MediPIET Summary report of work activities

Katerina Kirkovik Kolevska

North Macedonia, Cohort 4 (2021)

Background

1. About MediPIET

The Mediterranean and Black Sea Programme for Intervention Epidemiology Training (MediPIET) aims to enhance health security in the Mediterranean and the Black Sea region by supporting capacity building for prevention and control of natural or man-made threats to health posed by communicable diseases. It is a competency-based in-service two-year fellowship during which selected fellows conduct projects and field investigations at a MediPIET Training Site in their home country and attend MediPIET modules.

Since mid-2021, MediPIET has been implemented by ECDC as a part of the EU Initiative on Health Security. More information about the programme is available at: https://www.ecdc.europa.eu/en/training-and-tools/training-programmes/fellowships/medipiet.

2. Pre-fellowship short biography

Katerina Kirkovik Kolevska is a medical doctor, specialised in epidemiology, and works in the Department for epidemiology of communicable diseases in the Institute of Public Health, in Skopje, North Macedonia. During the COVID-19 pandemic, she was working in the Emergency Operation Center.

Fellowship

On 20 September 2021, Katerina Kirkovik Kolevska started her MediPIET fellowship at the Institute of Public Health, Skopje, North Macedonia. This report summarises the work performed during the fellowship.

National supervisors: Dragan Kochinski, Kristina Stavridis

Scientific coordinator: Kostas Danis

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Fellowship projects

3. Surveillance

Risk factors associated with COVID-19-related death during the Omicron period in North Macedonia, 2022

Introduction: During the Omicron period (December 2021–December 2022), when COVID-19 vaccines were already available, over 1500 COVID-related deaths occurred in North Macedonia. We aimed to identify factors associated with COVID-19-related death during this period.

Methods: Using the demographic, clinical and vaccination data obtained from the COVID-19 national surveillance database, we conducted a retrospective study among all people with laboratory-confirmed SARS-CoV-2 infection during the Omicron period (6/12/2021–31/12/2022). We used multivariable log-binomila regression to calculate adjusted risk ratios (aRR).

Results: During the study period, 128 804 COVID-19 cases occurred. The median age was 44 years (IQR:32-60); 55% were female, 40% were unvaccinated, and 58% received at least two COVID-19 vaccine doses. Overall, 1 541 deaths were registered, with a case-fatality of 1.2%; the median age at death was 76 (IQR: 69-82) years, 60% were male, 93% had at least one comorbidity and 60% were unvaccinated. Case-fatality was higher in males (aRR=1.7; 95%CI=1.5‑1.9), people ≥60 years (aRR=12; 95%CI=10–15), people with neurologic disease (aRR=4.5; 95%CI=3.2–4.3), carcinoma (aRR=3.0; 95%CI=2.3–3.9), kidney disease (aRR=2.5; 95%CI=1.9–3.2), cardiac disease (aRR=3.7; 95%CI=3.2–4.3), lung disease (aRR=1.8; 95%CI=1.5–2.2), diabetes (aRR=1.7; 95%CI=1.5–1.9). Compared with unvaccinated, case-fatality was lower in those vaccinated with two doses (aRR=0.37; 95%CI=0.34–0.41) or ≥3 doses (aRR=0.08; 95%CI=0.06–0.1).

Conclusions: Among SARS-CoV-2-infected people in North Macedonia during an Omicron-predominant period, males, older people, those with comorbidities, and unvaccinated people had a higher case-fatality. Targeting these high-risk groups for COVID-19 vaccination could help reduce mortality from COVID-19 in the future.

Role and outputs: principal investigator. The fellow wrote the protocol, analysed the data, presented at ESCAIDE 2023, and submitted a manuscript to a peer-reviewed journal.

Supervisors: Dragan Kochinski, Kristina Stavridis

Status: Completed

4. Outbreaks

Healthcare-associated Hepatitis B outbreak, Shtip, North Macedonia, August 2022 – January 2023

Background: On 23/01/2023, the regional Centre for Public Health (CPH) in Shtip reported a cluster of five cases of Hepatitis B in the Clinical Hospital Shtip (CHS). We investigated the outbreak to identify the potential source of infection and implement control measures.

Methods: A case was defined as any person hospitalised at the Department of Internal Medicine at CHC who was diagnosed with Hepatitis B from 25/08-10/09/2022. We searched for cases and conducted a retrospective cohort study among patients hospitalised at the same department during August and September 2022 (contacts). We interviewed all contacts in their homes using the Hepatitis B investigation form and tested them for Hepatitis B. We calculated attack rates (AR) using the number of contacts as denominator and risk ratios (RR).

Results: Of the 21 identified contacts, 11 (52%) lived in Shtip; 14 (67%) were males; the median age was 65 (range 32–86) years. Overall, we identified 8 cases (AR 38%); all were symptomatic, with the main reported symptoms being jaundice, nausea, malaise, and dark urine. The onset of symptoms occurred from 26 August 2022 to 16 January 2023. The highest ARs were among females (43%) and 60–69-year-olds (44%). Three deaths were registered among cases (case-fatality 38%). ARs were higher among those reporting potential sexual transmission (RR=2.9, 95% CI: 1.6–5.2), sharing a room with a case (RR=7.7, 95%CI:1.1–52), invasive diagnostic procedures (RR=1.10, 95%CI 0.37–3.27) and surgical interventions (RR=1.07, 95% CI:0.31–3.71). Environmental investigation indicated the use of common syringes for many patients during cannula lavage.

Conclusion: The occurrence of eight Hepatitis B cases in the department of internal medicine within five months, suggests ongoing hospital transmission of hepatitis in the department, requiring urgent measures. We recommended strict adherence to hygienic practices and aseptic and hygienic procedures during medical interventions to prevent further spread of the infection and to prevent the emergence of new cases.

Role and outputs: principal investigator. The fellow was involved in all the steps of the outbreak investigation, analysed outbreak data, wrote the final report with recommendations and actions and shared the results with the stakeholders.

Supervisor: Dragan Kochinski

Status: Completed

5. Research

Estimating COVID-19 vaccine effectiveness against severe acute respiratory infections (SARI) hospitalisations associated with laboratory-confirmed SARS-CoV-2 in North Macedonia

Background: Many questions remain about the effectiveness of different COVID-19 vaccines in preventing severe disease. We aimed to estimate COVID-19 vaccine effectiveness (VE) against laboratory-confirmed SARS-CoV-2 infection among SARI patients in North Macedonia.

Methods: We included adult patients who met the SARI case definition and were admitted to four SARI sentinel surveillance hospitals. Patients were tested for SARS-CoV-2 by RT-PCR. We conducted a test-negative case-control study, where cases tested positive and controls tested negative for SARS-CoV-2. We calculated adjusted odds ratios (aOR) using logistic regression and vaccine effectiveness (VE) as 1-aOR.

Results: Between 7 February and 10 December 2023, we enrolled 255 SARI patients; 43 cases and 212 controls. Of all SARI patients, the median age was 65 years (IQR: 54-73); years; 56% (n=143) were male; 36% were unvaccinated, 1,6% received one dose, 44% two doses, 17% three doses and 1,2% four doses. Of the 162 vaccines doses administrated, the most common COVID-19 vaccine brands were Pfizer 55 (34%), Sinopharm 23 (14%) and Sinovac 28 (17%). Compared with controls, cases were more likely to be males (65% vs. 35%, aOR=1.57, 95%CI=0.79–3.12), more likely to be 60+ years of age (84% vs. 16%, aOR=3.51, 95%CI=1.49–8.25), cases were 68% less likely to have been vaccinated with two doses (aOR=0.32 95%CI 1.14–0.68) and 80% less likely to have been vaccinated with three doses (aOR=0.20 95%CI 0.04–0.58) compared with controls. Cases were less likely to have been vaccinated with two COVID-19 doses (aOR=0.32 95%CI 1.14–0.68) and three doses (aOR=0.20 95%CI 0.04–0.58), indicating an adjusted VE of primary vaccine series (two doses) against infection of 68% (95%CI=32%–88%) and VE of three doses of 80% (95%CI=47%–96%).

Conclusions: During a period of Omicron-predominant circulation in North Macedonia, we found that COVID-19 vaccination protected against severe infection due to COVID-19. Our results could be used to raise awareness of the protective effect of COVID-19 vaccines and support an increase in uptake of COVID-19 boosters among at-risk population.

Role and outputs: principal investigator. The fellow adapted the WHO protocol and the questionnaire, conducted the trainings of study staff, did continuous monitoring, evaluation and performed weekly data checks, performed data entry and data analysis, submitted an abstract to ESCAIDE 2022, presented at a national conference (6th Macedonian Congress of Infectious Diseases with International Participation, November 2022, Struga, North Macedonia), and wrote a report.

Supervisors: Dragan Kochinski, Kristina Stavridis

Status: Completed

6. Scientific communication

Conference presentations

- **K. Kjirkovikj Kolevska**. COVID-19 Vaccine Effectiveness in preventing severe acute respiratory infections (SARI), North Macedonia, February 7th – October 2nd, 2022: Preliminary results. 6th Macedonian Congress of Infectious Diseases with International Participation, November 2022, Struga, North Macedonia.
- **K. Kjirkovikj Kolevska**. Risk factors associated with COVID-19-related death during the Omicron period in North Macedonia, 2022. ESCAIDE conference, 2023, Barcelona, Spain.
- D. Kochinski, **K. Kjirkovikj Kolevska**, et al. Re-emergence of Crimean-Congo Haemorrhagic Fever in North Macedonia, 2023. ESCAIDE conference, 2023, Barcelona, Spain.

Publications and outputs

K. Kjirkovikj Kolevska. Risk factors associated with COVID-19-related death during the Omicron period in North Macedonia, 2022. [submitted to a peer-reviewed journal]

7. Teaching activities

Estimating COVID-19 vaccine effectiveness against severe acute respiratory infections (SARI) hospitalisations associated with laboratory-confirmed SARS-CoV-2 in North Macedonia

Target audience: Hospital staff, doctors and nurses working in the departments involved in the SARI vaccine effectiveness study.

Date, duration, and location of the teaching activity:

4 February 2022, three hours, General Hospital '8th of September', Skopje

22 February 2022, three hours, Clinic for pulmology and allergology, Skopje

1 October 2022, three hours, Clinic for infectious diseases and febrile conditions, Skopje

Description of the teaching activity: The training aimed to train the hospital staff to collect data during the SARI vaccine effectiveness study. Presentations covered the study design, introduction of the protocol, objectives of the study, SARI case definition working process and results from the SARI surveillance. Participants also went through a practical training using KoBo toolbox software, where they took specimens, collected and stored enhanced surveillance data and filled in a questionnaire. During the last session, an open discussion took place including participants' questions, needs and possible issues and solutions.

Evaluation: All participants were able to complete the questionnaires and take specimens suggesting that the learning objectives had been achieved. Further monitoring of the activities during the study, including data-checking in the KoBo toolbox, timely reporting and sending specimens, suggested that the objective of the training were met.

8. Other activities

- COVID-19 surveillance, weekends on duty and on-call duty during the pandemic;
- Daily, weekly COVID-19 reports;
- Monthly communicable diseases reports;
- Annual reports of the national annual public health programs and surveillance of acute communicable diseases;
- Health education campaigns for COVID-19 and influenza;
- Field work during different outbreaks, contact tracing, and writing reports;
- National workshop on Strategic Risk Assessment; Introducing the Strategic Tool for Assessing Risks (STAR), May 16–18, 2022, Skopje, North Macedonia;
- United Nations BSAFE security awareness training, online;
- ECDC Training workshop in Risk Communication, 13–14 September 2022, Stockholm, Sweden;
- R training workshop by Epiconcept, online;
- Communicable diseases and HIV committee meetings;
- Euro-Save network meetings, online;
- CDC/CSTE Scientific Writing Workshop, 24–28 April 2023, Zagreb, Croatia;
- ECDC Consultation meeting of implementation and evaluation of NPIs in the EU/EEA, 24–25 May 2023, Stockholm, Sweden.

9. MediPIET modules attended

- Introductory Course – Part 1, 20 September – 8 October 2021, online.
- Inject day: Phylogeny, 20 October 2021, online.
- Inject days: Operational Research, 26–27 October 2021, online.
- Inject days: Data Collection, 10–11 November 2021, online.
- Outbreak Investigation module, 6–10 December 2021, online.
- Multivariable Analysis module, 14–18 March 2021, online.
- Multivariable Analysis inject day, 30 March 2022, online.
- Project Review module I & Introductory Course – Part 2, 20–29 April 2022, online.
- Rapid Assessment and Survey Methods (RAS) & Mass Gatherings, 6–10 June 2022, online.
- Project Review Module II, 29 August–2 September 2022, Lisbon, Portugal, face-to-face.
- Time Series Analysis module, 7–11 November 2022, Bilthoven (Utrecht), Netherlands, face-to-face.
- Chemical, Biological, Radiological and Nuclear Awareness and Mitigation (CBRN) module, 13–17 March 2023, Petrovac, Montenegro, face-to-face.
- Vaccinology Inject day, 29 March 2023, online.
- One Health & Vector-borne Diseases module, 2–4 and 15–17 May 2023, online.
- Project Review module 2023, 28 August – 1 September 2023, Lisbon, Portugal, face-to-face.

10. Supervisor conclusion

During the two-year MediPIET fellowship, Katerina Kjirkovikj Kolevska was involved in many activities, such as a study on COVID-19-related death, outbreak investigations, estimating COVID-19 vaccine effectiveness in preventing SARI and other assignments as required by the MediPIET programme and guide. Katerina conducted and finished all the assigned activities successfully. Her reports were well prepared, concise with findings and clearly stated recommendations. She was able to conduct her work as a team player with appropriate supervision, accepting feedback, suggestions and ideas. Her MediPIET assignments led to successful outcomes, including the implementation of recommendations and scientific publications. During the fellowship, she developed her skills for intervention epidemiology and especially for analytical epidemiological methods in cohort and vaccine effectiveness studies.

10. Personal conclusions of fellow

The MediPIET fellowship programme was a great opportunity to learn and practice more field epidemiology and data analysis. Learning by doing provided us with training and practical experience in applied epidemiology and guided us in public health interventions for communicable disease prevention and control. It was challenging, but totally worth it. The modules were well organised, and included useful lectures delivered by experienced speakers and real-life examples in field epidemiology. The whole programme was a valuable experience which helped me improve and update my knowledge, gain new skills in epidemiology and public health, and strengthen my skills to respond to future public health treats.

11. Acknowledgements

First, I would like to acknowledge my MediPIET supervisors Dragan Kochinski and Kristina Stavridis for their support, sharing their knowledge and experience, and providing me with project opportunities, and a lot of valuable information about epidemiology and public health. I also couldn't be more grateful to my frontline scientific coordinator, Kostas Danis, who was always available and supportive, teaching and guiding me during the whole fellowship, giving me great support and solving problems, and providing great advice for my future opportunities and career. I would also like to thank my project supervisors Mark Katz and Iris Finci from WHO Euro, for their support, help and advice, sharing their experience, consultation, and suggestions and helping me finalise my project assignment. I would also like to thank all my colleagues, colleagues from ECDC, for organising great modules and delivering useful training with a lot of productive lessons but also a lot of fun. Finally, I would like to thank all my colleagues from Cohort 4 for sharing their experiences and knowledge, and creating a family atmosphere over the last two years.