modules related to assignment/projects

EPIET/EUPHEM Introductory Course: Knowledge gained during Operational research Inject days was applied, including formulating the research question and calculation of sample size.

Multivariable Analysis Module: Knowledge of principles of logistic regression and multivariate model building as well as STATA syntax was applied to obtain adjusted OR and identify risk factors.

Rapid Assessment and Survey methods (RAS) module: Knowledge of principles of sampling and role of the design effect was applied to obtain the sample size.

Educational outcome

During participation in the surveys, the fellow developed several competencies. She selected an appropriate sampling strategy in a population and a sample from a source population, drafted a study protocol, developed evidence-based recommendations for target groups, calculated and interpreted point estimates and confidence intervals for measures of outcome frequency and association, drew conclusions from analysis results, performed statistical analyses with statistical software (STATA) including multivariable analysis. She adhered to ethical principles regarding data protection and confidentiality, and applied relevant laws in all steps of research.

4. Teaching and pedagogy

Analytical studies in the investigation of point-source outbreak: online workshop for Slovenian public health professionals

Supervisor: Veronika Učakar (MD, PhD), NIPH, Ljubljana, Slovenia

In Slovenia, outbreaks have been rarely supported with strong analytical epidemiological evidence. The online workshop of 1.5 hours for the public health professionals employed at the NIJZ aimed to refresh the principles of analytical epidemiology and present a simple tool developed by the Robert Koch Institute (RKI) for univariate analysis of data collected during a point-source outbreak. Online pre-course assessment and evaluation surveys were launched for participants.

Role of the fellow: Invited participants, prepared theoretical background presentation, prepared practical examples to train the use of the RKI tool, and drafted pre-course assessment and evaluation surveys.

Training modules related to assignment/projects

EPIET/EUPHEM Introductory Course: Knowledge of principles of learning needs assessment helped with the design of the workshop and knowledge of Bloom's verbs helped to formulate teaching objectives.

Educational outcome

During the teaching activity, the training competencies were developed. The fellow needed to create a suitable example to be able to stimulate the discussion on the results. She needed to adapt to the online environment with less direct feedback from the participants.

5. Communication

Publications related to the EPIET fellowship

1. **Klepac P**, Berlot L, Klavs I. Prevalence of and risk factors for sexually transmitted infection with Chlamydia trachomatis to guide control measures: findings from the Slovenian National Survey of Sexual Lifestyles, Attitudes, and Health in 2016–2017. *Acta Dermatovenerol APA* | 2021;30:141-147. doi: 10.15570/actaapa.2021.34
Petra Klepac, Tina Zupanič, Eva Leban, Aleš Korošec, Irena Klavs

Reports

2. **Klepac P**, Zupanič T, Leban E, Korošec A, Klavs I. Excess mortality during the first wave of covid-19 in Slovenia. In: The first wave of COVID-19 epidemic in Slovenia. Ljubljana: NIJZ, 2021. Available 15.8.2022
<https://www.nijz.si/sl/publikacije/prvi-val-epidemije-covida-19-skozi-prizmo-zdravstvene-statistike>

3. **Klepac P**, Fafangel M, Zaletel M, Leban E. Excess mortality surveillance and covid-19 in Slovenia in 2020. In: Surveillance report on communicable diseases in Slovenia in 2020. Ljubljana: NIJZ, 2022. Available 15.8.2022
https://www.nijz.si/sites/www.nijz.si/files/uploaded/epidemiolosko_spremljanje_nalezljivih_bolezni_v_sloveniji_v_le tu_2019_in_2020_0.pdf

4. **Klepac P**, Leban E, Kranjec N, Obid I, Galičič A, Kustec T et al. Surveillance report on confirmed COVID-19 cases in Slovenia in 2020. In: Surveillance report on communicable diseases in Slovenia in 2020. Ljubljana: NIJZ, 2022. Available 15.8.2022
https://www.nijz.si/sites/www.nijz.si/files/uploaded/epidemiolosko_spremljanje_nalezljivih_bolezni_v_sloveniji_v_le tu_2019_in_2020_0.pdf

Conference presentations

5. **Klepac P**, Fafangel M, Klavs I, Zupanič T, Leban E, Korošec A. Excess mortality during the first year of the COVID-19 epidemic in Slovenia, week 10/2020–week 10/2021. Poster. ESCAIDE 2021.

6. **Klepac P**, Berlot L, Klavs I. Prevalence of and risk factors for sexually transmitted infection with Chlamydia trachomatis to guide control measures: findings from the Slovenian National Survey of Sexual Lifestyles, Attitudes and Health, 2016–2017. Accepted as a poster to be presented at ESCAIDE 2022.

7. **Klepac P**, Galičič A, Kranjec N, Fafangel M. Social contacts during the COVID-19 epidemic: CoMix Europe survey in Slovenia, March–June 2021. Poster. Slovenian national public health conference, 2022.

Other activities

8. **Klepac P**, Učakar V. Compliance with nonpharmaceutical interventions in Slovenian adults during January–March 2021. SI-PANDA prevalence survey. Sent for review.

6. Other activities

The fellow participated in:

- implementation of the CoMix Europe study in Slovenia: translated and adapted the questionnaire, interpreted the results;
- implementation on the WHO survey on pandemic fatigue in Slovenia (SI-PANDA): cooperated in formulating the questions, interpreted the results;
- supervision of the contact-tracing call centre during the COVID-19 epidemic: coordinated meetings and organisation of work (e.g. during contact tracing involving large events), provided answers to contact tracers' questions regarding their work, interviewed cases with more complex history, provided connections of the centre with epidemiological service, clinics and laboratories;
- monthly on-call service at the Ljubljana regional unit of the NIJZ: responded to urgent events relevant to public health, e.g. outbreaks of COVID-19 in long-term care facilities and schools, an outbreak of gastrointestinal disease during mass gathering; collected data and organised response to possible cases of measles, invasive meningococcal disease, *legionella* in long-term care facility, monkeypox etc.; answering questions from clinicians related to epidemiological situation or public health recommendations etc.;
- ad-hoc COVID-19 epidemiological situation assessments and scientific literature review for development of the public health recommendations: e.g. cooperated in (re-)formulation of public health recommendations for cases and contacts of COVID-19, reviewed literature on the effectiveness of vaccination and non-pharmacological interventions in various scenarios to guide recommendations on public health measures (e.g. quarantine, working from home), wrote reports on the epidemiological situation in European countries for the Ministry of Health to guide decisions on public health measures at the entry to Slovenia;
- preparation of the national 'One Health meeting' with the presentation on coronaviruses in humans;
- preparation and interpretation of collected data on COVID-19 and excess mortality for the Slovenian Ministry of Health, media, and the general public.

7. EPIET/EUPHEM modules attended

1. Introductory Course part 1, (28.09.2020 – 16.10.2020), virtual
2. Introductory Course part 2 - Operational Research inject days, (9–10.11.2020), virtual
3. Outbreak Investigation, (07–11.12.2020), virtual
4. Introductory Course part 3, (26.04.2021 – 07.05.2021), virtual
5. Rapid Assessment and Survey Methods, (5–16.05.2021), virtual
6. Project Review 2021, (23–27.08.2021), virtual
7. Vaccinology, (14–18.02.2022), virtual
8. Multivariable analysis, (14–18.03.2022), virtual
9. Time Series Analysis, (4–8.04.2022), ISS, Rome, Italy
10. Management, Leadership and Communication in Public Health, (13–17.06.2022), ECDC, Stockholm, Sweden

Discussion

Coordinator's conclusions

One of the main goals of the EPIET programme is for fellows to develop core competencies in field epidemiology mainly through project or activity work, but also partly through participation in training modules and application of epidemiological methods to provide evidence to guide public health interventions for communicable disease prevention and control. This report summarises all the activities and projects conducted by Petra Klepac during her two-year EPIET fellowship (cohort 2020) as an MS-track fellow at the National Institute of Public Health in Ljubljana, Slovenia.

Petra's surveillance project contributed to the implementation of the European mortality monitoring (EuroMOMO) algorithm in Slovenia and enabled the country to join the EuroMOMO network. Petra's research project on the CT infection contributes and confirms the knowledge on disproportionate burden of the infection in young women and stimulates the discussion on the effectiveness of opportunistic testing. Petra's research protocol will enable to implement a study among high risk LTCF population that is expected to increase in the future.

Supervisor's conclusions

Petra achieved all the EPIET training objectives with a professional approach to all the tasks assigned. She was motivated to learn fast, and delivered products of scientific excellence. Her newly developed EuroMOMO surveillance system provided evidence for the high impact of COVID-19 on mortality among the elderly population in Slovenia and identified the importance of non-pharmacological interventions before vaccination was available. Her research on CT infection contributed to evidence-based proposal of opportunistic testing in young women as well as women reporting new sex partners during the previous year to be considered. Her teaching activity introduced a free and easy-to-use tool that will hopefully stimulate more analytical studies to be conducted during outbreak investigations at the regional level. Her completion of the EPIET training will contribute to the workforce capacity-building efforts in the area of communicable diseases and public health in Slovenia, and towards the achievement of the necessary critical mass of field epidemiologists trained according to EPIET standards in Slovenia.

Personal conclusions of fellow

This two-year programme allowed me to obtain knowledge on different aspects of epidemiology I previously had little experience in field (e.g. sampling, multivariable analysis and use of statistical software). The progress will hopefully allow me to conduct more in-depth analyses to provide solid evidence for prevention and control of communicable diseases in Slovenia.

Acknowledgements of fellow

I would like to acknowledge all my site supervisors for all their feedback and guidance during these two years. I would like to extend my acknowledgments to the whole Communicable Disease Department of the NIJZ. I would also like to acknowledge my front-line coordinators for all the support and constructive comments that helped me improve my knowledge and work practices.