



EPIET REPORT

Summary of work activities

Danai Pervanidou

European Programme for Intervention
Epidemiology Training (EPIET), 2011 cohort

Background

Pre-fellowship short biography

Danai Pervanidou has been working at the Unit for Vaccine Preventable Diseases, Department of Surveillance and Intervention, Hellenic Center for Disease Control and Prevention (KEELPNO) since 2008. Prior to that she studied medicine, specialising in neurology, and completed a Masters in Public Health (National School of Public Health, Greece).

EPIET assignment

On 19 January 2012, Danai Pervanidou was assigned to the Unit for Vector-borne Diseases, Department of Surveillance and Intervention, Hellenic Center for Disease Control and Prevention (KEELPNO), Athens, Greece (MS-track).

Fellowship projects

Surveillance project

Malaria enhanced surveillance systems

1.1 Active malaria case detection in affected areas, 2012

Title: Active case detection to prevent re-establishment of malaria, Greece, 2012

Background: Greece has been malaria-free since 1974. In 2011, *P. vivax* malaria re-emerged with 42 locally-acquired cases, 36 (86%) of which occurred in Evrotas, Lakonia, an agricultural area with many migrants from malaria-endemic countries. In 2012, we actively searched for cases to ensure early diagnosis and treatment. We evaluated this practice in terms of reduction of locally-acquired cases and timeliness of diagnosis.

Methods: We interviewed all reported cases in Greece regarding their travel history to identify locally-acquired cases. In areas with at least one locally-acquired case, we tested all immigrants for malaria using Rapid Diagnostic Tests

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(RDTs) and microscopy and screened all residents for fever on a weekly basis for one month. In Evrotas, we visited all the houses of immigrants, twice per month, and tested those with a fever for malaria. We compared the number of locally-acquired cases in 2011 and 2012 all over Greece and in Evrotas. We evaluated timeliness of diagnosis before and after the implementation of active-case-detection (ACD) in Evrotas by estimating the time between onset of symptoms and diagnosis.

Results: In 2012, 20 *P. vivax* locally-acquired cases were recorded in Greece (52% decrease compared with 2011). ACD identified 25 (27%) cases; 22 imported and 3 locally-acquired. In 2012 in Evrotas, 10 locally-acquired cases were recorded (72% decrease compared with 2011) and 17 imported; ACD identified 18 (67%) cases. The median delay between onset and diagnosis in Evrotas was three (range 0-15) days, down from six (range 2-17) in 2011.

Conclusions: ACD in Evrotas improved timeliness of diagnosis and may have contributed to a decrease in the number of locally-acquired cases. We recommend continuing ACD in all areas reporting locally-acquired cases to prevent re-establishment of transmission in Greece.

Role: Wrote the 2012 revised surveillance protocol and supervised its implementation all over Greece. Primary investigator in all areas apart from Evrotas. Collected and analysed the data.

Status: Completed, abstract accepted at ESCAIDE 2013¹.

1.2 Malaria screening of immigrants from endemic countries in detention centres and affected areas of the East Attica region

Background: We conducted screening to test immigrants from endemic countries for malaria.

Methods: We screened the asymptomatic migrants using Rapid Diagnostic Tests (RDTs) and the symptomatic - suspected cases (e.g. febrile) using both RDT and microscopy of blood smears.

Results: Between 6 August and 28 November 2012, we conducted malaria screening in eight detention centres, including five centres along the Greek-Turkish border. A total of 1 015 immigrants were screened using RDTs, 991 of whom with known nationality (20% from Afghanistan, 19% from Pakistan, 14% from Bangladesh, the rest from other African and Asian countries). The median age of screened immigrants was 26.5 years (range: 14-57 years) and 95% were males; 22% of the RDT-screened immigrants were symptomatic (16% had fever) or reported recent fever. We obtained seven blood smears. All RDTs and blood smears were negative for malaria. In Markopoulo, between 28 August and 28 September 2012, we screened 132 immigrants using RDTs. A total of 44 blood samples were taken for microscopy and PCR, in symptomatic individuals or those who had reported fever in the 15 days prior to examination or had a history of malaria. All RDTs and blood samples were negative for malaria. In Marathon, we screened 499 immigrants using RDTs between 25 June and 20 July 2012. A total of 145 blood samples were taken for microscopy and PCR, in symptomatic individuals or those having reported fever within 15 days prior to examination or had a history of malaria, or in order to study RDT sensitivity. All RDTs and blood samples were negative for malaria.

Conclusions: All screened immigrants were found negative for malaria. The negative test results of screening raised questions about the sensitivity and value of using RDTs in asymptomatic individuals.

Role: Primary investigator. Wrote the protocol and supervised its implementation. Collected and analysed the data.

Status: Completed. No official report was produced.

1.3 Timely detection of malaria cases among immigrants from endemic countries in Athens

The objective was to test for malaria (using Rapid Diagnostic Test) all suspected cases (e.g. febrile cases) among immigrants from endemic countries. The screening network included the KEELPNO mobile health units in the historical centre of Athens, the primary health centres of NGOs and specific hospitals in the centre of Athens.

Role: Primary investigator. Wrote the protocol.

Status: Completed. The project was not systematically implemented.

1.4 Malaria case investigation and management

Role: Drafted the revised malaria case management guidelines and the case and focus investigation guidelines for 2012, including a definition of suspected malaria cases to guide clinicians in testing for malaria. Performed or supervised the malaria case investigation (telephone or personal interviews with a structured questionnaire) in 14 locally acquired malaria cases (11 in 2012 and three in 2013). Organised and supervised the malaria focus investigation of the cases: weekly fever screening for all persons residing close to the case for one month after the case being reported (and one-round blood screening in household members and immigrants from endemic countries). Gave advice to physicians and local public health professionals for malaria case management and focus investigation (telephone help-line duties). Performed telephone help-line duties for the public. Performed or supervised the field investigation, in order to detect risk factors for local malaria transmission (environmental factors, possible vector breeding sites around the case, immigrants from endemic countries). Communicated with the malaria reference laboratory for information exchange. Prepared epidemiological reports on the investigation and communicated with national, regional and local authorities (the Ministry of Health, regional and local public health authorities, the Hellenic Co-ordinating Haemovigilance Centre) and the public (oral presentations on control and protective measures against

vector-borne diseases for the public in East and West Attica). Produced report on malaria investigations and communicated findings to European and international public health organisations (ECDC, WHO, CDC) and to EWRS. Revised the Malaria Notification Form of the Mandatory Notification System (2013) to obtain additional information on travel history, laboratory findings, case management, timeliness of diagnosis and treatment, classify cases as imported or locally-acquired and better estimate the WHO-recommended surveillance indicators.

Status: Completed.

Routine surveillance for vector-borne diseases: operation of the passive and active surveillance system for vector-borne diseases, especially malaria and West Nile Virus infection

Output: Surveillance reports for WNV (weekly during the transmission period and annually) and for malaria (bimonthly during the transmission period and annually), in Greek and English, published on the KEELPNO website. Available at:

<http://www.keelpno.gr/en-us/epidemiologicalstatisticaldata.aspx>

http://www.keelpno.gr/Portals/0/Files/English%20files/Malaria%20reports/Malaria_Report_EN_2013_11_16.pdf

Leishmaniasis surveillance: Increase of reported leishmaniasis cases in Thessaly region, 2013. During 2013, 31 cases of leishmaniasis were reported from Thessaly Region, compared with 1–14 cases reported annually in 2004–2012. We described this cluster in terms of time, place and person (clinical manifestations, outcome, laboratory methods), and recommended enhanced surveillance for human, animals and vectors and the implementation of preventive measures at local level. Enhanced diagnosis testing was performed for suspected cases of leishmaniasis at the local university hospital, which could partially explain the apparent increase in the number of reported cases.

Role: Primary investigator. Coordinated response to each notified case by local public health authorities. Monitored internal completeness of the system. Collected and analysed surveillance data and prepared the reports. Wrote the weekly and annual surveillance reports.

Status: Completed. Surveillance reports published at the KEELPNO website. Co-author of a published article².

Evaluation of the salmonellosis and shigellosis mandatory notification surveillance system (capture-recapture survey)

Role: Collected and analysed the data.

Status: Completed. Co-author of a published article³.

Outbreaks

West Nile virus outbreak in Greece, 2012–2013

Title: West Nile virus disease, Greece, 2012: third consecutive year of local transmission.

Background: In 2010, the first outbreak of West Nile virus (WNV) infections was recorded in Greece, the largest reported in Europe since 1996. In subsequent years, large outbreaks continued to occur. We investigated the 2012 outbreak to determine its extent and identify risk factors for severe disease.

Methods: We interviewed cases and treating physicians and recorded suspected place of exposure, clinical and laboratory findings, co-morbidities, and disease outcome. We used the EU-case definition for laboratory confirmed and probable cases. We estimated case fatality (CF) of neuro-invasive disease (WNND) and adjusted risk ratios (aRR) for fatal outcome using binomial regression models. PCR-positive samples were sequenced.

Results: In 2012, 161 cases were recorded, 109 of which were diagnosed with WNND, 18 fatal (CF=16.5%) and 58 WNND cases occurring in eight previously unaffected districts. Two main outbreak epicentres were identified: the urban southern suburbs of Athens in July and newly affected rural areas in East Macedonia-Thrace in August and September. The CF in the two epicentres was 7% (n=2) and 9% (n=4), respectively, whereas outside the epicentres the CF was 34% (n=12). Age >74 years (aRR=7.0, 95% CI: 2.2-22) and chronic renal failure (aRR=4.5, 95% CI: 2.7-7.5) independently predicted death. Sequences from three PCR-positive samples were WNV lineage 2, with high genetic similarity to the 2010 strain.

Conclusion: The occurrence of human cases in three consecutive years and in newly affected areas suggests that WNV has become established in Greece and is expanding. Higher CF outside the two epicentres might reflect insufficient physicians' awareness and under-diagnosis of WNV disease. Raising awareness among physicians and susceptible populations (the elderly and those with co-morbidities) throughout Greece is critical for disease prevention and control.

Role: Primary investigator. Performed enhanced case finding; awareness-raising among physicians; daily communication and information exchange with laboratories; investigated or supervised the investigation of all cases of West Nile virus disease within 24 hours of reporting (telephone interviews with a structured questionnaire); revised

the Case Investigation Form for the West Nile virus disease (2013); reported daily on the outbreak investigation and communicated to national, regional, local authorities, stakeholders and the public; exchanged information with other institutes participating in the outbreak investigation of the WNV infection in animals (equidae, birds) and vector surveillance (Ministry of Rural Development and Food, veterinary university schools, National School of Public Health); analysed the data and prepared weekly epidemiological outbreak reports.

Status: Completed, presented at 2013 ESCAIDE⁴, article published⁵.

Outbreak investigation of a cluster of five leptospirosis cases on the island of Zakynthos

We conducted case and environmental investigations to assess the extent of the outbreak. Based on descriptive epidemiological data, agricultural work, and especially vine harvesting, was a common type of exposure among cases.

Role: Primary investigator

Status: Completed

Outbreak investigation of a cluster of shigellosis cases (*Shigella flexneri*) in a day-care centre on the island of Corfu.

On 18–19 February 2013, a cluster of three shigellosis cases were reported to the Hellenic Center for Disease Control and Prevention at a day-care centre on the island of Corfu. We investigated the cases, and organised laboratory and environmental investigations to control the outbreak. Two shigellosis cases among children attending the same day-care centre led to inter-family clusters (nine cases in total in both families). Two additional confirmed and two suspected shigellosis cases were reported at the day-care centre, one and two months after the notification of the first cases. The index case of the cluster was not identified. Appropriate measures were recommended.

Role: Primary investigator. Produced final report

Status: Completed

Research

National vaccination coverage survey, 2012

Title: Structural barriers and socioeconomic factors are associated with incomplete childhood vaccination: a cross-sectional study in Greece, 2012

Background: To improve vaccine coverage (VC), factors influencing immunisation status of children need to be identified and addressed. We conducted a cross-sectional study among six year-old school-children and their parents/guardians to identify predictors of complete vaccination status.

Methods: We stratified the country into four regions and randomly selected school-classes (clusters) with probability proportional to the child-population size of each region. We asked all pupils within the selected clusters to provide their vaccination booklet and their parents/guardians to complete a questionnaire regarding beliefs and attitudes towards immunisation. Children were considered fully-vaccinated if they had received all vaccinations according to the Greek National Vaccination Programme. We calculated adjusted-Prevalence Ratios (aPR) and 95% Confidence Intervals (95% CI) allowing for the stratification and the clustering, using binomial regression.

Results: Of all 1 046 (84%) participating children in 79 selected school-classes, 63% (95% CI 58-67) were fully-vaccinated. Parental positive opinion regarding immunisation was not associated with complete vaccination status of their children (PR=0.95; 95% CI:0.77-1.2). Children were less likely to be fully-vaccinated if they had ≥ 2 other siblings (aPR=0.68; 95% CI:0.51-0.90); if they were Roma (aPR=0.44; 95% CI:0.15-0.99) or immigrants (aPR=0.82; 95% CI 0.67-1.00) and if their parents had <9 years of formal education (aPR=0.77; 95% CI:0.69-0.86). Complete VC was lower in children of parents/guardians who perceived long distances to immunisation facilities as a major barrier to immunisation (aPR=0.80; 95% CI:0.72-0.90).

Conclusions: Structural barriers and socioeconomic factors rather than parental attitudes towards immunisation were associated with incomplete vaccination. Comprehensive approaches are warranted to overcome these barriers and improve vaccine coverage in the high-risk groups identified in this study.

Role: Collected and analysed the data

Status: Completed. Presented at 2013 ESCAIDE⁶.

Long-term outcomes of West Nile Virus (WNV) infection in Greece

Background: We conducted a survey to (i) investigate and describe long-term outcomes (physical, cognitive, and functional) after West Nile virus infection in Greece, (ii) estimate the prevalence of long-term symptoms among persons diagnosed with WNV during 2012 in Greece, (iii) determine the association of age, sex, neuroinvasive disease status (severity of the initial clinical syndrome), underlying illness and time since acute infection of the most common long-term individual symptoms and determine whether these factors affected the likelihood of recovery.

Methods: We conducted telephone interviews with all cases of WNV disease detected in Greece in 2012, 6–12 months after their acute illness, to collect information on their physical, cognitive and functional health status after WNV disease, symptom duration and severity (on a 1–10 scale), the need and duration of assistance after the disease, the time required for full recovery and work or school absenteeism. We collected information on demographic characteristics, hospitalisation, WNV disease manifestation, and co-morbidities from the surveillance database.

Role: Primary investigator. Wrote the protocol, collected and analysed data

Status: Final report in progress

Scientific communication

- One article published⁵.
- Two oral presentations at international conferences^{1,4}.
- One poster presentation at an international conference⁶.
- Co-author of three published articles^{2,3,8}.
- Two oral presentations to joint ECDC/WHO mission to Greece on vector-borne diseases, entitled 'Malaria in Greece: epidemiological surveillance data, 2012' and 'WNV in humans in Greece, 2012', November 2012, Athens (not publicly available).
- Four oral presentations at national conferences:
 - 'Malaria surveillance in Greece, KEELPNO, 2012', 15th National Meeting on Haemovigilance, 14 Dec 2012, Athens (not publicly available)
 - 'Active malaria case detection in Greece, 2012', 39th Annual Pan-Hellenic Medical Congress, Athens, 22–25 May 2013 (not publicly available).
 - 'West Nile virus outbreak in Greece, 2012', 39th Annual Pan-Hellenic Medical Congress, Athens, 22–25 May 2013 (not publicly available).
 - 'Haemorrhagic fevers (West Nile virus, Dengue). New threat for the mega-cities. Now Athens too?', 19th Pan-Hellenic Congress of Pathology, Athens, 11–14 December 2013 (not publicly available).
- Co-author in one abstract presented as oral presentation at international conference⁷.
- Two abstracts accepted as poster presentations at the 2013 International Meeting on Emerging Diseases and Surveillance (did not participate in the meeting due to financial constraints).
- Several epidemiological reports on WNV disease (weekly, annually) and malaria (bimonthly, annually), in Greek and English, published at the official website of KEELPNO (Available at: <http://www.keelpno.gr/en-us/epidemiologicalstatisticaldata.aspx>).
- Two articles in the KEELPNO newsletter (May 2012: 'Malaria and West Nile Virus infection epidemiological data and control measures in Greece in 2010–2012', April 2013: '2013 World Malaria Day').

Teaching experience

- Lecture on case-control studies and facilitation of the case study 'Trichinosis outbreak' for the MSc programme 'International Medicine and Health-Crisis Management' of the Athens University, Faculty of Medicine (three hours).
- Lecture on cohort studies and facilitation of the case study 'Gastroenteritis outbreak' for the MPH programme of the National School of Public Health in Athens (three hours).
- Lecture: 'Confounding and effect modification' and the case study: 'Haemorrhagic fever outbreak' for the MPH programme of the National School of Public Health, in Athens (three hours).
- Nine training seminars (90 minutes each) in 2012 for local public health professionals and clinicians on malaria diagnosis, treatment, case and focus investigation and surveillance: in four hospitals and four primary health centres in affected areas and one at the National School of Public Health in Athens (total: 13.5 hours).
- Lecture on malaria surveillance in Greece for the MSc programme 'Health-Crisis, Mass disasters and Emergency Situations Management' of Athens University, Nursery Department (30 minutes).
- Eleven training seminars (45 minutes each) in 2013 for local public health professionals and clinicians on malaria and West Nile virus disease diagnosis, management, epidemiological data, and surveillance: at two hospitals and nine primary health centres in affected areas (total: nine hours).
- Preparing or updating educational material on the diagnosis and management of malaria, West Nile virus disease, Crimean-Congo haemorrhagic fever and Dengue cases. This was sent to clinicians working in the public sector and uploaded to the KEELPNO website.

Miscellaneous

Participated in the KEELPNO working group for vector-borne diseases. Worked on the KEELPNO malaria action plan 2012–2015 and the classification of all prefectures according to the risk for local malaria transmission. This risk

classification guides local public health interventions. Participated in the national working group for the design of the national action plan on vector-borne diseases. Participated in the multi-sectoral working group for the definition of areas affected by vector-borne diseases (guidance for blood-safety measures). Prepared informative material for the public on Dengue fever, Crimean-Congo haemorrhagic fever and protective measures against tick bites which was then uploaded to the KEELPNO website. Nominated as the National Focal Point for Emerging and Vector-borne Diseases.

Supervisor's conclusions

During her fellowship at the Hellenic Center for Disease Control and Prevention, Danai Pervanidou was successfully involved in a wide variety of learning-by-doing activities on surveillance, field epidemiology and applied research. Danai was a hard-working, enthusiastic and positive colleague and it was a pleasure working with her. She successfully carried out all her projects and the outcomes of her work were outstanding. Her competencies have been further developed and she has acquired new skills.

Danai had the opportunity to be actively involved in the management of two emerging vector-borne diseases in Greece; malaria and West Nile Virus infection. She gained knowledge and expertise on these diseases that very few scientists in the country or even in Europe currently have. Danai's work during her fellowship experience was not only important from a training or scientific point but also from a practical point of view. Since the surveillance and the management of vector-borne diseases was something new for the country, her work was used by public healthcare services as a basis for organising public health action.

During these two years of intense work Danai has had the opportunity to take initiatives and work independently on a number of occasions, which I believe is something that will help her a lot in her future professional career.

Next steps

Danai already belongs to the active public health workforce of her country. Her intention is to continue working in her current position, in the Department of Surveillance and Intervention, as a field epidemiologist. In March 2014 she became the Head of the Vector-borne Diseases Unit.

References

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