Generalitat de Catalunya
Agència de Salut Pública de Catalunya

ISGlobal Institut de Salut Global Barcelona

Meeting Report:

“Risk of introduction of Zika Virus and other arboviruses in Catalonia”

Held in Barcelona

Agència de Salut Pública de Catalunya

June, 2016

Glossary

ASPCAT	**Agència de Salut Pública de Catalunya**
ASPB	**Agència de Salut Pública de Barcelona**
CHIKV	**Chikungunya virus**
CEAB	**Centre d'Estudis avançats de Blanes**
CREAF	**Centre de Recerca Ecològica i Aplicacions Forestals**
CReSA	**Centre de Recerca en Sanitat Animal**
CSIC	**Consejo Superior de Investigaciones Científicas**
IRTA	**Institut de Recerca i Tecnologia Agroalimentàries**
DENV	**Dengue virus**
IC3	**Institut Catalá de Ciencies del Clima**
ISCIII	**Instituto de Salud Carlos III**
ISGlobal	**Institut de Salut Global de Barcelona**
PROSICS	**Programa de Salut Internacional de l'Institut Català de la Salut**
SCM	**Servei de Control de Mosquits**
UPF	**Universitat Pompeu Fabra**
WHO	**World Health Organization**
WNV	**West Nile virus**
ZIKV	**Zika virus**

Contents

1. Acknowledgements and Participants

ISGlobal and ASPCAT members would like to thank all participants for their contribution to this report and to the facilitators who worked behind the scenes to support the event.

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2. Background

Zika virus (ZIKV) is an arbovirus (arthropod-borne virus) belonging to the family Flaviviridae, genus *Flavivirus*, related to Dengue virus (DENV), Yellow Fever virus, Japanese Encephalitis virus and West Nile virus (WNV). It is transmitted by the bite of infected mosquitoes of the genus *Aedes*, including *Aedes aegypiti* [1].

ZIKV was named after the Zika forest in Uganda (Africa) where it was first isolated in Rhesus monkeys in 1947. Serological studies in 1952 provided evidence of ZIKV infection in humans, initially considered an occasional guest, but it was not until 1968 that ZIKV was isolated from human samples in Nigeria. Since its discovery, epidemiological, serological and entomological studies confirmed the circulation of the virus in several African countries (Nigeria, Sierra Leone, Ivory Coast, Cameroon and Senegal) and Asia (Pakistan, Indonesia, Philippines, Malaysia, Cambodia and Thailand) [2]. Phylogenetic studies have shown the existence of two main lineages of this virus: the African and the Asian strains.

In 2007 an epidemic was reported for the first time in the Island of Yap (Micronesia), where approximately 80% of the population was infected [3]. In 2013 the epidemic reached and spread through several territories of French Polynesia. ZIKV was detected in Brazil in early 2015 and since then, the epidemic has been spreading across the Americas. To date of June 2016, 39 countries or territories presented mosquito-borne transmission in the region [4]. Moreover, the circulation of the virus has been reported during 2016 outside the Americas in Asia, the Pacific and Africa (WHO).

The most common symptoms of infection by ZIKV are mild fever and rash, often accompanied by conjunctivitis, muscle or joint pain, and malaise. They begin between two and seven days after the bite of an infected mosquito and are self-limited. Symptoms are similar to those of DENV or Chikungunya virus (CHIKV), which also are transmitted by the same type of mosquito. While ZIKV infection was initially considered as a mild disease, reports on the possible association with Guillain-Barré syndrome and congenital malformations after vertical transmission raised major concerns around the world. The WHO recognized the epidemic as a public health emergency of international concern on 1 February 2016 [5]. In April 2016, the first evidence showing a link between fetal abnormalities and ZIKV infection was published [6]. Since then, great efforts have been made globally in order to show evidence of causality between infection and congenital and other neurological complications, to better understand the pathophysiology of the disease, and to improve disease detection and containment.

The emergence of Bluetongue virus in northern Europe, the large-scale outbreaks of WNV fever in North America and several CHIKV and DENV fever outbreaks in Europe (France, Italy and Greece), remind us of the very real risk of introduction of exotic pathogens into Europe in a rapidly changing, interconnected world. Such connectivity also increases the probability of importing disease vectors, particularly mosquitoes and ticks, and this has created new scenarios in which the established exotic vectors potentially facilitate the transmission of pathogens previously restricted to tropical and subtropical regions. In the current context of global alert due to the ZIKV epidemic in the Americas, and the health burden due to increased global diseases caused by arboviruses such as DENV and CHIKV, the WHO developed a series of activities in order to assess the risk of arbovirus introduction into Europe. Spain and the Mediterranean region, where *Aedes albopictus* is present, were considered to be at medium-to-high risk for the introduction and circulation of the virus. Catalonia, because of its technical and scientific capacity in public health, its geographical location within the Mediterranean countries, the consistently reported presence of the potential vector (*Aedes* spp.), and the high intensity of migration and trade flows, has a unique interest in assessing the impact of these diseases on public health in the near future.

The Public Health Agency of Catalonia has implemented two protocols addressing interventions for the prevention and early detection of autochthonous cases of arbovirosis, and the follow-up of pregnant women exposed to the virus, and their babies[7, 8].

3. Purpose of the meeting

In response to the international ZIKV epidemic alert, the Public Health Agency of Catalonia (ASPCAT), with the support of the Barcelona Institute for Global Health (ISGlobal) has established an initiative to comprehensively address the challenges in public health related to the global emergence of arbovirus infections, with a particular focus on the current ZIKV epidemic.

In order to promote cooperation between the relevant institutions and establish an initial consensus for future action, ASPCAT invited experts from different areas relating to the surveillance, prevention and response to arbovirus in Catalonia for a one-day meeting, held in Barcelona the 20th of June 2016.

The main objectives of this meeting were:

1. To review the epidemiological, entomological, clinical, microbiological and environmental conditions related to the potential introduction of ZIKV and other arboviruses in Catalonia.
2. To review the capabilities and limitations in surveillance and response to limit potential autochthonous transmission.
3. To assess the risk of introduction and transmission in Catalonia based on the analysis of the above in order to support communication and public health risk management.
4. To decide whether there is a need for additional assessments through more complex approaches and to identify those organizations responsible for their implementation and development.
5. To establish a framework of consensus that allows systematized data collection and analysis, optimize communications and strengthen capabilities regarding surveillance, prevention and control of arboviral infections in Catalonia.

4. Risk of introduction

a. Epidemiological factors

Estimations from surveillance data show that around 15,000 travellers returning from subtropical and tropical regions to Catalonia seek medical attention every year (15% of the estimated total number of travellers). Two per cent of those are confirmed as suffering an arboviral infection and a range of 36-80% of the patients are viremic at arrival. This gives an estimation of between 100 and 240 symptomatic patients per year that can potentially transmit an arbovirus. Yet, the number of viremic asymptomatic patients is unknown and a proportion of symptomatic patients might not seek medical attention. Thus, the total number of patients with capacity to transmit arbovirus probably exceeds that range. It is worth noting that up to 70% of the cases in returning travellers are reported between May and September, with a peak in July and August (50% of the total).

Aligned with these estimations and taking into account that there are preliminary data, a total number of 639 suspected cases of imported arboviral infections were notified to the ASPCAT between 01/2014 and 06/2016. A total of 434 cases were laboratory confirmed (68%). This represents an average of 255 suspected and 173 confirmed cases per year in the last 3 years. During the years 2014 and 2015, before the Zika global alert, cases were confirmed as DENV and CHIKV infections. Between January and June 2016, a total of 69 cases of ZIKV infections were confirmed, representing more than 50% of the total of cases during the period. Gender distribution shows a slight trend towards females (71%). Regarding geographical distribution, the majority of the cases were reported in Barcelona and its vicinity. The main reported region is Latin America for CHIKV and ZIKV infections, while for DENV confirmed cases, South East Asia is reported first, followed by the Caribbean.

b. Entomological factors

There are over 3,000 known species of mosquitoes worldwide and 47 species are known to be reported in Catalonia. The most relevant species in the territory are *Culex pipiens, Ochleratatus caspius, Anopheles artroparvus* and *Aedes albopictus.*

Culex pipiens, widely distributed in Spain, is the theoretical main vector for WNV. While several equine cases as well as few human cases of WNV have been reported in Andalusia, south of Spain, no cases have been reported in Catalonia up to date. To note is that most of positives for the virus in mosquitoes in Andalusia have been detected in *Culex perexiguus* while *Culex pipiens* reported only few.

Nowadays, *Aedes albopictus* is the only *Aedes* spp. associated with human arbovirus transmission reported in Catalonia. *Aedes albopictus* has been mainly associated with CHIKV transmission, especially the East Central and South African (ECSA) strain, and its capacity and competence for transmitting ZIKV and DENV is considered limited. However, it is worth noting that *Aedes aegypti,* the main vector responsible of the current ZIKV epidemic, was reported in Spain up to the 1940s, when it definitely disappeared. Thus, one cannot exclude its potential reintroduction in the future, especially considering its recently established presence in Madeira and in the Eastern shore of the Black Sea.

Aedes albopictus was first reported in Spain in 2004, in Sant Cugat del Vallès, a residential area in the vicinity of Barcelona, and rapidly spread remaining established in the Mediterranean Basin. In Catalonia, *Aedes albopictus* has been reported until 2015 in 452 municipalities (48% of the total) mainly located in the coastal area with high population density. The mosquito is known to be highly adapted to the urban environments such as Barcelona. Mapping of the populations shows *hot* areas in the city usually associated with water containment that serve as breeding sites. *Aedes albopictus* is known to follow seasonal patterns with a diapause (overwintering period) between November and May and a peak in density during the months of July and August. Entomological surveillance capacities are mostly concentrated in coastal areas of Girona and areas surrounding Tarragona and Barcelona, representing 9% of the total of the territory, but probably a much higher percentage of human population. Studies performed at CReSA-IRTA in 2014 and 2015 showed that local populations of *Aedes albopictus* are competent for transmission of the CHIKV (ECSA strain) as well as DENV (serotype 2). Nevertheless, there is stil a lack of knowledge regarding surveillance-related factors, such as insecticide resistance rates, population densities or biting rates. Similarly, intrinsic factors for transmission such as arbovirus vector capacity and vector competency including incubation period and infectivity for the strains present in Catalonia have not been systematically evaluated.

To date, no outbreak of human arbovirus has been reported in Catalonia, as has occurred in France and Italy for DENV and CHIKV. In 2006, following surveillance for WNV, Usutu Virus RNA was detected in a pool of *Culex pipiens* obtained in Barcelona province. In addition, DENV serotype III was detected in a pool of 29 *Aedes albopictus* specimens obtained in Barcelona province in September 2015. Moreover, several species of flavivirus considered not pathogenic to humans have been isolated upon entomological surveillance in 9 different mosquito species including *Aedes albopictus*, *Aedes vexans*, *Anopheles atroparvus* and *Culex pipiens.*

c. Environmental factors

Climate change footprints can be consistently detected in Catalonia. Among the 1950-2015 period, annual trends show an increase in temperature (+0.23 ºC per decade) and a decrease in precipitation (-1.5% per decade). The effect is even more visible when evaluating summer temperatures (increase +0.34ºC per decade) and precipitation (decrease 2.1% per decade). These environmental factors might directly impact the survival and adaptation of the vector and affect vector features such as density or competence for viral transmission. Moreover, climate change impacts human behaviour in a way that may favour vector adaptation. For example, increases in temperature and decreases in precipitation lead to an increase in water containment and therefore availability of breeding sites, challenging vector control. Nevertheless, the precise manner in which climate change could impact the risk of arboviral introduction and transmission in the short future remains unclear, as well as its role in the introduction of new vectors in the region.

5. Surveillance and response capacities

a. Integrated Management Strategy

As a result of the increasing global impact of mosquito-borne viral infections in the past decade, together with the presence of potential vectors in Catalonia, the ASPCAT implemented an integrated strategy for the management of arboviral diseases, resulting in the development and approval in September 2015 of the "*Protocol for surveillance and control of arboviral infections in Catalonia*"[8]. The objective was to guide and coordinate preparedness for the surveillance, prevention and control of arbovirus of public health relevance in Catalonia. The protocol initially included WNV, DENV and CHIKV, and ZIKV was added in January 2016. It includes guidelines for individualized urgent notification of cases, communication circuits between the different bodies, entomological interventions and assessments after confirmation of cases, standardized preventive measures for personal protection, vector control, and management of blood and tissue banks. The protocol also includes an evaluation scale for risk estimation of autochthonous transmission as well as risk-based public health management algorithms.

b. Clinical surveillance and case management

Surveillance of mosquito-borne diseases relies mainly on cases identified by primary health care centres and reference centres receiving returning travellers. Thus, involving primary care health workers in surveillance to include ZIKV and other arbovirus in the differential diagnostics as well as providing them with guidance for sampling and laboratory confirmation at reference centres is essential for optimizing surveillance. Notification to the ASPCAT through the epidemiological surveillance territory services is mandatory and must be done when cases are suspected, while waiting for laboratory confirmation, in order to quickly trigger further epidemiological and entomological investigations. Main limitations of arboviral surveillance are patients not willing to attend consultations, as well as asymptomatic but nevertheless viremic patients which, in the case of ZIKV, can represent a ratio of 3:1 asymptomatic:symptomatic. Management of the patients, which is mainly supportive treatment, can be performed at primary care settings following consensus guidelines. If complications arise, patients are redirected to the hospital level.

For the surveillance and management of ZIKV infection in pregnancy, a consensus protocol has been developed and implemented since February 2016 [7]. Pregnant women who have travelled to epidemic regions or those with sexual partners having travelled to endemic regions and returning with symptoms, are identified at primary care level when attending routine obstetric follow-up. These cases are notified to the ASPCAT through the surveillance network that coordinates referral of samples for laboratory testing. All cases fulfilling epidemiological criteria are screened for ZIKV infection, regardless of symptoms. When positive cases are identified, patients are derived to one of the two specialized reference centers (Hospital Clínic-San Joan de Déu and Hospital Vall d'Hebron), where they are further followed-up following international clinical guidelines. Up to date, June 2016,17 pregnant women have been confirmed with ZIKV infection, one of them diagnosed with fetal abnormalities.

c. Laboratory surveillance

Diagnosis of ZIKV infection can only be confirmed by detection of viral RNA or by detection of virus-specific antibodies. While molecular detection is the most reliable diagnosis, it can only be performed during the initial phase of the infection, when viremia in blood is high. Therefore, antibody detection plays an important role when patients attend health care settings at later stages of the infection. Diagnosis of ZIKV in Catalonia is centralized in two reference laboratories (Hospital Vall d'Hebron and Hospital Clinic) which have capacity to perform diagnosis confirmation. In both laboratories, quality assurance guidelines are followed. RT-PCR is used for viral RNA detection as virus isolation is not performed because is time and resource consuming and has a limited sensitivity. While use of serum/plasma is the standard, urine samples are also tested in parallel, which can extend the period of detection up to 10 days after symptoms onset, and sometimes even longer. Serology is used when molecular diagnosis is negative or at later phases of infection. The standard in this case is to demonstrate seroconversion of IgM and/or IgG in paired samples (acute phase sample plus convalescent phase sample). However, cross-reactivity is relatively common when patients have been previously exposed to other flaviviruses such as DENV. When this is the case in pregnant women, samples are confirmed by neutralization assays, which are performed at the Spanish national reference laboratory ISCIII. This usually increases turnaround times and might have a negative impact on patient management. To date, PCR testing has been performed in 404 and 276 samples in both centres with a positive rate of 6% and 17%, respectively. IgM determination has been performed in 418 and 149 samples with a positive rate of 4% and 8.7%, respectively IgG has been performed in 422 and 154 samples with a positivity rate of 48% and 61%, respectively. Interestingly, only 3.5% of IgG positives were true positives because of cross reactivity with past DENV infection. The main challenge currently faced is the submission of samples with incomplete clinical and epidemiological information.

d. Entomological surveillance and management

Due to the alert of WNV, entomological surveillance of arbovirus was developed in Catalonia between 2001 and 2005 involving the three catalan SCM, under the coordination and funding of the Spanish National Reference Laboratory, ISCIII. From 2006 to 2012, WNV surveillance involved again the different SCM and incorporated CReSA-IRTA. Up to 2009, entomological surveillance in maritime ports and airports was coordinated by the Spanish Ministry of Health (Barcelona-El prat, Girona and Tarragona) and included within the Spanish national plan but only continued in Barcelona after 2012. The "*Protocol for surveillance and control of arboviral infections in Catalonia"* implemented in 2014 includes guidelines for urgent notification of cases to vector control teams as well as for vector control interventions after detection of human cases. CReSA-IRTA, with biosafety level III facilities has the capability for arbovirus detection and isolation in entomological samples. Routine entomological surveillance as well as vector control interventions are not centralized and are currently depending on municipalities. In terms of entomological surveillance, only about 9% of the territory is covered by public bodies. The three SCM actually perform routine mosquito control in their areas and not only surveillance.

6. Risk assessment evidence-based approaches for facilitating public health management

Risk characterization must include the hazard, the exposure and the context assessment, aligning with the WHO recommendations. Considering ZIKV (and other arboviruses) as the "hazard", relevant questions such as "who is susceptible?" and "in which environment?" should be considered for evidence-based characterization of the risk. Two main approaches are possible: a quantitative process (number of expected cases in our population) and a qualitative process (likelihood estimation).

a. Qualitative assessment

Qualitative assessment feeds from data and experts' opinions to allow the generation of a risk matrix estimating the likelihood of an event (local transmission of ZIKV) and the further association of the different risk levels with the potential consequences, facilitating algorithms for risk management. There are a few qualitative assessments addressing the risk of introduction of arboviruses in Europe. Qualitative risk assessment of introduction of ZIKV and other arboviruses in Catalonia is feasible based on available data, and can be a useful and rapidly available tool for public health communication and management.

b. Quantitative assessment and modelling

Quantitative assessment aims to predict the number of expected cases in the population. It can estimate the event with a grade of certainty depending on factors such as risk of bias, imprecision or grade of response.

When developing quantitative models for epidemics of vector-borne diseases such as ZIKV or CHIKV, several factors are usually taken into account: the virus, the vector, climate facilitation for vector suitability and impact on pathogen life-cycle and ecology, and the social behavior of the human host and its role on infection spreading. Thus, one of the main challenges when developing computational or mathematical models, such as the SEIR (Susceptible, Exposed, Infected, Recovered) compartmental model is to have the variables required with enough grade of confidence. Moreover, quantitative models might give a false feeling of precision in their conclusions. However, computational and mathematical models can help us understand spatiotemporal dynamics of vector-borne infections at a mid and large geographical and global scale, and network structures might be useful for predicting different epidemic scenarios which can be inform public health management.

Citizen science data is currently used in Catalonia to improve the *Ae. albopictus* surveillance through a citizen platform called Mosquito Alert. Mosquito Alert is a platform for the research, surveillance and control of disease-carrying mosquitoes and gathers citizen scientists, professional scientists and surveillance and control managers. This novel scientific initiative, developed form CEAB-CSIC and CREAF, allows the assessment of mosquito distribution models and the predictions about its potential spreading through citizen reporting of mosquito occurrence and breeding sites from mobile phones. A key aspect of modelling with citizen data is data quality. Moreover, models using threshold quality data have the same predictive capacity as common scientific data, but contrary to standard scientific methods, citizen science offers powerful scalability.

7. Conclusions

- The risk of introduction of ZIKV and other arboviruses in Catalonia, as well as the outbreak response capacities, have been systematically reviewed and discussed by a panel of experts in relevant fields related to arboviruses.
- The estimated number of symptomatic cases of arboviral infections arriving in Catalonia with capacity to transmit the disease in Catalonia could be high: 100-240 cases/per year. Moreover, asymptomatic patients (except pregnant women) as well as patients not attending health care facilities are escaping from clinical and epidemiological surveillance, making the scenario more challenging and decreasing the likelihood of detecting index cases at an early stage.
- *Aedes aegypti*, considered the most important vector for DENV and the main vector in the current ZIKV epidemic, has not been reported in the territory since the establishment of modern entomological surveillance.
- However, the endemic vector *Aedes albopictus* is well established in Catalonia favored by environmental and climatic conditions and reported in nearly 50% of the territory since its introduction in 2004. The vector has adapted to urban and rural settings and is present in areas with the highest population density such as the city of Barcelona and its metropolitan area.
- The three SCM in Catalonia have been performing routine mosquito control and study since 1982 in their areas, thus general data and knowledge are available. Vector sentinel surveillance is being performed in Catalonia since 2001, it is related to few diseases (WNV), discontinuous in time, and there is currently a lack of knowledge related to some important variables for effective vector control measures such as biting behaviour, larval habitats, seasonality, daytime/night time activity, and resistance to insecticides, among other things.
- There is a lack of knowledge regarding the specific ZIKV transmission competence of endemic *Aedes albopictus* strains. Moreover, *Aedes albopictus* is an extremely competent vector for CHIKV transmission, especially the ECSA strain, and there is already evidence of wild mosquito infection in Catalonia with DENV and other flaviviruses including Usutu virus.

- Protocols and circuits for prevention and control actions have been developed and implemented, coordinated by the ASPCAT and ensuring rapid and integrated interventions when suspicious and positive cases are identified.
- Clinical management is performed through the primary and hospital health care networks in coordination with two International Health reference centers with well-trained specialists, especially focusing on symptomatic cases and pregnant women arriving from the affected countries.
- Specific protocols for managing infection in pregnancy have been developed and implemented to guarantee alignment with international guidelines.
- There is a strong clinical laboratory capacity and circuits to ensure accurate and rapid diagnosis. However, some challenges such as saturation of clinical and laboratory services may occur due to the high number of suspected cases in some seasons.
- Guidelines and circuits for entomological interventions have been developed and distributed. Strong laboratory capacities for arboviral detection in entomological samples are available. Vector control interventions depending on municipalities are being monitor and evaluated by ASPCAT. Moreover, challenges such as vector control in private areas and proprieties with unidentified owners, as well as public communication when pesticide compounds are used, have been reported and might benefit from coordinated data collection and analysis and development of protocols for social communication.
- Overall, due to the presence of competent vectors, the lack of immunity of the population and the significant number of imported cases, Catalonia could considered at a high risk of introduction of arboviruses and will be specifically challenged by the current ZIKV epidemic during the following months.
- The territory will benefit from further evidence-based risk assessment to better identify areas for improvement, evaluate potential epidemic scenarios and optimize resources.
- Capacity for rapid detection, management of cases, especially vulnerable populations, and outbreak response is strong, particularly in the areas where the likelihood of introduction is higher. Nevertheless, there is still a need for

enhancement of capacities for better preparedness and ensure any potential outbreak is mitigated at an early stage.

- Because arboviruses are not currently circulating in Catalonia but one of the potential vectors (*Aedes albopictus*) is present, risk management should focus on maintaining and strengthening the strategies to reduce the risk of transmission: rapid investigation of sporadic cases (clinically suspected or laboratory confirmed) to determine whether they are imported or locally-acquired, regular monitoring of vectors and their abundance (particularly in areas with recorded or suspected cases) and integrated vector management. Routine knowledgeable management of vectors when/where needed, is a good starting point for emergency operations.
- Due to the potential introduction of other arbovirus vectors such as *Aedes aegypti,* entomological surveillance at points of entry (ports, airports, ground crossing) should be maintained and education of the health-care providers and the community about the risk of arboviral infection in travelers, its diagnosis and reporting requirements should be enhanced. If a locally-acquired case is confirmed, the response should be escalated to epidemic level in order to prevent further spread.
- Novel initiatives such as Mosquito Alert, a platform which enables geolocalized citizen reporting of mosquitoes and breeding sites from mobile phones can certainly help in filling gaps in surveillance as well as supporting management and control strategies by the development of prediction models of spreading.

8. Recommendations and way forward

a. Epidemiology:

- Epidemiological surveillance is key for the timely detection of cases and rapid response with active participation from all stakeholders.
- ZIKV and other arboviruses surveillance and prevention plans should be maintained and strengthened by building on the existing arbovirus management strategy.
- Reported suspected and confirmed cases must elicit rapid epidemiological investigations through the catalan epidemiological surveillance network in order to evaluate the source of infection (imported or autochthonous transmission) and rationally develop prevention measures
- A detailed cost-effective Emergency Response Plan addressing potential autochthonous transmission needs to be developed/enhanced and routinely updated for preparedness establishing plans of action with clear roles and evidence-based priorities and ensuring rapid availability of resources.
- Collection of clinical and laboratory surveillance data should be maintained within the current strategy including quality assurance. Additional relevant entomological and environmental surveillance information should be provided by partners. Data should be then analyzed in an integrative manner. Public health-driven data analysis and production of relevant conclusions could be performed on an annual basis ensuring circulation within the relevant bodies in order to monitor, feed-back data providers, and enhance evidence-based and cost-effective preparedness.

b. Clinical surveillance and management:

- Clinical surveillance of imported cases is critical for risk evaluation of introduction as well as for rapid detection of cases in case of local transmission.
- Suspected and confirmed cases should be rapidly notified to ASPCAT by established circuits to ensure adequate response.
- Network collaboration and communication between reference centers and primary care settings are needed to ensure awareness and rapid identification of

cases.

- Consensus guidelines for clinical diagnostics, laboratory circuits and management of arboviral diseases should be, routinely updated and shared within the primary care network and relevant health services (International Health, Gynecology and Obstetrics, Intensive Care Units, Neurology, Rheumatology, Pediatrics) through the catalan surveillance network of ASPCAT [9]. Guidelines should also include criteria for derivation from primary care settings to specialized reference centers in case of severe illness and disease in vulnerable populations including children, elderly, pregnant women and immune-compromised patients.
- Communication plans should be developed and implemented within the clinical and epidemiological surveillance network in order to increase attendance to pre and post-travel visits and counseling especially for tropical and sub-tropical destinations. Reference centers should ensure the provision of information on preventive standard measures against vector-borne diseases during pre-travel advice and counseling in case symptoms present during travel or upon return.

c. Laboratory surveillance and capacity:
   - Reference laboratories have a key role in the surveillance for ZIKV introduction and spread.
   - Resources and capacities for maintaining molecular and serologic techniques in reference laboratories for the diagnostic evaluation of ZIKV and other epidemic arbovirus should be available. Ongoing training of laboratories for updates in arbovirus detection is needed.
   - Collaboration within network partner laboratories is important in order to optimize resources and guarantee turnaround times
   - Reference laboratories should develop, with other public health partners, sample triage plans and circuits to avoid laboratory overload.

d. Entomological surveillance and management:
   - Following international recommendations, Integrated Vector Management (IVM) should be implemented upon existing entomological capacities. An IVM approach is evidence-based and an essential feature in the development of the capacity to

generate local data on disease epidemiology and vector ecology. Integration at the level required for IVM is not a simple task; national leadership and adequate local capacity are essential.

- It is important to differentiate vector control from vector surveillance and to promote national structures in both senses.
- Successful IVM for ZIKV and other arboviruses requires trained experts in entomology and vector control.
- IVM is not an emergency time activity. Vector management is done systematically by most local authorities. Therefore, existing control actions are the base for enhancement when emergency arises
- IVM would benefit with the implementation of novel evidence-based strategies, such as citizen platforms for surveillance of mosquitoes, which can help to fill gaps and optimize resources.
- In order to achieve a maximum impact on vector-borne disease IVM should include:
    - Coordinated routine and timely entomological surveillance under a national robust framework ensuring appropriate data collection and sharing with stakeholders.
    - Activities aiming to ensure the availability of the knowledge related to factors influencing local vector biology (including competence and resistance features) as well as management strategies (insecticide resistance data).
    - Synergistic use of interventions through coordinated and protocoled plans.
    - Enhanced collaboration within the health sector and with other public and private sectors as well as engagement with local communities and other stakeholders. It is worth noting that *Aedes albopictus* is a non-native mosquito, adapted to urban life and thus easier to control by human behaviour than other mosquito species. Public education campaigns should be a major part of entomological management.
    - Validation and continuous evaluation of surveillance and control activities to measure efficacy, to ensure that staff who are adequately trained and

are following appropriately technical guidelines.

- The development of a public health regulatory framework for vector control and vector surveillance.

e. Environmental sciences:

- Environmental surveillance should be implemented and integrated within the arbovirus surveillance strategy. Relevant seasonal environmental factors including climatic proxies impacting on vector population dynamics, survival and competence should be identified, routinely collected and analyzed.
- Based on scientific evidence, the surveillance strategy will benefit from the use of qualitative assessments as well as quantitative computational and mathematical models evaluating potential epidemiological scenarios. This will facilitate optimization of resources and management by identifying the most cost-effective interventions as well as strengthening preparedness

f. Risk communication and advocacy

- Leadership of the ASPCAT and involvement of municipalities, non-governmental, and community-based organizations for public risk communication and advocacy should ensure coordination, production and circulation of health education material.
- Rational communication of risk to the public, addressing modes of disease transmission, unavailability of specific treatment, available means of symptomatic and supportive treatment and adoption of control measures is crucial for sensitization and community participation.
- It is important to reassure the population that these are preventable and self-limiting diseases. People should follow ASPCAT guidelines and if traveling to endemic regions should be encouraged to use personal protection measures in the form of full-sleeved clothing, mosquito repellent preparations over the exposed body parts, and insecticide-treated bed nets.
- The communication has to be targeted at modifying behaviors (practices of storage of water and personal protection) and eventually special campaigns may be carried out with the involvement of the mass media (TV, radio, newspapers, billboards), particularly before mosquito seasons.

- Synergic efforts engaging policy-makers at national and international levels are crucial, and should highlight the need for resources availability, surveillance strengthening, prevention and control measures and developing cost-effective and sustainable strategic plans for combatting vector-borne diseases.
- Lattermost, an approach for preparedness and response should include activities for international networking and coordinated collaboration in Public Health, especially within the South European and Mediterranean region.

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