Summary of work activities
Dr Isabel Martínez-Pino
European Programme for Intervention
Epidemiology Training (EPIET), 2011 cohort

Background

Pre-fellowship short biography

Dr Martínez-Pino is a Spanish medical doctor with a four-years specialisation in preventive medicine and public health. Her education includes a master's degree and a PhD, both in public health. Prior to EPIET, Isabel Martínez-Pino worked for more than six years in the field of epidemiology/public health and infectious diseases. She has worked in infectious disease surveillance and outbreak alert and response at the regional, national and international level.

EPIET assignment

On 19 September 2011, Isabel Martínez-Pino was assigned to Epicentre, Paris (France). She joined the Intervention and Training Department, where she was involved in surveillance activities, training, outbreak investigations and operational research in the field of infectious diseases, mainly in African countries. Supervision was provided by Dr Klaudia Porten.

Fellowship projects

Surveillance project

Evaluation of cholera surveillance system at the Health Community/Health Unit of Petit Rivière, La Chapelle et Verrettes (UCS PRVL), Departement of Artibonite, Haïti

Background: Cholera became endemic in Haiti following the large cholera outbreak of 2010. We conducted an evaluation of the cholera surveillance system to i) improve the information provided and ensure that cholera is effectively monitored and to ii) promote early warning and response if a new increase of the number of cases occurs.

Methods: The evaluation was conducted between 15 January and 6 February 2012 in the Unité Communale (UCS) de Santé Petit Riviere de l'Artibonite, Verrettes and La Chapelle (PVRL) in the Department of Artibonite and consisted of three steps: (1) description of the public health importance of cholera in UCS PVRL; (2) description of the cholera surveillance system in Artibonite, specifically at the UCS PVRL; and (3) description of the attributes and performance

of cholera surveillance system (simplicity, flexibility, data quality, acceptability, sensitivity, representativeness and timeliness). A series of semi-structured questionnaires was completed through face-to-face interviews with the staff of the Health Department of Artibonite (DSA), cholera treatment units, 'brigadiers', and several other health structures in the UCS (namely, two primary-care clinics, one health centre and two hospitals). We also used administrative data (such as registers, forms, electronic databases), reports and scientific articles on cholera surveillance in Haiti, and, more specifically, the UCS PVRL.

Results: In the UCS PVRL, a total of 19 929 cases were registered in a total population of 315 660 inhabitants (attack rate 6.3%). Artibonite is the only department which receives epidemiological support to its health structures from UCS. Cholera surveillance is integrated in the national surveillance system and was reinforced during the epidemic. Cholera surveillance is organised in different levels: community ('brigadiers'); regional level, including health structures (dispensaries and health centres); specific cholera treatment centres (CTC and UTC), whose data are reported to the UCS, DSA or to both; and a central level (DSA) which notifies cases to the Ministry of Health. There is no national surveillance guide available for the system users. There is no threshold to declare/detect an outbreak. Human and material resources may be insufficient to control a new outbreak. Confirmation of cholera cases is not routinely performed, as there is lack of material and rapid diagnostic tests in the laboratories. The global system is well accepted by the users. Cases reported at the community level (brigadiers) are not included in the national figures neither it is the geographical origin of the cases (under commune level).

Recommendations: A better preparedness plan in case of a new outbreak is needed. The staff at the central level should regularly provide training and feedback. Specific recommendations include: 1) Strengthen surveillance activities at the UCS, the central level (DSA), and remote areas to detect the first cases of a new outbreak in a timely manner; 2) set up a community surveillance system; 3) improve cholera prevention activities and access to health centres.

Contribution/role: Principal investigator

Status: Completed

Output: Internal report

Retrospective study of the origin of cholera cases, Artibonite Department, Haiti

Background: Cholera hit Haiti in October 2010 and spread rapidly along the Artibonite River before reaching the rest of the country. A first epidemic peak was observed in January 2011, followed by a decline. In May 2011, a second peak was recorded. The health authorities set up a surveillance system that did not take into account the origin of registered cases.

Methods: A retrospective analysis of the origin of reported cases since the beginning of the epidemic was conducted in order to elucidate transmission patterns. An analysis by locality of origin for each *commune* was performed (specifically the *commune* of Desdunes, Grande Saline and Sant Marc).

Results: Data records from 11 cholera treatment centres (CTC), 22 cholera treatment units (UTC) and 46 oral rehydratation sites (PRO) were collected between December and February 2012, including 84 030 cases of cholera coming from Artibonite and registered between October 2010 and December 2011.

Conclusions: This study allowed the description of cases of cholera by locality during the last two peaks (October 2010–January 2011 and May 2011–September 2011).

Contribution/role: Co-investigator

Status: Completed

Output: Internal report, manuscript in progress[1]

Outbreak

Typhoid fever outbreak investigation, Harare, Zimbabwe, 2012

Background: An outbreak of typhoid fever occurred in Harare City, Zimbabwe, in October 2011. We conducted an investigation to identify priority areas for water and sanitation intervention through mapping of the most affected suburbs, Kuwadzana (KU) and Dzivaresekwa (DZ).

Methods: We used individual data from all typhoid fever suspected cases (clinically diagnosed patients) to describe the epidemic in Harare. This information was provided by the Ministry of Health. We calculated attack rates (AR) by gender, age and place of residence. Data collection for mapping was limited to KU and DZ. We recorded GPS coordinates of the residence of cases included in the typhoid fever registers and generated 2 000 random points serving as controls within shape files of KU and DZ. We used K functions and kernel smoothing techniques to detect clustering.

Results: From 10 Oct 2011 to 17 Mar 2012, 3 795 suspected cases of typhoid fever were reported in Harare, 2570 of whom (67.7%) were in DZ and KU. The median age was 16 years [interquartile range 4–30 years] and 54.2% were

female. The AR in DZ was 0.80% and 1.37% in KU. We traced and recorded 2 212 (86.1%) GPS coordinates of suspected cases in DZ and KU. Cases were more clustered than controls (p<0.001). Two clusters were identified in KU and DZ (the latter was apparent already within the first week of the outbreak), both of which were located next to a water source. Conclusions: We could highlight two clusters (surrounding boreholes), indicative of high typhoid fever transmission. Spatial analysis is a useful tool to identify potential sources of transmission and to target water, sanitation and health education interventions to contain outbreaks.

Contribution/role: Principal investigator

Status: Completed

Output: Internal report, manuscript in progress [2]; two presentations at international conferences[3,4]

Research

Cholera rapid diagnostic test after vaccination: proportion of positive tests and time for vaccinated persons to test negative, Forecariah, Guinea, June 2012

Objectives: To estimate the proportion of positive results of a cholera rapid diagnostic test in recipients of the cholera vaccine at different time points after vaccination and estimate the mean time for vaccinated persons with an initial positive test to test negative again after vaccination.

Methods: Prospective study of the proportion of positive tests and time to become negative after ingestion of the killed whole-cell oral cholera vaccine Shanchol (Shantha). The study population corresponded to the population targeted by the MSHP/MSF-OCG vaccination campaign (all residents of Forécariah aged one year and above).

Study site and period: The study took place on the island of Kabak, in the Forécariah prefecture (Guinea), during the second cholera vaccination round conducted by MSF-OCG in June 2012. The inclusions took place on two consecutive days, and the people included were followed up for a maximum duration of seven days.

Results: A total of 94.3% of cholera vaccine recipients had a positive result with the Crystal VC rapid test after vaccination. Starting with the third day after vaccination, the proportion of people testing positive decreased to a half. On day four of the follow-up, only one fifth still tested positive. The median time it took to test negative (in those with an initial positive test) after vaccination was four days. None of the specimens tested with the rapid test on the seventh day of follow-up (D7) was positive, although five persons for whom the last follow-up specimen was positive could not be tested at D7, either because they were absent or because they were not able to produce stools at D7. Almost all positive results were positive for the T1 line only (*V. cholerae* O139).

Conclusions: It is important to take into consideration the possibility of a false positive result to the Crystal VC® rapid test in individuals recently vaccinated against cholera. From the first to the fourth day after vaccination, a positive result will remain inconclusive (i.e. it is not possible to conclude whether the test is positive for cholera or the vaccine). A positive result with the rapid test can be considered as a true positive (not due to vaccination) with quasi-certainty from the fifth day after vaccination on (<3% of positives among vaccinated cases) and in all cases one week after vaccination.

Contribution/role: Co-principal investigator

Status: Completed

Output: Internal report, article published in PLoS Neglected Tropical Diseases[5], one internal presentation at Epicentre[6], one poster at ESCAIDE 2013[7], one poster for Epicentre Scientific Day 2013[8].

Follow-up of the mass vaccination campaign with Shanchol: surveillance of pregnancy-related side effects

Objectives. General: To determine whether there was a difference in the outcome of pregnancy for pregnant women exposed to oral cholera vaccine (OCV) compared with unexposed women. Specific: (1) To compare the incidence of pregnancy loss (miscarriage and stillbirth) in a retrospective cohort of vaccinated and unvaccinated pregnant women by conducting a population survey; and (2) to compare the incidence of malformations in a retrospective cohort of children born to vaccinated and unvaccinated women in a population survey.

Methods: Cohort study. We will carry out a population survey which will enable the creation of a retrospective cohort of pregnant women, and determination of the incidence of pregnancy loss (miscarriage and stillbirth). The study will be carried out in Boffa (Guinea).

Contribution/role: Co-principal investigator

Status: Protocol submitted to the MSF Ethics Review Board and to the Guinean ERB, awaiting response

Output: Internal protocol

Incidence of pregnancy loss before and after the introduction of the Shanchol vaccine in Guinea: interrupted time series analysis

Objectives: General: to determine differences in pregnancies outcomes among pregnant women exposed and unexposed to the Shanchol oral cholera vaccine (OCV). Specific: To determine through a retrospective analysis of historical clinical records if the historical trend of birth and pregnancy loss (miscarriage and stillbirth) in Boffa prefecture in the health centers has changed after the mass vaccination campaign with Shanchol.

Methods: a retrospective data entry from clinical registries (follow-up visits and pregnancy outcomes) will allow calculating the historical trend and comparing it with data collected after the mass vaccination campaign with Shanchol in the vaccinated and unvaccinated areas of the prefecture. The eight health centres in Boffa prefecture offering antenatal care will be the study sites for the time series analysis. The follow-up registries of pregnant women will be entered in a separate database.

Contribution/role: Co-principal investigator

Status: Field visit to Guinea done (28 April–3 May). Data collection done, data entry ongoing. Quality control done, first analysis ongoing.

Output: Internal protocol

Vaccination coverage with the oral cholera vaccine Shanchol in pregnant women in Boffa prefecture, Guinea

Objectives: To estimate the vaccination coverage in pregnant women of the mass vaccination campaign conducted by the Ministry of Health with the support of MSF using the oral cholera vaccine (OCV) Shanchol in Boffa prefecture between April and June 2012.

Methods: Two-stage cluster survey

Results: 105 women who were pregnant during the vaccination campaign were recruited in Boffa centre and Koba, with a mean age of 26 years (IQR: 20–30); 27.6% (95% CI 19, 6–37.5) of these 105 women were vaccinated with one dose; 49.5% (95% CI 38, 2–60.9) with two doses (fully vaccinated), and 77.1% (95% CI 67, 5–84.6) with at least one dose. 43.2% of the vaccinated women kept the vaccination card. Main reason for not getting vaccinated was absence during the vaccination campaign.

Conclusions: Vaccination was well accepted by pregnant women although coverage is lower than in the general population. Even if mass vaccination campaigns are a complementary tool for standard interventions during cholera epidemics, sensibilisation campaigns should be specifically addressed to this particular group.

Contribution/role: Co-principal investigator. Status: Completed (field visit 28 April–3 May)

Output: Internal report finished and shared with partners (field and MSF headquarters)

Scientific communication

- One article published in a peer-reviewed journal[5]
- Three oral presentations at ESCAIDE 2012[3], Epicentre Scientific Day 2012[4] and Epicentre internal scientific seminars[6]
- Two posters at Epicentre Scientific Day 2013[8] and ESCAIDE 2013[7]
- Three manuscripts in progress[1-2,9]

Teaching experience

Responding to outbreaks, training organised by Epicentre for Médecins Sans Frontières (MSF) medical coordinators

During the first week of December 2012, I was a member of the teaching staff for a five-day training course organised by Epicentre entitled 'Responding to outbreaks' for MSF medical coordinators (medical doctors and nurses) with experience in at least one outbreak investigation and a basic knowledge of epidemiology.

The course was divided in a morning session with theoretical presentations and an afternoon session with case studies that illustrated the theoretical presentations. I taught a one-hour session on outbreak investigation and facilitated a four-hour case study based on an outbreak of jaundice in Sudan.

Contribution/role: Teacher

Status: Completed

Output: Presentation and case study

Training during international missions

In each of the international missions we trained the staff we recruited. We trained them in the collection of surveillance data (Haiti), use of GPS devices (Zimbabwe), the application of rapid diagnostic tests for cholera and cholera prevention and control (Guinea).

Contribution/role: Teacher

Status: Completed

Output: PowerPoint slides, material for participants

Diploma 'L'aide humanitaire dans l'attention aux populations affectées par désastres', training organised by the Spanish Society of Humanitarian Medicine together with the Spanish Agency for International Development Cooperation (AECI).

During the third week of April 2013, I taught a course leading to a diploma in 'L'aide humanitaire dans l'attention aux populations affectées par désastres', organised by the Spanish Society of Humanitarian Medicine and the AECI

I organised the epidemiology module, prepared the lectures, and, for four days, delivered the lectures and case studies together with another epidemiologist.

Contribution/role: Teacher

Status: Completed

International missions

- Haiti (15 January 2012–6 February 2012). Surveillance project
- Zimbabwe (3–21 March 2012). Outbreak investigation
- Guinea (4–21 June 2012). Research project
- Senegal (14–19 April 2013). Training
- Guinea (28 April–3 May 2013). Vaccination coverage survey and research project on OCV and pregnancy phase I (interrupted time series analysis)

Supervisor's conclusions

Isabel was involved in a large variety of public health activities during the two-year fellowship at Epicentre: outbreak investigations, surveillance, descriptive and analytical epidemiology. She has reached a high level of expertise and qualification. She was highly appreciated as a very flexible, constructive and enthusiastic colleague, and it has always been a pleasure to work with her. Her project work at Epicentre, carried out with MSF and international partners, resulted in excellent outcomes which were published in high-impact international journals and/or practically applied in the humanitarian sector. We can highly recommend Isabel Martínez-Pino for any kind of public health work.

Next steps

Medical epidemiologist in Spain. Keep collaborating in international health projects.

References

[1] Allan M, Grandesso F, Pierre R, Magloire R, Coldiron M, Martinez-Pino Isabel et al. High-resolution spatial analysis of cholera cases reportedin Artibonite Department, Hait in 2010-2011. [work in progress]. [2] Polonsky J, Martínez-Pino I, Nackers F, Chonzi P, Manangazira P, Simons S, et al. Mapping cases of typhoid fever to identify spatial clustering during an outbreak in Harare, Zimbabwe, 2012. [work in progress]

[3] Martínez-Pino I, Polonsky J, Nackers F, Simons S, van Herp M, Maes P, et al. The use of mapping to identify priority areas for intervention during a typhoid fever outbreak in Harare, Zimbabwe, 2012. Oral presentation at: ESCAIDE 2012, European Scientific Conference on Applied Infectious Disease Epidemiology; 2012 Oct 24–26; Edinburgh, UK.

[4] Isabel Martínez-Pino. The use of mapping to identify priority areas for intervention during a typhoid outbreak in Harare, Zimbabwe. Oral presentation at: Epicentre, 22nd Scientific Day, 31 May 2012, Paris, France.

[5] Martínez-Pino I, Luquero FJ, Sakoba K, Sylla S, Haile M, Grais RF, et al. Use of a cholera rapid diagnostic test during a mass vaccination campaign with in response to an epidemic in Guinea, 2012. PLoS Negl Trop Dis. 2013 Aug 15;7(8):e2366.

[6] Martínez-Pino I. Proportion de cas positifs et temps de négativation d'un test de diagnostic rapide du choléra après la vaccination: Forécariah, République de Guinée, Juin 2012. 9 Novembre 2012 Séminaire interne, 1 heure. Epicentre, Paris, France.

[7] Martínez-Pino I, Luquero FJ, Sakoba K, Sylla S, Haile M, Grais RF, et al. Use of a cholera rapid diagnostic test during a mass vaccination campaign with in response to an epidemic in Guinea, 2012. Poster presentation at: ESCAIDE 2013, European Scientific Conference on Applied Infectious Disease Epidemiology; 2013 Nov 5–7; Stockholm, Sweden.

[8] Martínez-Pino I, Luquero FJ, Sakoba K, Sylla S, Haile M, Grais RF, et al. Proportion of positive tests and time to become negative of a cholera rapid diagnostic test after vaccination: Forecariah, Guinea, June 2012. Poster presentation at: Epicentre, 23nd Scientific Day, 30 May 2013, Paris, France.

[9] Luquero FJ, Rodrigues A, Martínez-Pino I, Remartinez D, Palma PP, Eiros JM, et al. Family members suffering from cholera: main risk for women taking care of the household during an outbreak in Guinea-Bissau, 2008. [work in progress]