Background

ECDC's Fellowship Programme is a two-year competency based training course offering two paths: the field epidemiology path (EPIET) and the public health microbiology path (EUPHEM). After the two-year training course, the graduates will have extensive expertise in applying epidemiological or microbiological methods to guide public health interventions for communicable disease prevention and control.

Both curriculum paths provide training and practical experience through a ‘learning by doing’ approach at 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’ which is why 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 Martina Del Manso, cohort 2019 of the Intervention Epidemiology path (EPIET) at the Istituto Superiore di Sanità (ISS).

Pre-fellowship short biography

Martina Del Manso has a bachelor’s degree in Statistics for Demographic and Social Analysis and a Master’s Degree in Health, Social Statistics, and Demography. Martina is permanent staff member at the Italian National Institute of Health (Istituto Superiore di Sanità). Before starting the EPIET fellowship she worked for nine years in the Department of Infectious Diseases (Epidemiology Unit). Her main tasks included design and implementation of surveillance systems for several infectious diseases at national level including measles, rubella, arboviruses and invasive bacterial diseases. She was also responsible for the production of several surveillance outputs (12 routine reports and ad hoc analysis). She also worked as an analyst and a coordinator on the set-up and implementation of an Italian event-based surveillance system in the Italian Epidemic Intelligence network, supporting the organisation of training and event-based surveillance activities. Martina has also contributed to several epidemiological studies in the field of communicable diseases and vaccination. While at the Italian National Institute of Health, she was also involved in various national and international surveillance system projects, as well...
as in outbreak investigations. She also had the opportunity to collaborate with senior epidemiologists from different backgrounds. During the pandemic, she helped to coordinate the Italian integrated SARS-CoV-2 surveillance system and was responsible for outputs such as epidemiological bulletins and dashboards, coordination of data collection for the generation of the weekly risk assessments and the set-up and coordination of routine evaluation of the surveillance system.

On 12 September 2019, Martina Del Manso started her EPIET fellowship at the Italian National Institute of Health (Istituto Superiore di Sanità), Rome, Italy, under the supervision of Patrizio Pezzotti (main supervisor) and Flavia Riccardo (co-supervisor). Daniel Thomas was the frontline coordinator (FLC) until December 2020, when he was replaced by Alastair Donachie. This report summarises the work carried out during this fellowship.

**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 and summarising and communicating scientific evidence and activities with a specific epidemiological 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, with the exception of those prohibited for reasons of confidentiality.

**Results**

The objectives of the 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**

1.1 Outbreak investigations

**COVID-19 outbreak in Lombardy region, February 2020**

Supervisors: Patrizio Pezzotti, Flavia Riccardo

On 20 February 2020, when the first autochthonous case was detected in Lombardy region followed by a rapid increase in cases, the Infectious Diseases Department of the Istituto Superiore di Sanità were contacted by the Lombardy Region Health Department to support the activation of contact tracing activities and the first epidemiological analysis during the initial phase of the outbreak. Martina was selected to provide this support to the Local Health Unit in Milan.

A total of 305 cases of SARS-CoV-2 were confirmed by regional reference laboratories, 51 (16.7%) of which were confirmed by the national reference laboratory (ISS), and seven deaths were identified. At the time of analysis, the symptom onset date was only available for 26 of the 305 cases. A total of 197 cases were male (64.8%) with a median age of 60 years (interquartile range: 45-74 y; min 4y; max 92y). All cases were of Italian nationality. At least 66 cases (41.9%) were hospitalised and 20 (30.3%) of these were hospitalised in intensive care. No cases reported a history of travel to countries with SARS-CoV-2 transmission during the presumed 14-day incubation period (no index case was identified). Not all patients were traced back to a single chain of transmission. Martina was one of the co-investigators, supporting the collection of case data, contact tracing, collection and analysis of data and the drafting of the outbreak report.

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Training modules related to assignment/projects

**EPIET/EUPHEM Introductory Course**
This course reviewed basic concepts of epidemiology which helped in the analysis of data and the use of statistical software for the analysis. It was also helpful to review the procedure for notifying cases in surveillance systems and the data collection instruments used to retrieve information.

**Outbreak Investigation Module**
This module was key for all activities. For example, it reviewed the importance of creating a case-definition (and a contact definition) in the first instance.

**Educational outcome**
The involvement in these activities helped to develop several skills. From a technical point of view, Martina improved her skills in applying theoretical frameworks for outbreak investigation to a practical situation. She also learnt about the importance of standardising data collection and extracting useful information from the database to translate into public health action. Martina also had to interact with several other professionals working at regional and local level and she learnt how important it is to understand their priorities and realities, so that instruments designed at national level can be used effectively.

1.2 Surveillance

**COVID-19 surveillance: design, implementation, and analysis**
Supervisors: Patrizio Pezzotti, Flavia Riccardo

SARS-CoV-2 infection in humans causing clusters of severe pneumonia (1–3) was first detected in the city of Wuhan, China, in December 2019. On 20 February 2020, the first case of locally-acquired SARS-CoV-2 infection was diagnosed in northern Italy. At this stage, Istituto Superiore di Sanità (ISS) was involved in implementing a surveillance system to collect data. On 27 February 2020, a case-based surveillance system for all laboratory-confirmed human SARS-CoV-2 infections was established in collaboration with the Italian National Institute of Health (ISS), the Italian Ministry of Health, and the regional and local health authorities using the case definition from the European Centre for Disease Prevention and Control (ECDC) [13].

Through a web platform, the system collects individual data on laboratory confirmed cases of SARS-CoV-2 infection and additional information. Results for different levels of aggregation and risk categories are now published daily and weekly on the ISS website and made available to national and regional public health authorities. These results are one of the information sources for the regional monitoring and risk assessment system. The role of the fellow was to coordinate the exchange at national and regional level, to prepare the results for dissemination at public level, to develop the risk assessment system and to coordinate the data quality controls.

Martina worked on almost all stages of the COVID-19 surveillance. She helped develop the protocol and designed the system for data collection. She was responsible for preparing an infographic with an automatic dashboard for epidemiological updates (https://www.epicentro.iss.it/coronavirus/sars-cov-2-dashboard) and epidemiological analysis on a daily basis. Each week, she prepared a bulletin with the epidemiological update, an epidemic intelligence bulletin, and regional reports on data quality for internal use. In total, she prepared 58 monitoring reports on the risk classification of an uncontrolled and unmanageable epidemic. She also submitted a manuscript as first author and this was published in a peer-reviewed journal [1] and she participated in the preparation of several other manuscripts [2-5, 13-16].

**Monitoring the risk of a COVID-19 uncontrolled and unmanageable epidemic**
Supervisors: Flavia Riccardo, Patrizio Pezzotti

After the first wave of COVID-19 in Italy (February–April 2020) there was a need to set up a system to monitor the pandemic at sub-national level in order to help decision-makers decide what measures to implement, when and how. In this context, on 30 April 2020 the national government signed a new decree setting out indicators that would define the epidemiological risk and impact of the pandemic in each Italian region. These indicators would be used alongside other parameters to establish non-pharmaceutical Interventions (NPI) at regional level.

Together with the Ministry of Health, the ISS was given the responsibility for collecting data, calculating these indicators and producing a weekly risk assessment of every region. The system used ECDC’s methodology to assess 21 indicators, looking at the probability of infection and the impact of the pandemic. Martina participated in the preparation of a manuscript (under revision) on this risk assessment monitoring [12].

Martina played a key role in developing and adapting the design of the monitoring system and data collection procedures. She used data from different sources (COVID-19 integrated surveillance system, aggregated data from the Ministry of Health and ad hoc data collected from the regions) to calculate and analyse indicators and prepared draft reports with weekly risk assessments which were later presented to a committee designated by the national government.
Training modules related to assignment/projects

EPIET/EUPHEM introductory course
The EPIET/EUPHEM introductory course familiarised the fellows with the core concepts in surveillance. It covered the development and evaluation of a surveillance system as well as key aspects of the analysis of surveillance data. This knowledge helped me to be aware of the key aspects of a surveillance system and provide the appropriate input.

Time Series Analysis module
The Time Series Analysis module built on the EPIET/EUPHEM introductory course and the Multivariable Analysis Module. It represents a cornerstone in the preparation of the fellows for a more in-depth analysis of surveillance data. The module helped me to plan and execute impact analysis of measures (e.g. COVID-19 vaccination) on COVID-19 related outcomes.

Multivariable Analysis Module
The Multivariable Analysis Module builds on the EPIET/EUPHEM Introductory Course and strengthens the fellows’ statistical skills. The module introduced a variety of regression methods that we applied for surveillance data analysis to produce institutional reports and scientific articles.

Educational outcome
The design and implementation of the systems in both projects has taught me how to set up surveillance in an emergency and/or in a complex administrative context. It has also taught me how various stakeholders have different priorities and how to take these into consideration. The analysis of large databases has taught me a lot about how to automate processes. Finally, the analysis aspect has given me the opportunity to further develop my methodological skills by learning more about which methods are appropriate for each type of situation.

2. Applied public health research

Initial impact of SARS-Cov-2 vaccination on healthcare workers in Italy
Supervisors: Patrizio Pezzotti, Massimo Fabiani

In Italy, the COVID-19 vaccination campaign began in December 2020 with the vaccination of healthcare workers. To analyse the actual impact that vaccination was having on this population group, we measured the association between week of diagnosis and healthcare worker status using log-binomial regression. By the weeks 22–28 of March 2021, we observed a 74% reduction (PPR 0.26; 95% CI 0.22-0.29) in the proportion of cases reported as healthcare workers and an 81% reduction in the proportion of symptomatic cases reported as healthcare workers, compared with the week with the lowest proportion of cases among healthcare workers prior to the vaccination campaign (31 August – 7 September 2020). The reduction, both in relative and absolute terms, of COVID-19 cases in healthcare workers that began around 30 days after the start of the vaccination campaign suggests that COVID-19 vaccines are effective in preventing infection in this group.

Martina worked as a co-investigator on this project. She contributed to the design of the study, performed data analysis and was the second author on a manuscript which was published in a peer-reviewed journal [4].

Risk of SARS-CoV-2 infection and subsequent hospital admission and death at different time intervals since first dose administration; an analysis of the first 7.3 million vaccinated people in Italy
Supervisors: Patrizio Pezzotti, Massimo Fabiani

There is a need to assess the real-world impact that vaccines have on COVID-19 related outcomes. We analysed data on over seven million people who had been vaccinated. Compared with the period 0–14 days post-first dose, we found risk reductions for SARS-CoV-2 infection, hospitalisation, and death of 78% (95% confidence interval (CI): 0.21-0.24), 89% (95% CI: 0.09-0.15) and 93% (95% CI: 0.04-0.11) respectively 35–49 days post-first dose. These results provide an opportunity for public health authorities to promote participation in the ongoing COVID-19 vaccination campaigns.

Martina worked as a co-investigator on this project. She contributed to the design of the study, performed data analysis and was a co-author of the manuscript which was published in a peer-reviewed journal [9].

Epidemiological characteristics of COVID-19 cases in non-Italian nationals diagnosed in Italy: results from the national integrated surveillance system
Supervisors: Massimo Fabiani, Flavia Riccardo

International literature suggests that disadvantaged groups could be at higher risk of morbidity and mortality from SARS-CoV-2 infection due to poorer living/working conditions and barriers to healthcare access. Yet, there was no concrete evidence of this disproportionate impact on non-national individuals, including international migrants, short-term travellers, and refugees.
We analysed data from the Italian integrated surveillance system of all COVID-19 cases diagnosed at the beginning of the local epidemic on 20 February 2020 up until 3 May 2020. We used multi-level negative-binomial regression models to compare the attack rate, the case-fatality rate, and the rate of admission to hospital and intensive care unit (ICU) between the Italian and non-Italian nationals. The analysis was adjusted for differences in socio-demographic characteristics and differences in the week and region of diagnosis.

Overall, we analysed 179,361 COVID-19 cases, including 10,286 (5.7%) non-Italian nationals. Compared to Italian nationals, non-Italian nationals had a lower attack rate [adjusted rate ratio (ARR)= 0.65, 95% confidence interval (CI): 0.52-0.81]. However, non-Italian cases were more likely to be hospitalised (ARR=1.44, 95% CI: 1.32-1.57) and admitted to ICU (ARR=1.66, 95% CI: 1.46-1.89), with differences being more pronounced in those coming from countries with a lower human development index (HDI). We also observed an increased risk of death in non-Italian cases from low-HDI countries compared to Italian cases (ARR=1.49, 95% CI: 1.03-1.18).

Martina worked as a co-investigator on this project, involved in the data analysis and interpretation of the results. She was also co-author of a manuscript which was published in a peer-reviewed journal [8].

**Analysis of influenza vaccination response in elderly**

**Supervisors:** Silvia Vendetti, Patrizio Pezzotti

Influenza represents an important public health and medical challenge and a significant burden on society in terms of morbidity, mortality, hospitalisations, and lost working time. An urgent public health problem is understanding the weak vaccine responses observed in a high percentage of the population, predominantly in the elderly, and to identify a correlation between a low immune response to influenza vaccination in the elderly and host factors.

This knowledge could be also relevant when evaluating new vaccinations with enhanced protection for this population. The aim of the project is to identify a correlation between immune responses to influenza vaccination in the elderly and host factors. The study was a monocentric prospective study with a healthy patient enrolment carried out among general practitioners in Rome and its provinces.

The descriptive and analytical data analysis was carried out to identify a probable correlation between a low immune response to influenza vaccination in patients >65 years and a certain host factor.

Given the complexity and size of this project (duration three years), Martina was asked to create a data input mask in SurveyMonkey which could be used for all the project periods.

**Study protocol for the impact of the anti-rotavirus vaccination on hospitalisation for infant gastroenteritis in Italy**

**Supervisors:** Fortunato D’Ancona, and Patrizio Pezzotti

Anti-rotavirus vaccination in Italy has only been introduced in some regions since 2013 and until 2018 there was no national strategy for offering universal vaccination to new-borns. In order to gather evidence on the impact of the regional-based vaccination strategy, this study aims to measure the impact of vaccination on hospitalisation due to infant gastroenteritis (GEA) by comparing regions that have progressively introduced vaccination against those where immunisation had not been introduced in 2017. Furthermore, within the regions which had introduced vaccination during the study period, a comparison will be made between the hospitalisation rate before and after introduction of vaccination.

Time series analysis techniques will be applied to assess monthly hospitalisation rates taking into account seasonality, age, sex, geographical area and the vaccination coverage. Finally, multivariable linear regression techniques will be applied to assess the effect of vaccination on the mean length of stay, controlling for other characteristics. Afterwards, the study will be repeated to verify the impact in those regions that introduced vaccination in 2018 (as requested under the National Immunisation Plan (NIP)).

Martina contributed to the development and finalisation of the study protocol. She will be the responsible for the collection and analysis of data from national discharge registers. The next step will be for her to support the writing of the report and to prepare a manuscript.

**Training modules related to assignment/projects**

**EPIET/EUPHEM Introductory Course**

The introductory course familiarised the fellows with the core concepts of operational and applied research. It covered the development of study protocols and the drafting of aims and objectives relevant to a national public health institute, as well as data analysis and presentation for the other modules to build on.

**Outbreak Investigation Module**

The Outbreak Investigation Module was useful for refreshing data input methods.

**Multivariable Analysis Module**

The Multivariable Analysis Module builds on the EPIET/EUPHEM Introductory Course and helped to strengthen statistical skills. The methods covered in this module were used to carry out the analysis the analysis detailed in the work activities.
**Time Series Analysis module**
The Time Series Analysis module built on the EPIET/EUPHEM introductory course and the Multivariable Analysis Module. The methods covered were particularly useful when working on the project ‘Initial impact of SARS-COV-2 vaccination on healthcare workers in Italy’.

**Educational outcome**
Participating in these research projects and even being in the lead on some of them, was an important educational experience. I learnt and applied new epidemiological methods and data management skills. Furthermore, it was a great opportunity to learn from and work with others in different departments.

**4. Teaching and pedagogy**

*Indagine di focolaio epidemico (Outbreak investigation)*
This course was designed to train the national health system personnel in each Region to enhance their identification and intervention skills during an epidemic and/or outbreak and thus build a network at national level. Martina developed a case study for performing the activities involved in the 10 steps of an outbreak investigation. The course was held from 29-31 October 2019.

*Continuous training of the Italian Epidemic Intelligence Network (EI)*
In recent years, a new group has been formed in Italy called the Italian Epidemic Intelligence Network (EI) and this course was primarily aimed at healthcare professionals who are part of the EI network. The objective was to strengthen their technical competency as event-based surveillance analysts and offer them an overview of the activities and methodologies related to this discipline as used internationally. Martina prepared lectures and case studies. The course was held on 28-30 January 2020.

**Training modules related to assignment/projects**

**EPIET/EUPHEM Introductory Course**
The main take-home-message from the introductory course was the importance of retaining the learner's attention through the use of various communication techniques.

**5. Communication**

**Publications related to the EPIET fellowship**


12. Flavia Riccardo, Giorgio Guzzetta, Alberto Mateo Urdiales, Martina Del Manso, Xanthi D. Andrianou, Antonino Bella, Patrizio Pezzotti, Simona Carbone, Tiziana De Vito, Francesco Maraglino, Vittorio De Micheli, Claudio Dario6, Enrico Coscioni, Giovanni Rezza, Andrea Urbani, Stefano Merler, Silvio Brusaferro on behalf of the Italian COVID-19 monitoring group; Data for action in COVID-19 response: effectiveness of upscaling mitigation measures on the basis of weekly quantitative rapid risk assessments in Italy (under revision).

National reports


Conference presentations


Other presentations


21. Webinar ‘From the spread of infectious diseases in Tuscany to the COVID-19 epidemic in European countries: evidence and reflections’ - Presentation ‘Case fatality rate in patients diagnosed with SARS-CoV-2 in Italy: variations by epidemic phases and between regions’ - 3/2/2021 – Ars Toscana


6. EPIET/EUPHEM modules attended

1. Introductory Course, 23/09/2019 – 11/10/2019, Spetses, Greece
2. Outbreak Investigation, 09/12/2019 – 13/12/2019, Nicosia, Cyprus
3. Multivariable Analysis, 20/04/2020 – 24/04/2020, Online
5. Time series Analysis, 25/01/2021 – 29/01/2021, Online
6. Rapid Assessment and Survey Methods, 27/04/2021, 05-06/05/2021, Online
7. Vaccinology, 14/06/2021-18/06/2021, Online.

7. Other training

- Scientific meeting at ISS - presentation: ‘Update on the evolution of the COVID-19 pandemic’
- Webinar ‘Dalla diffusione delle malattie infettive in Toscana all'epidemia COVID-19 nei paesi europei: evidenze e riflessioni’ [From the spread of infectious diseases in Tuscany to the COVID-19 epidemic in European countries: evidence and reflections] – Presentation: ‘Case fatality rate in patients diagnosed with SARS-CoV-2 in Italy: variations per fasi epidemiche e tra le regioni’ [Case fatality rate in patients diagnosed with SARS-CoV-2 in Italy: variations by epidemic phases and regions].

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 through participation in training modules and the application of epidemiological methods to provide evidence to guide public health interventions for communicable disease prevention and control. This report summarises all activities and projects conducted by Martina during her two-year EPIET fellowship (cohort 2019) as a Member-State track fellow at the Istituto Superiore di Sanità (ISS) in Rome, Italy.

Martina has had a successful fellowship and achieved all her learning competencies. In particular, she further developed her skills in surveillance where she played a key role in developing and adapting the design of the newly integrated surveillance system for COVID-19 in Italy. Furthermore, she improved her skills in teaching and developed case studies for the continuous training of the Italian epidemic intelligence network. Finally, her research projects have allowed her to develop her skills in operational research, particularly in protocol writing, data analysis and most notably in the preparation of manuscripts highlighted by her impressive contribution to several publications in peer-reviewed journals as both first and co-author.

It has been a real pleasure working as Martina’s frontline coordinator. I have found her to be highly motivated, hard-working with a really positive ‘can do’ attitude during what has been a difficult and challenging time. The fellowship has allowed her to further develop her competencies and given her the opportunity to implement many of the skills she has acquired from the programme in her daily work. I wish her all the very best for her future career.

Supervisor’s conclusions

Martina is a versatile researcher who shows initiative and has a very positive overall attitude. Her communicative and flexible personality has allowed her to interact and engage very well, not only with the staff unit but also with people working within the Italian national health system. As a fellow, she has achieved the EPIET training objectives, showing a professional approach to all the tasks assigned and a high degree of independence in completing them. She has been a very dedicated and hard worker and has grown in her infectious disease field epidemiology competencies. She worked independently in conducting and leading studies and training courses and in disseminating results, coordinating and engaging well with the project supervisors. All the activities she has been involved in have been finalised and disseminated through presentations and peer-reviewed articles.
Personal conclusions of fellow

EPIET has been an immensely enriching experience. I came into the programme with a relatively solid background in disease surveillance (predominantly at national level) and some experience in outbreak investigation and operational research and I was looking to further develop these last two areas. Unfortunately, my EPIET fellowship has been strongly affected by the pandemic. My experience was a little limited and although I searched for opportunities in the area of outbreak investigation at regional and local level, it proved possible. However, it was still a very formative period, both in terms of the support from the entire cohort and from the frontline coordinators who supported me and the modules in which I had the opportunity of participating. It was immensely valuable to share knowledge, science and values among European colleagues and networks and to undertake cross-border collaboration. This enabled me to gain a strong sense of how the field and surveillance systems function and the methods used for their interpretation, evaluation, improvement, enabling me to turn data into knowledge with practical implications for action and interventions. I hope I will continue to contribute to the knowledge cascade, sharing experiences and ideas within and outside Italy, strengthening the role of epidemiology and public health in promoting quality intervention and decision-making to maximise well-being in complex situations.

Acknowledgements of fellow

First of all, I would like to thank ECDC for having selected me as an EPIET fellow.

I would like to thank my site supervisors, Patrizio Pezzotti and Flavia Riccardo, as well as my colleagues Xanthi Andrianou, Alberto Mateo Urdiales, Antonino Bella, Paolo D'Ancona, Matteo Spuri, and Daniele Petrone for mentoring and supporting me through these two years, for being so flexible and helpful with my plans and ideas and for always looking for ways to help me. To Xanthi, I would like to say thank you for being the best office mate ever and an important source of inspiration and serenity who always found kind words for me. Thank you to all my project supervisors for having devoted their time to mentoring me. Thank you to my Frontline Coordinators (first Daniel Thomas and then Alastair Donachie) as well as to all the module facilitators and organisers because their hard and inspiring work was vital to making our fellowship great. Special thanks to Giulia Errico for surviving with me. Finally, I would like to thank my EUPHEM/EPIET/EAP fellows of cohort 2019 for these wonderful two years. It will be longer than expected before we see each other again but until then I will always smile when I think about the brief but wonderful time we spent together (Forza Ragazzi!!!).