MISSION REPORT

Dengue outbreak in Madeira, Portugal

March 2013

ECDC MISSION REPORT

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Abbreviations

CEVDI	Centro de Estudos de Vectores e Doenças Infecciosas
DENV-1	Dengue virus 1
DGS	Directorate-General of Health, Portugal
DNA	Deoxyribonucleic acid
DDT	Dichlorodiphenyltrichloroethane
GIS	Geographic information system
IASAÚDE, IP-RAM	Instituto de Administração da Saúde e Assuntos Sociais, IP-Região Autónoma da Madeira
ICPC-2	International Classification of Primary Care 2
ICT	Information and communications technology
IHMT	Instituto de Higiene e Medicina Tropical
INSA	Instituto Nacional de Saúde Dr Ricardo Jorge
MDSS	Madeira Dengue Surveillance System
RAM	Região Autónoma da Madeira
RT-PCR	Reverse-transcriptase polymerase chain reaction
SESARAM, E.P.E.	Serviço de Saúde da Região Autónoma da Madeira, E.P.E.
SOP	Standard operating procedure
SRPCBM	Serviço Regional de Protecção Civil e Bombeiros da Madeira

1 Summary

From 26 September 2012 to 3 March 2013, the autonomous province of Madeira, Portugal, reported its first dengue outbreak (Dengue-1 virus). Of the 2 168 probable cases, 1080 were confirmed. No severe clinical forms were reported, and there were no fatalities. As of 3 February 2013, seventy-eight patients have been diagnosed in other European countries with dengue infection after returning from Madeira (continental Portugal 11, United Kingdom 23, Germany 19, Finland 7, Sweden 5, France 3, Denmark 2, Austria 2, Norway 2, Croatia 1, Slovenia 1, Spain 1, and Switzerland 1). The latest case was reported on 1 February 2013 from Finland. Phylogenetic studies showed that the virus was most likely introduced from South America (Venezuela, Colombia, or northern Brazil). Between week 4 and 19 (2013), three imported cases from Angola (2) and Brazil (1) were identified in Madeira.

The outbreak was mainly located in Funchal and neighbouring areas, notably Câmara de Lobos, São Martinho, and Caniço. Few cases were reported in other municipalities; these cases were most likely acquired in foci of active transmission.

The presence of *Aedes (Ae.) aegypti* mosquito, the main dengue vector, was detected for the first time in Funchal in 2005 and its presence was then recorded along the southern coast of the island, at low altitudes and in urban settings that provided an ecological niche for the establishment of the mosquito in Madeira.

ECDC conducted a first mission in October 2012 to set up a specific epidemiological surveillance system based on information from the public healthcare system, the *Madeira Dengue Surveillance System*. Using this tool, the local authorities were able to follow the spatio-temporal evolution of the outbreak. Results were published in an epidemiological bulletin for the main stakeholders.

In March 2013, ECDC conducted a second mission to Madeira to retrospectively assess outbreak epidemiology as well as the public health measures and activities implemented between September 2012 and February 2013 and to discuss with the local health authorities response and preparedness planning with regard to future scenarios. Upon request from the Portuguese Directorate-General of Health, the team conducted a SWOT analysis (strengths, weaknesses, opportunities, and threats) of main activities related to dengue prevention and control in Madeira. The main outcomes of this analysis are presented in this report.

After the first *Ae. aegypti* mosquito notification in 2005, vector control campaigns were initiated: measures were taken to reduce the number of breeding sites, mosquito adulticides were applied, and vector surveillance was implemented for the entire island. In addition, the Portuguese Directorate-General of Health published technical guidance to reduce the risk of importation and introduction of *Ae. aegypti* to continental Portugal. During the outbreak, health education activities (websites, flyers and posters, publications, news media activities) were conducted and reinforced, particularly at the community level and at healthcare centres.

The archipelago of Madeira is well connected with tropical countries where dengue is endemic. Therefore, the reintroduction of the dengue virus – as demonstrated by the regular notification of imported cases – is always possible. Also, new mosquito populations from tropical endemic areas could establish themselves. Thus, there is a need for a contingency plan which covers vector-borne disease outbreaks and efficient vector-control measures.

Possible outbreak scenarios were discussed with local health authorities and proposed to be included in an intersectoral contingency plan describing response activities in relation to the phases of an outbreak. The implementation of sustainable intersectoral cooperation and coordination (as well as adequate human and financial resources) was another main topic of discussion during the mission.

Vector surveillance needs to be maintained and enhanced to monitor the geographical spread of the vector and to insure proper evaluation of control activities. Additional scientific knowledge about the vector's behavior, its population genetic characteristics, and its insecticide resistance pattern is needed. Work in this direction should be prioritised in the coming years, together with improving local entomological expertise. Insecticide testing should be performed on site in order to insure the efficient implementation of vector surveillance and control measures. In the insular context of Madeira, an elimination programme in combination with preventive measures against the re-introduction of the mosquito might be considered. Further innovative vector control approaches presently under technical assessment for mid- and long-term interventions were also discussed.

In conclusion, the establishment of *Ae. aegypti* mosquito in Madeira and the dengue outbreak that occurred in 2012–2013 emphasise the necessity of a sustainable vector surveillance system and the implementation of long-term strategies for vector control. In addition, enhanced mosquito surveillance should be implemented at strategic points (e.g. harbours and airports) in other geographic areas, for example the Canary Islands and continental Portugal.

Experiences acquired through this vector-borne outbreak in Madeira are of interest to EU Member States which potentially face the introduction of tropical vector-borne diseases in areas infested by *Ae. albopictus* mosquitoes.

2 Objectives

General objective

The goal of the second mission to Madeira following the dengue outbreak (September 2012 to January 2013) was to assess the already implemented response measures and activities and support the planning of new measures based on the current situation and possible future scenarios.

Specific objectives

To review in detail the epidemiological situation of human dengue cases (September 2012 to February 2013):

- Retrospective analysis of collected data (descriptive epidemiology: time, place, person)
- Case management

To assess the general coordination and planning of the response measures which were taken to contain the 2012 outbreak of dengue (September 2012 to February 2013):

- A review of the surveillance of the disease, focus investigations, disease management, and laboratory activities
- A review of the entomological surveillance, retrospective review of preventive/control measures through field visits

To propose further measures in order to enhance preparedness and improve the control of dengue transmission in the island:

- Support the partners in the Autonomous Region of Madeira (Região Autónoma da Madeira, RAM) by discussing the development of a contingency plan for dengue
- Review of laboratory planning and capacities for case confirmation
- Evaluation of transmission risks through blood donation (presentation of EUFRAT tool)
- Identification of gaps and opportunities for the implementation of sustainable surveillance of *Aedes aegypti* (guidelines, infrastructure, monitoring of control activities, coordination) to support assessment of possible re-emergence (data collection, analysis, etc.)
- Evaluation of risks associated with a possible (re-)emergence of dengue and identification of possible control strategies for *Ae. aegypti.*

A debriefing of the mission with experts from the National platform took place at the Directorate-General of Health in Lisbon on 15 March 2013.

A summary of the team activities, stakeholder meetings, and the mission agenda are presented in Annexes 1, 2 and 3, respectively.

3 Epidemiological analysis

Materials and methods

Prior to week 43/2012, the epidemiological data available were collected from:

- voluntary reports from healthcare system of the Autonomous Region of Madeira (Serviço de Saúde da Região Autónoma da Madeira, SESARAM E.P.E.); and
- the regional laboratory, where all samples were analysed.

In week 43/2012, the Madeira Dengue Surveillance System (MDSS) was operative, and the extraction of epidemiological information was automated. A detailed case definition was published by the Directorate-General of Health in Lisbon in October 2012 [5].

Probable cases must meet both the clinical and epidemiological criteria. Clinical criteria include acute onset of fever and at least two of the following symptoms or signs: headache, retro-orbital pain, myalgia, arthralgia, exanthema, haemorrhagic manifestations or leucopoenia. Epidemiological criteria: resident in, or visit to, a dengue-affected area during the 21 days prior to onset of symptoms (the whole Autonomous Region of Madeira was considered an affected area at the time of the outbreak).

A confirmed case is defined as a probable case with at least one of the following laboratory results: presence of dengue virus-specific IgM antibodies in blood or cerebrospinal fluid (CSF); significant increase in the concentration of dengue virus-specific IgG antibodies (seroconversion), or detection of dengue virus nucleic acid or antigen in blood or CSF.

All cases were geo-localised using the street address and epidemiological information, which was then entered into a geographic information system (GIS). The spatial data infrastructure of Madeira contains numerous map features, e.g. streets, buildings, hotels, restaurants, hospitals, clinics, schools, sewage systems, and irrigation networks, which allows for the analysis of vector control measures in relation to case occurrence.

This analysis covers the period up until 2 March 2013 (week 9/2013).

Results

Between 26 September and 3 March 2013, 2168 probable and confirmed cases were notified during the 23-week outbreak; the epidemiological curve is shown below as Figure 1.

Figure 1: Dengue cases (probable and confirmed) by week, weeks 39/2012 to 9/2013, Autonomous Region of Madeira
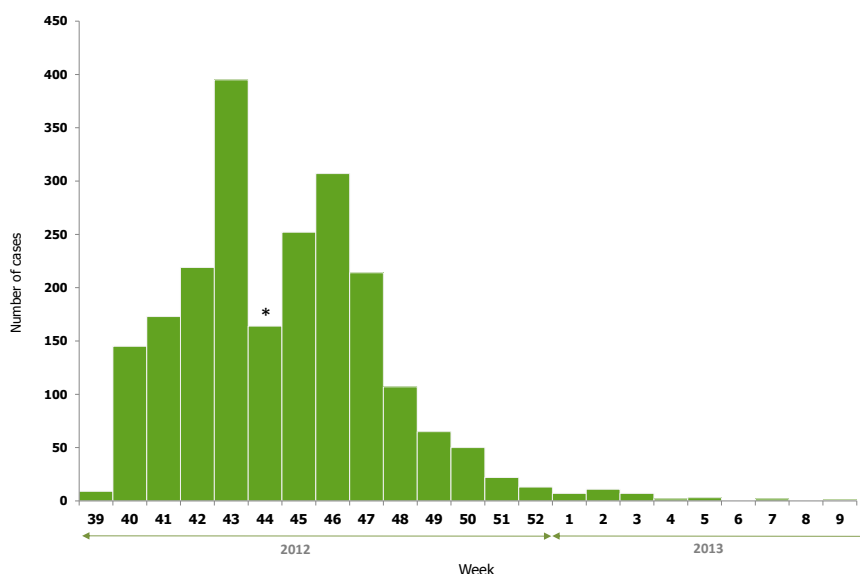
* Introduction of MDSS

The first two cases with dengue had onset of symptoms on 26 September (week 39/2012). The outbreak curve reached its peak in week 43. The marked increase between weeks 39 and 40 could be the result of delayed notifications during the early days of the outbreak. There is a decrease of reported cases in week 44, the first week

after the introduction of the MDSS (see * in Figure 1); there is no clear explanation for this marked change in the weekly pattern.

The numbers pick up again in weeks 45 and 46, followed by a gradual decrease, which continues well into 2013. This bi-modal pattern can also been seen in the epidemiological curve for cases imported to the EU. Imported cases were reported through the EWRS platform by Member States and the independent MDSS notification system. Spearman's Rho (correlation coefficient) between weekly data from EWRS and MDSS is 0.87, p<10–4), which points to environmental conditions as the cause for the bi-modal distribution, rather than a notification bias at the start of the MDSS.

The figure below correlates daily mean temperature, long-term seasonal temperature (long-time series decomposition between 1999 and 2012, see Annex 4), and daily precipitation (meteorological station in Funchal, Madeira, January 2010 to December 2012). The three relevant vector thresholds are hatching (13 °C), emergence (18 °C), and oviposition (22 °C) [6]. The vertical grey bars represent the period during which the seasonal component is above the oviposition threshold.

The outbreak occurred at the end of period with ideal conditions for the *Ae. aegypti* population and was characterised by high mosquito activity (data not shown), a positive temperature anomaly, and plenty of rainfall. Overall, data indicate that the optimal period for oviposition, with regard to temperatures, is between July and October. During this time there is an increased risk for the emergence of vector-borne outbreaks transmitted by *Ae. aegypti*.

Figure 2: Daily mean temperature, long-term seasonal temperature, and daily precipitation in Funchal, January 2010 to December 2012
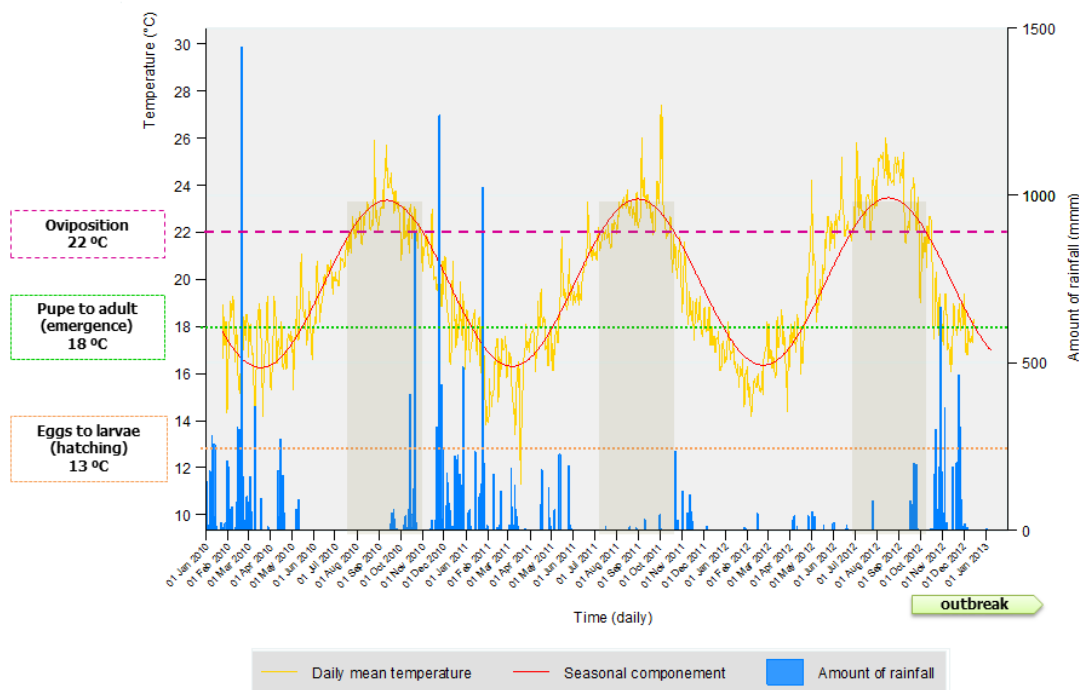
An outline of the main outbreak parameters is given in Table 1. The cumulative incidence rate was 78 per 10 000 inhabitants over the outbreak period. The majority of cases were notified in the three neighbouring municipalities: Funchal (77%), Santa Cruz (8.3%), and Câmara de Lobos (5.8%), representing 91.1% of the total number of cases (Figure 3).

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Table 1: **Epidemiological parameters by residence, weeks 39/2012 to 9/2013, Autonomous Region of Madeira**

Municipality of residence	Population	Number of cases	Cumulative number of cases	Cumulative %	Attack rate per 10 000 persons	Week of occurrence of first case	Number of weeks with cases
Funchal	111892	**1670**	1670	77.0	**149.3**	39	**21**
Santa Cruz	43005	**180**	1850	85.3	**41.9**	39	**17**
Câmara de Lobos	35666	**124**	1974	91.1	**34.8**	41	**14**
Machico	21828	**44**	2018	93.1	**20.2**	39	**15**
Porto Santo	5483	**10**	2028	93.5	**18.2**	41	**2**
São Vicente	5723	**10**	2038	94.0	**17.5**	40	**7**
Ribeira Brava	13375	**19**	2057	94.9	**14.2**	41	**9**
Santana	7719	**9**	2066	95.3	**11.7**	41	**4**
Porto Moniz	2711	**3**	2069	95.4	**11.1**	43	**2**
Calheta	11521	**12**	2081	96.0	**10.4**	41	**5**
Ponta do Sol	8862	**9**	2090	96.4	**10.2**	42	**5**
Other		**78**	2168	100.0			
Total (Madeira)	**267785**	**2168**			**78.0**	**39**	**21**

The cumulative incidence rate map indicates that the higher attack rates in southern municipalities. Likely, this results from the higher population density in these areas and the distribution of the *Ae. aegypti* vector present only along the southern coastline (see Annex 4, Figure 10). Still, it should be noted that cases are recorded according to their residence place and since *Ae. aegypti* mosquitoes are mostly active during the day, some cases may have likely been infected when working or studying away from their residence.

Figure 3: **Cumulative incidence rate for probable and confirmed dengue cases per 10 000 inhabitants, by parish of residence, weeks 39/2012 to 9/2013, Madeira Island**

Source: IASAUDE; discretisation method: natural break (Jenks); map projection: EPSG:3061 – Porto Santo/UTM zone 28N; software: Quantum GIS 1.8; map reference: ECDC_CIR_n2168

As three municipalities of Funchal, Santa Cruz and Câmara de Lobos represent the vast majority of notified probable cases, the standardised incidence ratio (SIR) by 'block' (the lowest administrative division for the 2011 census) has been calculated for these three municipalities (Figure 4).

The centre of the outbreak was in Funchal, with 82% of all cases; the highest incidence rates were reported from Santa Luzia parish and Nazaré locality. One case was reported in S. Martinho parish. The neighbouring municipalities of Santa Cruz and Câmara de Lobos also notified cases but at a lower level (Table 1).

Figure 4: Standardised incidence ratio for probable and confirmed dengue cases, by 'block' of residence in the municipalities of Funchal, Câmara de Lobos and Santa Cruz, weeks 39/2012 to 9/2013), Madeira island
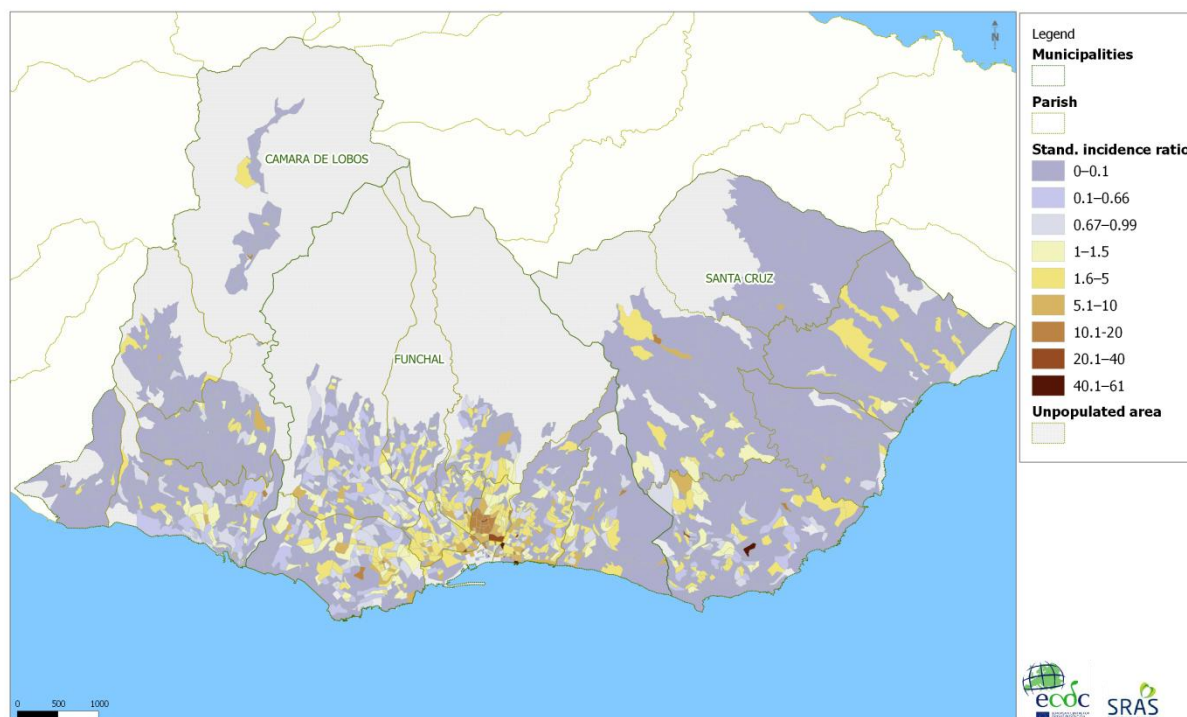
Source: IASAUDE/ECDC; discretisation method: pretty breaks; map projection: EPSG:3061 – Porto Santo/UTM zone 28N; software: Quantum GIS 1.8; map reference: ECDC_SIR_Madeira.

In order to better delimit the spatial distribution of dengue between the municipalities of Funchal, Câmara de Lobos and Santa Cruz, a spatial and/or temporal clusters analysis was performed using space-time scan statistics. Chen et al. describe this method as follows:

> Most syndromic surveillance systems make use of spatial scan statistic and its variations. Using such methods for spatial analysis, a large set of circular windows with varying sizes is imposed on the map in different locations to search for clusters over the entire region. … The spatial-temporal version of the scan statistic uses cylinders instead of circles, where the height of the cylinder represents time … [while] the circular base defines a geographic area …[1]

For each combination of cylinder position and time, the occurrence of observed cases is compared with the number of expected cases number and the relative risk.

Data from the 2011 census were used, with the smallest administrative unit being a 'block'[2]. The generalised likelihood ratio was computed with the Poisson model (high detection rate). The significant level (p-value) was generated with Monte Carlo hypothesis testing of 999 randomly simulated data sets. The cluster with the highest p-value was considered the 'primary' cluster (cluster number 1 in red, see figure below); secondary clusters were labelled in the figure according to their p-value value (clusters 2 to 11 are based on increasing p-value, indicated by shades of green). Several cluster analyses were run ('space', 'time' and 'space-time') by varying the maximum size of the circular window (200 m, 400 m, 600 m, 800 m and 1000 m).

The cluster with the largest surface was found in Funchal, with a maximum window of 600 m, with one primary cluster centred in Santa Luzia parish between 1 October and 23 November (first cluster, but also finishing earlier than the other clusters) and 10 secondary clusters mainly occurring between October and November. Overall, the scan process identified 1118 observed cases versus 152 expected with a median relative risk of 5.7. Details on the used software can be found in Annex 6.

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[1] Chen H, Zeng D, Yan P. Infectious disease informatics: Syndromic surveillance for public health and bio-defense. New York, London, Heidelberg: Springer; 2009.

[2] Instituto Nacional De Estatística. Statistics Portugal: resident population. [internet]. 2012 [cited 2013 Oct 9]. Available from: http://www.ine.pt/xportal/xmain?xpid=INE&xpgid=ine_indicadores&indOcorrCod=0005889&selTab=tab0

Figure 5: Standardised incidence ratio of probable and confirmed dengue cases, by 'block' of residence and primary/secondary cluster, municipalities of Funchal, Câmara de Lobos and Santa Cruz (weeks 39/2012 to 9/2013), Madeira Island
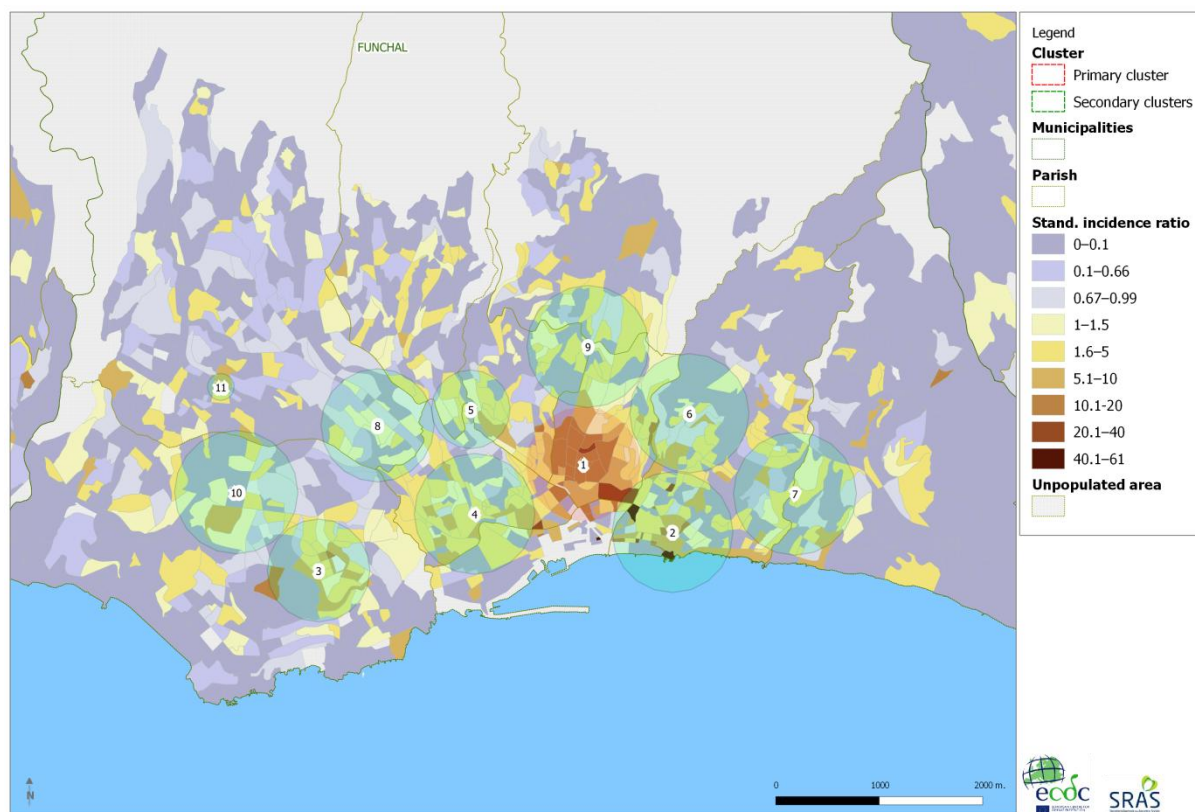
Source: IASAUDE/ECDC; discretisation method: pretty breaks; cluster analysis (type: space-time; probability mode: Poisson; detection: high rate; time span: daily; total population included: 50% at risk; maximum radius: 600m); map projection: EPSG:3061 – Porto Santo/UTM zone 28N; software: Quantum GIS 1.8; map reference: ECDC_cluster_Madeira.

In Figure 5, the primary cluster (see map: circle #1, Santa Luzia) is composed of residential areas located in the hills overlooking the city centre. Most houses are surrounded by small courtyards, often with terraces full of ornamental plants – potential breeding sites for *Ae. aegypti*. A substantial number of houses are vacation homes and stay empty most of the year, which makes access almost impossible during breeding site reduction campaigns. The neighbourhood also features a few abandoned houses, which usually have numerous breeding sites, particularly after rain. Successful vector control interventions are only possible if these buildings are mapped so control measures can be taken.

During the outbreak, considerable efforts were made to reduce breeding sites in the Santa Luzia cluster and increase awareness about dengue and the need to remove all potential breeding sites (see sections 'Summary of outbreak response activities' and 'Vector control').

Cluster 2 differs substantially from Cluster 1: residential and commercial buildings are located in the flat part of Funchal and very close to the city centre. Here, the sewage system provides *Ae. aegypti* with several breeding sites.

Cluster 3 is located on the hilltop, with wide roads and residential buildings. An investigation identified some courtyards with a high density of breeding sites and numerous ornamental plants.

All three clusters – despite their apparent differences – are suitable for the vector and thus potential areas for the transmission of dengue. This reinforces the importance of including different topological settings when planning vector control strategies. An in-depth understanding of the main breeding sites types is also essential.

It is assumed that population immunity is high after the outbreak, notably in Santa Luzia parish (see Annex 7). The ratio between symptomatic and asymptomatic cases is estimated at 20:80. Areas with a high dengue herd immunity will most likely not experience a re-emergence of DENV-1 in the coming years but will remain vulnerable to the introduction of other serotypes, which might lead to more severe cases (Figure 13, Annex 8).

The female-to-male ratio was 1.41, with the attack rate for men (AR_{men}=68.6 per 10 000) lower than for women (AR_{female}=86.5 per 10 000). Figure 6 shows the attack rate for gender and age group (population data: 2011 census for Madeira Island).

When looking at age distribution, men and women are affected differently. The youngest male age group shows the highest AR. Conversely, the female age group between 35 and 64 years is more affected than its male counterpart. A field investigation showed that the higher risk for women in this age group could be related to the fact that more women stay at home during the day than men, which leaves them more exposed to the diurnal activities of *Aedes aegypti*.

Figure 6: **Dengue incidence rates for probable and confirmed cases by age group and gender, 26 September to 11 November 2012, Madeira**
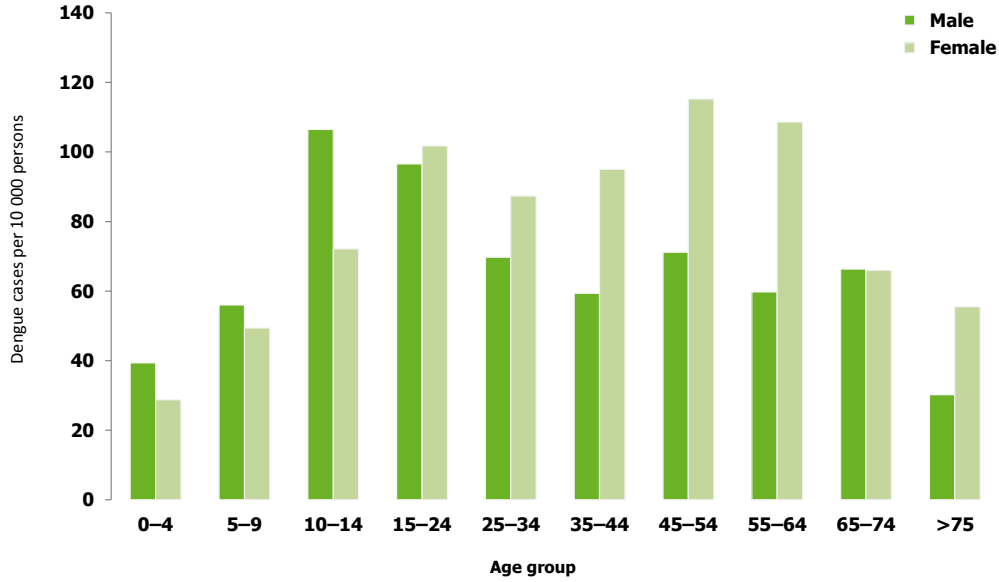
4 Summary of outbreak response activities

This section summarises the main measures taken between the start of the dengue outbreak up until February 2013. As there is no commercially available dengue vaccine, activities focus on vector control, treatment of symptomatic cases and prevention measures. Since the end of the outbreak, activities have shifted to disease and vector surveillance (in order to detect dengue cases, both locally acquired and imported, as early as possible), raising awareness in the local population (to promote the reduction of breeding sites), the preparation of a contingency plan, and regular control activities. This outline provides a retrospective overview of major activities and is no detailed review of actions conducted during the outbreak.

Epidemiological surveillance

Epidemiological surveillance started with the detection of the first confirmed case (week 39). An automatic epidemiologic surveillance system, based on information drawn from the local healthcare system (SESARAM) was implemented and maintained until the end of the outbreak. The system is intended to remain operative throughout 2013. During the outbreak, IASAÚDE received data from the SESARAM database twice a week, so the data could be included in IASAÚDE's weekly epidemiologic bulletin.

ECDC recommended that laboratory results should be included in the weekly data reports to make the epidemiological update more pertinent and to better integrate clinical and laboratory results. In addition, a normative document is planned which endorses the extension of data collection through the local healthcare system SESARAM: for all probable cases, both the place of work and the exact place of residence should be included to allow conclusions on the diurnal activities of the mosquitoes. This information could also support epidemiological investigations, inform vector control measures, and guide entomological investigations.

A notification form for private medical practitioners was posted on the IASAÚDE website. By the end of the outbreak, the retrospective analysis of the 30 notifications collected online showed that all patients had already been included in the SESARAM and the laboratory database. The online notification form will remain active, as will the MDSS.

Routine phone interviews with sporadic cases were implemented; these interviews are considered routine activities and should be conducted for all new cases during low-intensity outbreaks.

An epidemiologic bulletin was produced every week and passed on to the Directorate-General of Health, local health authorities, and the medical committee for dengue in the Autonomous Region of Madeira. The bulletin presented the results of outbreak monitoring, followed the evolution of the outbreak, and presented further material for decision-makers who needed to decide on tailored response measures.

The frequency of routine laboratory confirmation for probable cases was adapted to the intensity of the outbreak. A subset of approximately 10% of all probable cases was tested during the peak of the outbreak, following previous recommendations. In addition, all severe cases were tested to detect the potential circulation of new serotypes. In the last weeks of the outbreak, all probable cases were tested for new serotypes.

Public health measures

The following measures were introduced at the start of the outbreak: case management, patient follow-up, blood safety measures. The objectives were clearly defined: to detect early severity signs, avoid complications, diminish dengue transmission, and ensure the safety of blood transfusions as well as tissue and organ transplants.

Experts provided guidance to all healthcare centres in Madeira, managed cases, and referred critical cases to emergency wards at Dr Nélio Mendonça Hospital. Authorities installed a clinical consultation unit dedicated to dengue fever at the Health Centre of Bom Jesus and Santa Luzia to ensure proper follow-up and the prevention of complications. In November and December 2012, at total of 1741 consultations was recorded, including initial consultations for suspected cases of dengue and follow-up visits.

IASAÚDE published guidelines for the care of dengue patients, which was sent to all healthcare facilities and medical practitioners in Madeira. Probable cases were systematically followed up by telephone interview and/or medical consultation. Appointments for the follow-up were usually made during the initial consultation.

On 6 October, the day when the health alert was announced, blood donations were put under embargo. From 6 October to 4 November, 397 blood donations were tested by RT-PCR in Lisbon and six DENV-1-positive blood donors were detected. On 5 November, RT-PCR assay was introduced at the laboratory of Dr Nelio Mendonça Hospital.

Communication plan

A communication plan was regularly updated during the outbreak; media included television, text message alerts, the IASAÚDE webpage, and direct communication with healthcare workers through focus group and meetings. Again, messages were mostly educational, with an emphasis on personal protection measures, and urged the public to reduce the number of breeding sites around their private residences.

Leaflets, posters, websites, TV and radio messages informed the general public about dengue fever (transmission mode, symptoms, treatment) and personal protection measures such as insect repellents and domestic insecticides. The campaign focused on areas under public administration, touristic areas and transit areas, namely, the airport and the harbours. A number of activities were tailored to groups of special relevance, for example staff at healthcare centres, teachers at schools and high schools, and the scientific and non-scientific staff at universities and community associations (see Annex 12).

Intersectoral collaboration and partnerships

Intersectoral collaboration and partnerships were built up at regional, national and international levels. Collaboration of all regional sectors (health, transport and tourism, urban development, education, and administrative authorities of affected municipalities) involved in vector control and outbreak management was coordinated by IASAÚDE. A first intersectoral committee meeting was conducted on 25 October 2012 during which the main tasks in response to the outbreak were defined: communication, vector control activities, and activities with regard to the tourism sector. This led to a series of activities such as integrated vector control and an improved organisational structure (see Annex 13).

Collaboration was with national institutions (DGS, IHMT and INSA) was promoted; also, Madeira cooperated with research groups which had field entomology expertise (monitoring of vector populations, scientific advice on vector control strategies). The DGS summoned a team of experts as a task force to provide technical advice and guidance. Further contacts and coordination efforts included ECDC and WHO.

In October 2012, ECDC supported a first field mission in Madeira, providing support and technical/scientific advice: advice ranged from setting up a surveillance system to epidemiological analyses to the use of a geographical information system. ECDC also offered technical expertise on integrated vector control activities. Details can be found in a mission report available at: http://ecdc.europa.eu/en/publications/Publications/dengue-outbreak-madeira-mission-report-nov-2012.pdf

5 SWOT analyses

DGS requested a SWOT analysis (strengths, weaknesses, opportunities, and threats) of the various sectors of dengue prevention and control in Madeira. The results of this analysis can be found below.

Epidemiological surveillance

Outline

In September 2012, the epidemiological surveillance system in Madeira faced a complex challenge: the first outbreak of dengue fever in 100 years presented health authorities with an unexpected challenge. IASAÚDE, national authorities and ECDC had to closely collaborate in order to quickly set up an automated surveillance system based on data from the local healthcare information system. Another essential point was an epidemiologic case definition. An online questionnaire was prepared, and the local surveillance system was tweaked to accommodate a database that then could be used to produce a twice-weekly summary of the epidemiological situation. An epidemiological bulletin produced to inform on the evolution of the outbreak.

The surveillance system is very comprehensive because most citizens of Madeira are enrolled in the public healthcare system. Only a small number of patients were treated by the private healthcare sector, and even they were eventually captured by the local dengue surveillance system and the IASAÚDE database when they attended follow-up consultations conducted at public healthcare facilities.

Local authorities depend on data when preparing the epidemiological bulletin or carrying out field operation responses. In addition to patient characteristics and a constantly updated epidemiological curve, geo-location (of a patient's household address) and assumed place of exposure are valuable information because this enables field workers to implement vector control measures in close proximity of the possible place of exposure.

Efforts made during the outbreak period aimed to build local capacity and strengthen the local authorities' commitment. Sharing expertise and resources from other administrative sectors – notably the geographical information system – demonstrated the improved information exchange between partners. However, the limited availability of technical resources and the lack of experience in vector-borne disease outbreaks made it difficult to properly analyse the epidemiological parameters. However, the increase of capacity will definitely be an asset for future vector-borne disease outbreaks in Madeira and Portugal.

One of the most important benefits of the geographical information system (GIS) used in Madeira is the detailed information it provided for the most affected (most notably the Santa Luzia neighbourhood) areas, where the circulation of the virus in the community was high. In the coming years, this type of information will remain valuable and support the local health authorities in monitoring the potential re-emergence of the dengue virus. Furthermore, GIS data are also helpful to notify the population if dengue-like symptoms are reported in their neighbourhoods, particularly if the outbreak is caused by a new serotype. ECDC experts recommended that biological results should be reported to the dengue surveillance system in order to improve monitoring.

Epidemiological surveillance has become a useful advocacy tool for supporting an intersectoral approach. The ECDC team suggested that regular simulation exercises should be held, involving all sectors under various emergence scenarios to stress-test the surveillance system and the workflows.

SWOT analysis epidemiological surveillance

	Helpful	Harmful
Internal	**Strengths** • Flexibility • Timely • Central system • Excellent coverage of healthcare facilities (hospitals and healthcare centres) • Medical staff understands local epidemiology • Acceptance by population • Case management and follow-up consultation • Laboratory facilities • Integrated and linked vector control (GIS)	**Weaknesses** • Laboratory results should be integrated into the information technology (IT) system workflow. • Place of work in IT workflow • Lack of capacity building for epidemiological analyses • Improve information flow for the private health sector (reminders, newsletters)
External	**Opportunities** • Collaboration and external expertise • Comprehensive knowledge about the outbreak to produce a contingency plan • Support advanced epidemiological analysis • Lessons learned • Experience can benefit other Member States, EPIET programme, etc.	**Threats** • Communication

Health services and organisation

Outline

The health sector is managed by the Regional Secretariat of Health and Social Affairs (Secretaria Regional dos Assuntos Sociais). Activities are divided between two departments:

- IASAÚDE, IP-RAM (Instituto de Administração da Saúde e Assuntos Sociais, IP-Região Autónoma da Madeira)
- SESARAM, E.P.E. (Serviço de Saúde da Região Autónoma da Madeira, E.P.E.).

The Regional Secretariat of Health and Social Affairs also operates the civil security services (SRPCBM, Serviço Regional de Protecção Civil e Bombeiros da Madeira), which deals with health emergencies and natural disasters.

The health information system captures information in two main areas, using a unique identifier for each user:

- public sector; includes two hospitals: Dr Nelio Mendonça Hospital in Funchal and Hospital dos Marmeleiros, as well as 14 primary healthcare centres, one in each municipality and four in Funchal; outpatient and discharge diagnoses are reported to a central database operated by SESARAM.
- private sector; under the responsibility of IASAÚDE, with eight registered private clinics and 412 registered medical doctors, 11 of which are general practitioners.

The healthcare system in the Autonomous Region of Madeira reacted quickly to the dengue outbreak. Command and control activities were put in place in order to ensure the proper assessment of the situation, identify gaps and carry out activities developed before the outbreak. Priority was given to disease surveillance and case management.

During the first week of the dengue outbreak, patients were directed to the emergency ward at the Dr Nélio Mendonça Hospital; later, medical consultation centres were set up in or near dengue clusters (e.g. Santa Luzia) to ensure early access to medical care and follow-up consultations in the affected neighbourhoods. In addition, health authorities reviewed the capacity of the Madeiran health system to treat dengue fever. Incidentally, a contingency plan should contain a section on medical supplies and the healthcare system's capacity to offer tailored treatment for dengue, or other diseases, for that matter.

A strong effort was made to avoid nosocomial transmission. As there is a real risk of transmission inside and outside of medical facilities, mosquito control measures were taken: screen windows, mosquito nets for hospital beds, regular insecticide spraying, and vector surveillance in the proximity of the centre. As with medical supplies, the procurement and logistical aspects of mosquito control materials should be anticipated in the contingency plan (i.e. emergency stock provisions).

From early on in the outbreak, the clinical management of cases included early detection and follow-up consultations. A more detailed retrospective analysis of the clinical aspects is recommended and would be of interest to local general practitioners and specialists. The analysis should pay attention to the duration of hospital stays, biological parameters, and other factors such as paediatric status and co-morbidity. The rate of follow-up consultations would indicate access to medical care and patient participation in the follow-up consultations. This study would also provide background information for a cost analysis of the outbreak – essential information for the

management of further outbreaks. Financial information from this study could also be used for the contingency plan.

The laboratory facilities will be described below. All in all, laboratory management was adequate, but the shortages of laboratory reagents (dengue rapid test, PCR testing) could have been dealt with better.

In general, local communication about outbreaks and healthcare management can promote early patient consultations and curb secondary transmission. The dengue media campaign in Madeira (radio, TV, social media) was implemented in an appropriate manner. During the outbreak, local health authorities sought external advice to assess and refocus their public health message.

SWOT analysis health

	Helpful	Harmful
Internal	**Strengths** • High use of public health sector • Well-organised public health sector • Experience with natural disasters • Case management • Contingency plan 2013 • Dengue will be included in the hospital emergency plan (contingency plan) • Intersectoral approach • Support from municipalities	**Weaknesses** • Lack of outbreak scenario • Limited technical resources • Laboratory results not yet integrated in the IT workflow • Place of work not added as geographical variable in IT workflow (diurnal activities of the vector) • No simulation exercises conducted
External	**Opportunities** • External support and external review of contingency plan • Experience sharing	**Threats** • Virus re-emergence • Virus re-introduction • Partial population immunity (DENV-1) and outbreak of dengue fever with a new-serotype

Laboratory analysis

Outline

Laboratory analysis is a key component in a dengue outbreak because it can provide case confirmation.

- Under routine surveillance, conducting a laboratory assay will allow the early confirmation of cases and provide information on the type of strain that is circulating – either a new dengue strain or a re-emerging strain. Initial case detection should always be combined with serotype identification, molecular assays and sequence analysis. Rapid tests are helpful because they yield results in a few hours' time, so response activities in the field can start sooner. Additional laboratory assays (RT-PCR and sequencing) should be conducted quickly to confirm the preliminary results.
- During the course of a large outbreak it is not possible to test the entire cohort for suspected or probable cases. A sample of approximately 10% of probable cases should be routinely laboratory tested to monitor outbreak patterns and check for co-circulation of other dengue serotypes.
- At the end of an outbreak (i.e. when the surveillance system only reports sporadic cases) every probable case should be laboratory tested, which would also help to determine the official end of the outbreak.

Only one laboratory – Dr Nélio Mendonça Hospital – in the public health system in Madeira is equipped to conduct the entire set of laboratory analyses for dengue (rapid test, serology assays and molecular detection). In addition, five privately owned laboratories in Madeira are capable of conducting rapid tests. Up until 11 March, only 5% of cases were tested in the private sector, with most specimens sent to the central laboratory for confirmation.

Using a structured questionnaire developed by ECDC experts before the actual mission, the mission team discussed retrospective and prospective laboratory issues with Dr Graça Andrade, director of the laboratory at Dr Nélio Mendonça Hospital in Funchal. All laboratory results can be retrieved through a central database; laboratory results, however, are not automatically transferred to the MDSS surveillance system.

At the beginning of the outbreak, no interpretation algorithm was available; it became available at a later point in time. An evaluation grid on how to classify patient as positive or negative based on laboratory test results was shared with medical practitioners.

Retrospective evaluation

According to the protocol in place, rapid tests were used for diagnosis of early acute dengue infection. Due to limited stocks in Europe, different rapid tests for dengue were used during the outbreak:

Dengue NS1 antigen detection:

- SD BIOLINE Rapid Dengue Test Dengue NS1 Ag + Combo Test IgG/IgM test (Standard Diagnostics Inc., Korea)[3]
- Dengue Virus NS1 Antigen (Bio-Rad, USA)[4]
- Dengue IgG and IgM virus detection by in vitro immunochromatographic test (serotypes 1, 2, 3 and 4)
- NADAL Dengue Virus test cassette (*nal von minden* GmbH, Germany)[5]

In addition, RT-PCR was performed systematically for specimens taken from patients within onset of fever less than seven days ago. The PCR used in Madeira did not differentiate DENV serotypes. If the onset of symptoms was longer ago than seven days, serology confirmation was conducted by dengue IgM and IgG capture enzyme-linked immunosorbent assay (ELISA: NovaLisa, Novatech, Germany). Sequence analysis identified the same DENV-1 strain during the course of the outbreak as in viruses circulating in South America (Colombia, Venezuela, and the Roraima region in northern Brazil [6]).

From October to December 2012, a total of 183 patient samples were submitted, and 95 cases were confirmed; 39 of these cases were only confirmed by serology, and the remaining ones were confirmed by RT-PCR or RT-PCR in conjunction with serology. After December, only samples from severe and imported cases were sent to the reference laboratory for laboratory confirmation. After the end of the outbreak, all samples are routinely referred to the national reference laboratory for confirmation. In total, 3285 clinical samples were tested between 26 September and 3 March. A total of 1080 cases were confirmed during this period.

All positive serum samples (regardless of the test method) are stored at −20 °C for approximately two months, together with some of the negative samples. Samples were professionally shipped by a company which had provided services to laboratories before. However, the average shipping time to INSA of about one week was considered too long.

A retrospective detailed analysis of the laboratory results and performance is ongoing, together with an internal quality laboratory control. To that regard, both Dr Nélio Mendonça hospital and INSA laboratories participated in a external quality assessment on dengue molecular diagnostics (EQA, April 2013) organised by the ECDC-funded ENIVD network[7].

In order to confirm test results and ensure their comparability (e.g. interpretation of potential false positive and false negative results), it remains essential to maintain a shared database of patients between both laboratories, namely the one at Dr Nélio Mendonça hospital (Madeira) and the national reference laboratory at Instituto Nacional de Saúde Dr Ricardo Jorge (mainland Portugal).

Prospective evaluation

The team at the hospital laboratory has four experienced technicians and can request more support from the private sector and INSA if needed. The hospital laboratory is able to test around 90 samples a day with RT-PCR and NS1 rapid tests and can handle approximately 180 samples for serology. Under this high-workload scenario, business continuity for other pathogen tests cannot be maintained. There are no plans to install sequencing capacity in Madeira. An agreement with a laboratory to deliver three test kits a week is already in place (one kit contains 90 rapid tests). Support in terms of reagents can also be requested from INSA.

So far, laboratory costs have not been assessed.

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[3] http://www.standardia.com/html_e/mn03/mn03_01_00.asp?intId=98

[4] www.bio-rad.com/en-ca/sku/70700-dengue-ns1-ag-strip

[5] http://www.medxpert.hu/en/orvosi-gyorstesztek/tropusi-betegsegek-a-parazitak/Details/103/11/orvosi-gyorstesztek/tropusi-betegsegek-&-parazitak/nadal%C2%AE-dengue-virus-tesztkazetta

[6] http://www.eurosurveillance.org/ViewArticle.aspx?ArticleId=20398

[7] www.enivd.org

Blood safety

Outline

Three topics were discussed with the director of the blood bank, Dr José Bruno Freitas: i) analysis workflow for the screening of blood donor samples, ii) blood donor population characteristics for the European Up-Front Risk Assessment Tool (EUFRAT)[8], and iii) sustainability of routine testing of blood samples for dengue. As for laboratory analysis, a structured questionnaire developed by ECDC experts was filled in.

There is only one blood bank in Madeira (Dr Nélio Mendonça Hospital in Funchal) and there are no mobile blood donation stations. Precautions and screening procedures for the prevention of dengue transmission through blood transfusion were implemented as soon as the first case was confirmed: since then, all blood donations have been systematically tested for dengue at the central public laboratory. Blood samples from September were deferred.

In total, 43 of 1948 donations tested positive for DENV-1 between 9 September and 11 March 2013 (Table 2). After systematic screening (RT-PCR), almost all positive donors could called in to be retested for IgM and IgG. Of the 43 positive donors, only two had become symptomatic during the follow-up period (one with IgM^+ & IgG^+; no serological follow up available for the other donor). Only three donors had detectable seroconversion, one also developed symptoms, while the other two remained asymptomatic. The number of PCR-positive results is high; a low PCR threshold or a potential environmental contamination with PCR DNA amplicons cannot be ruled out. Note that the six first original samples were sent to INSA and tested positive by PCR, arguing against false positive results.

Of the 397 blood donations collected between 6 October and 4 November, six were DENV-1-positive (RT-PCR in Lisbon). Since 5 November, Nelio Mendonça Hospital has been using RT-PCR assay for both case detection and blood donor screening.

Before each donation, all donors have to go through a routine screening questionnaire and an interview. The questionnaire has been fine-tuned at the early stage of the outbreak to screen for dengue. An information leaflet is distributes to ensure that donors who develop symptoms after donating blood will seek medical care.

Table 2: Blood safety screening results

Date of blood collection	Blood donations	RT-PCR-positive dengue cases	Elisa+ (IgM) post-donation testing/n; sample tested with PCR+	Estimated number of positive cases (PCR)s/1 000 blood donation	Follow-up
6 Oct 2012 – 5 Nov 2012	397	6	0/3	15	All – no symptoms
6 Nov 2012 – 30 Nov 2012	392	13	1/9	38	All – no symptoms
1 Dec 2012 – 31 Dec 2012	437	22	2/20	48	All – two donors with symptoms
1 Jan 2013 – 31 Jan 2013	531	2	0/1	3.7	All – no symptoms
1 Feb 2013 – 13 Feb 2013	191	0	0	0	–
Total	**1 948**	**43**		**22.6**	

Several proposals were discussed with the heads of the blood bank and the laboratory at Dr Nélio Mendonça Hospital: a retrospective analysis of the entire laboratory dataset, a quality control scheme, and RT-PCR assays for the screening of blood or plasma donors, to be carried out by the laboratory of the blood bank.

EUFRAT's on-site demonstration to the head of the blood bank drew on local and ECDC information. The overall prevalence of infection in the donor population was estimated at 83 per 100 000 (see Annex 10).

The Madeiran authorities will continue to screen blood donations until further notice from the Instituto Português do Sangue (IPS). The issue of spoiled or tainted specimens was raised: the more samples are transported between the collection site and the testing site (even if distances are short and samples are transported in a cold chamber at 4–8 °C), the higher the risk that specimens are not suitable for testing. In order to facilitate dengue screening, it would be helpful if the blood bank laboratory would develop the capability to perform PCR assays.

Follow-up consultations for positive donors (detection of symptoms and seroconversion) will be continued.

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[8] http://eufrattool.ecdc.europa.eu/

SWOT analysis laboratory and blood safety

	Helpful	Harmful
Internal origin	**Strengths** • Adaptability • Fast response to emergencies • Ad hoc local infrastructure	**Weaknesses** • External quality assessment to be implemented • Laboratory interpretation protocol • Stock planning based on scenarios • Serotype identification workflow with INSA • Protocol for biobank and storage facilities
External origin	**Opportunities** • Collaboration with INSA • ECDC support for EUFRAT tool • Retrospective analysis of laboratory results • Population immunity study – scientific collaboration with external partners	**Threats** • Additional costs for blood screening (blood safety)

Vector surveillance

Outline

A retrospective review of entomological surveillance activities and findings was carried out. The review was based on consultations with Professor Carla Sousa, stakeholders of the Funchal dengue control plan, and a group of high school teachers who conducted a study of *Ae. aegypti* breeding sites on school premises. In addition, the ECDC team reviewed maps and inspected the network of traps used for *Ae. aegypti* vector surveillance.

Figure 7 presents the main axis of progressive spread since the first notification in Funchal in 2005. The vector spread from the likely point of initial introduction to the west and the east of the island, following the southern coastline. Note that the vector did not establish itself in the northern part of the island (Porto Moniz municipality), where it was detected in 2011.

Figure 7: *Ae. aegypti* evolution in Madeira between 2005 and 2012
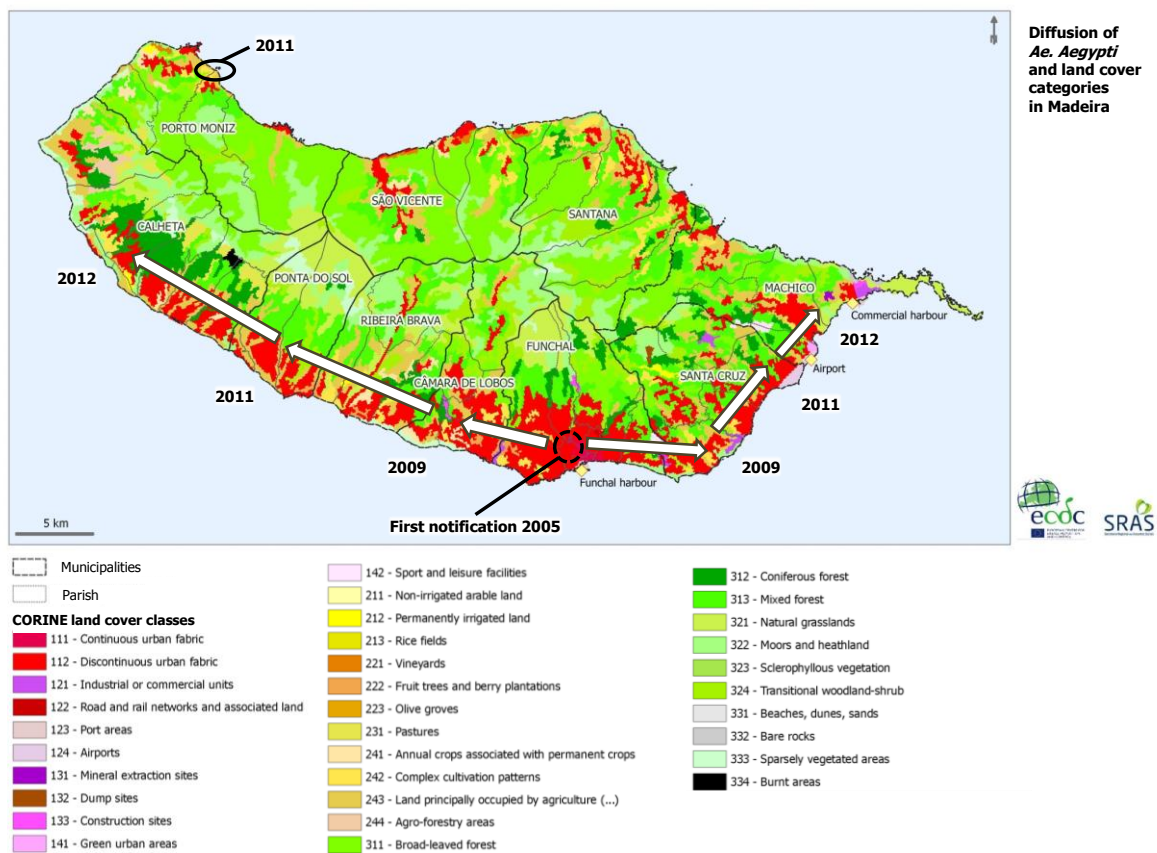
Surveillance activities started in 2005 when *Ae. aegypti* was detected for the first time in Santa Luzia parish and ovitraps were placed in the municipality of Funchal. The network has being progressively extended to neighbouring municipalities, the airport (Água de Pena) and the commercial harbour (Caniçal).

In 2009, 45 additional ovitraps were placed in an equidistant grid pattern proposed by the entomological team of the Museum of Natural History (Municipal Museum of Funchal). Twenty-seven were placed in Funchal municipality (27), the remainder in 10 other municipalities. *Ae. aegypti* was also detected in the neighbouring municipalities: Câmara de Lobos (parish of Câmara de Lobos) and Santa Cruz (parish of Caniço). Monitoring was continued up until 2013, in conjunction with the EU-funded MOSQIMAC project (2007–2013).

In 2011, an entomological survey was carried out in Madeira and Porto Santo, using 273 ovitraps. It showed that the *Ae. aegypti* population had expanded to the west (parishes of Canhas and Ponta do Sol, municipality of Ponta do Sol) and the east (parish of Santa Cruz, municipality of Santa Cruz). A positive ovitrap was also found on the north coast in the parish of Ribeira da Janela (municipality of Porto Moniz). No positive ovitraps were recorded in Porto Santo, the other inhabited island of the archipelago.

Between February and September 2012, surveillance of adults was implemented with 15 BG-Sentinel traps which covered Funchal and the neighbouring municipality of Câmara de Lobos and were checked biweekly.

In October 2012, surveillance activities were enhanced to a) record the transmission level in infested and neighbouring areas and b) monitor the species' spread:

- Ovitraps were deployed in areas with high activity of *Ae. aegypti*. A total of 136 ovitraps were placed, including 35 near airports and harbours (Madeira Airport: 9, Porto Santo Airport: 2, harbour of Funchal: 10, harbour of Caniçal: 10, harbour of Porto Santo: 4), one in the parish of Madalena do Mar, one in Jardim do Mar, and three in Paúl do Mar (east of the municipality of Ponta do Sol). In addition, five ovitraps were placed on the northern coast (Porto Moniz: 1, Ribeira da Janela: 1, São Vicente, Ponta Delgada: 1, Porto da Cruz: 1).
- The 16 BG adult mosquito traps (including one at Madeira airport) were checked daily.

In addition, door-to-door entomological surveys were performed to estimate the infestation indexes in private and public buildings (house, container and Breteau indexes). Gutters and water drainage sewers in Funchal's city centre were surveyed to detect the presence of *Ae. Aegypti*.

Ae. aegypti has been detected, below the elevation of 200m, along the entire southern coast, with the exception of the easternmost municipality (Caniçal) where the commercial harbour is located. However, the vector was detected in the northeast of Machico City, less than five kilometres from the harbour.

In the northern part of Madeira, *Ae. aegypti* was detected (positive ovitrap) in Ribeira da Janela in 2011, on the western part of the coast. The mosquito did not establish itself in the area and has not been detected since, which indicates an isolated incident due to human-assisted transportation. Events like this can occur again and can lead to the mosquito's establishment if the location is favourable (high population density and low elevation, as in Ponta Delgada).

On the southern coast, the establishment of *Ae. aegypti* is characterised by the high density of potential and actual breeding sites. Figure 8 shows the potential (red dots) and actual (pink dots) breeding sites of *Ae. aegypti* on the premises of Escola Secundária Jaime Moniz in Funchal during the 2012 transmission season.

Figure 8: Breeding sites on the premises of Escola Secundária Jaime Moniz, Funchal, 2012–2013

Ae. aegypti uses a wide variety of breeding sites (tires, plants, vases, gutters, water tanks, canvas covers, etc.); larvae have also been found in small amounts of water, for example empty beer cans and shards of brown glass.

Table 3: **Summary of vector surveillance**

	Larvae	Adults
Pre-epidemic 2005–2012	• Ovitraps since 2005, mainly in Funchal, but progressively in neighbouring municipalities • Placement of traps in a grid pattern since 2009	• BG traps checked twice a week since February 2012 (Funchal and neighbouring municipalities)
Epidemic 2012	• Grid placement of ovitraps maintained • Additional ovitraps deployed to monitor *Ae. aegypti* activity	• BG traps daily checked since October 2012
Perspectives	• Grid placement of ovitraps maintained • Re-location of the 'emergency' ovitraps to cover almost all areas favoured by the mosquito (most of the southern coast, some regions of the northern coast) and Madeira airport/harbours	• BG traps checked daily

SWOT analysis of vector surveillance

	Helpful	Harmful
Internal origin	**Strengths** • Surveillance started before outbreak • Placement of traps in a grid pattern (since 2009; trend) • Adaptability (new locations of *Ae. aegypti* establishment) • Reliable information • Commitment of population and authorities • Intersectoral activities with good collaboration at the operational level • Certain expertise available locally	**Weaknesses** • Limited human resources • No specific financial resources • Vector surveillance not identified as a specific task • No clear coordination of vector surveillance and local expertise (e.g. insecticide test) • Vector population structure (multiple introductions of the vector?)
External origin	**Opportunities** • Collaboration (DGS, experts, etc.) • For Madeira: get a coordinator with experience in dengue surveillance • For Europe: learn from Madeira (surveillance of invasive mosquitoes in Europe) • ECDC guidelines on surveillance of invasive vectors	**Threats** • Lack of sustainability (emergence of other priorities or loss of interest in the future) • Fewer complaints from citizens of Madeira • Risk of importation of new strains of *Ae. aegypti* to Madeira • Risk of exportation of *Ae. aegypti* to Europe

Vector control and responses strategies

Outline

Control activities in Madeira started in 2006. Measures included breeding site reduction campaigns and the treatment of breeding sites with *Bacillus thuringiensis israelensis* (Bti) and insecticide spraying for adult mosquitoes. Biocide treatments were performed between 2005 and 2008 (Oct 2005 to Jan 2006, May 2006 to Jan 2007, Sep to Dec 2007, April 2008, and May 2008).

In 2009–2010, WHO tests were used to estimate the susceptibility of *Ae. aegypti* to several insecticides: dichlorodiphenyltrichloroethane (DDT) 4%, malathion 5%, permethrin 0.75%, and deltamethrin 0.05%[9]. Results showed high susceptibility of the vector to malathion, intermediate resistance to deltamethrin, and high resistance to DDT and permethrin. This profile is characteristic of *Ae. aegypti* populations in the Caribbean[10]. To survey possible knockdown resistance (kdr) mutations, DNA was extracted from 35 mosquitoes previously characterised as resistant to DDT, permethrin and deltamethrin. This kdr mutation was found in only one DDT-resistant homozygote and in two permethrin-resistant heterozygotes, corresponding to 6% of the analysed mosquitoes[13]. One DDT-resistant mosquito was found homozygote for kdr mutation, and two permethrin-resistant mosquitoes were heterozygotes for the same mutation (overall corresponding to 6%). New resistance profiles assays should be conducted soon.

In October 2012, when the first cases of dengue were detected, control activities were enhanced.

•   Larvae control activities such as breeding site reduction were carried out in a more systematic way and involved additional partners (IASAÚDE, the municipality of Funchal, and the community). In addition, salt and salt water were used in water drainage to dispose of immature mosquito stages.

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[9] World Health Organization. WHO Pesticide Evaluation Scheme (WHOPES). [internet]. 2013 [cited 2013 Oct 22]. Available from: http://www.who.int/whopes/resistance/en/

[10] Seixas G. *Aedes* (Stegomyia) *aegypti* (Diptera, Culicidae) from Madeira Island: geographical origin and insecticide resistance. Master thesis. Lisbon: Instituto de Higiena e Medicina Tropical, Universidade Nova de Lisboa; 2012. 123pp.

- In November 2012, in order to reduce larvae and adult mosquitoes, pesticides were applied in one hospital, one health centre, and one school – all located in the most affected area of Funchal:
  - Outside the buildings: spraying of alpha-cypermethrin (9.86%), fogging of tetramethrin (2%), cypermethrin (10%) and piperonyl butoxide (5%) and Bti application.
  - Inside the buildings: fogging of tetramethrin (2.2%), phenothrin (4.4%) and piperonyl butoxide (9.6%)
- Door-to-door information campaigns regarding *A.e aegypti* source reduction and protection against mosquitoes bites were carried out. Flies swatters, insecticides and insect repellents were promoted at the community level.
- In December 2012, a two-year plan (2012–2014) to control dengue transmission in urban Funchal was introduced. Available from: http://www.cm-funchal.pt/todoscontraomosquito/

The following activities were conducted to prevent exportation of *Ae. aegypti* to mainland Portugal and other countries:

- Since 2005, guidance documents have been published to promote the implementation of ISR recommendations in ports and airports. Available from: http://iasaude.sras.gov-madeira.pt/mosquitos/, see 'Circulares e Comunicados'.
- On 30 October 2012, guideline documents on mosquito control measures for harbours and airports were published (elimination of possible breeding sites, aircraft disinsection according to WHO recommendations, communication on board of ships).
- Solid waste and goods transportation:
  - Waste (glass and tyres) are sent to Portugal to be treated. Old tyres are centrally collected at the solid waste treatment facility (Estação de Tratamento de Resíduos Sólidos) at Meia Serra (elevation: 1130 m), where they are shredded and then transported by vessel to Portugal (Setúbal).
  - Bananas are packed into boxes in São Martinho and transported by vessel.
  - Flowers are usually transported by aircraft.

The following documents were produced in preparation for another outbreak:

- A list of public buildings for anti-mosquito measures (to be carried out by private contractors)
- Treatment protocols to be agreed between IASAÚDE and private contractors
- SOPs for breeding site reduction

A summary of vector surveillance activities is presented in Table 4.

The following issues regarding the control of *Ae. aegypti* have been identified for Madeira:

- Access to abandoned houses (10% of the buildings visited during the door-to-door campaign); geolocation included in the geographic information system (GIS).
- Integration of GIS in vector control and response (Figure 14).
- Short-term control strategy:
  - identify efficient insecticides (insectarium; field tests needed) and authorisation to import and use them
  - improve the involvement of all affected municipalities
  - establish treatment protocols with private contractors
  - ensure that measures are implemented at airports and in airplanes.
- Mid- and long-term control strategies: comparison of various options and identification of promising solutions (expert workshop).

The following issues regarding the risk of *Ae. aegypti* importation were identified for mainland Portugal:

- Surveillance of airports where aircrafts directly arrive from an area with an established *Ae. aegypti* population
- Surveillance of location where the containers are opened that arrive from an area with an established *Ae. aegypti* population
- Identification of harbours with vessels from an area with an established *Ae. aegypti* population.

Table 4: **Summary of vector control activities**

	Larvae	Adult
Pre-epidemic 2005−2012	• Since 2006: breeding site reduction + Bti (2006−08)	• Since 2006−08: Insecticide spraying • Insecticide tests (2009)
Epidemic 2012	• Breeding sites reduction in a systematic way in the areas at risk (Municipality of Funchal/community/IASAÚDE) and around cases (IASAÚDE) • Use of salt in storm drainage • Bti: one hospital, one health centre, one school	• One run of insecticide spraying: one hospital, one health centre, one school (hot spot) • Flies swatter (community) • Insecticide/repellent (community)
Perspectives	• Test of insecticides for larval stage • SOP for breeding site reduction in function of epidemiological phase	• Test of insecticides for adult stage • Evidence for alternative strategies (*Wolbachia;* genetically modified mosquitoes)

SWOT analysis of vector control activities

	Helpful	Harmful
Internal	**Strengths** • Experienced private contractors • Commitment • Some specific expertise available locally	**Weaknesses** • No public service equipment for vector control • Public health sector had no previous experience in vector control during an outbreak • No mosquito control unit • No coordination of vector control activities • No updated information about resistance of mosquitoes to insecticides • No dedicated bodies for vector control evaluation (external evaluation)
External origin	**Opportunities** • Operational and scientific support (DGS, experts, etc.) • For Madeira: get a coordinator with experience in dengue control • For Europe: learn from Madeira (control of an invasive mosquito vector) • Workshop in Madeira with mosquito control experts	**Threats** • Lack of political will and insufficient human and economic resources • Lack of sustainability (emergence of other priorities/loss of interest) • Other diseases transmitted by *Ae. aegypti* • Complexity of the legal process for public contract with private companies • Lack of legal advice from National Health Authority about access to abandoned houses for public health emergency

6 Contingency plan

Outline

A contingency plan is a document focused on a specific risk; it anticipates what could happen and establishes operating procedures. The main objective of such a plan is to make decisions in advance about the management of human and financial resources, coordination and communication procedures, and raise awareness with regard to a range of technical and logistical responses. However, contingency plans are dynamic documents that must be tested and continually updated.

A draft proposal for a dengue contingency plan in Madeira was drawn up before the mission, based on information retrieved from IASAÚDE and DGS websites, documents sent by IASAÚDE, dengue outbreak data, documents from French Overseas Departments in the Caribbean.

A draft version was discussed and updated with stakeholders (IASAÚDE: Drs Ana Nunes, Ana Clara Silva) and Prof. Carla Sousa (see Annex 11 and 12). In particular, the organisation of an intersectoral committee, as agreed and formalised between IASAÚDE and all major partners on 30 November 2012, was discussed. The health group (hospital, health centres and laboratory) was also included with their respective tasks.

IASAÚDE organised a workshop with all partners (environment, agriculture, harbours and airports, education, tourism, and the health group) to discuss and agree on the developed draft and prepare an agenda to finalise the contingency plan.

The different phases of a dengue outbreak were discussed (Figure 9), assuming a re-emergence scenario for dengue in Madeira.

Figure 9: Example of outbreak epi curve and outbreak phases (endemic setting)
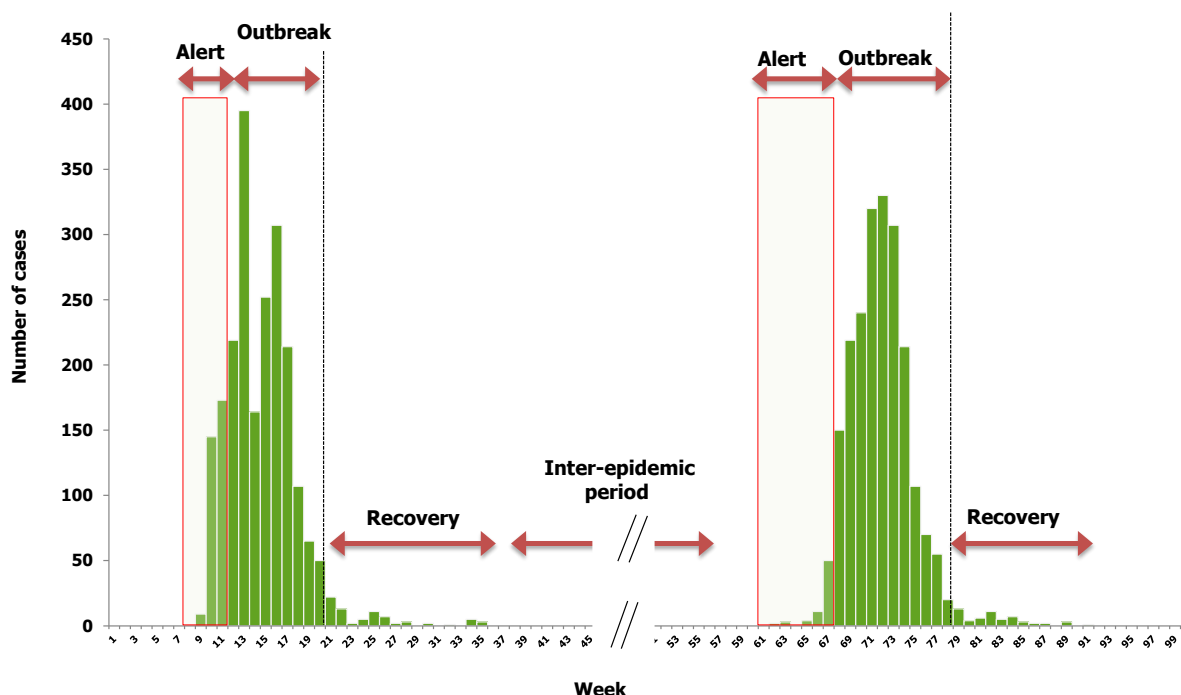
The following main features of the contingency plan were agreed upon during the workshop:

- Definition of a 'worst case' outbreak scenario:
  - New serotypes: with DENV-1 already present, new serotypes are introduced through endemic countries; worldwide worsening of the dengue situation due to favourable climatic factors (mosquito season from July to December).
  - Spread. The vector is present in most of the inhabited areas of the southern part of the island and climatic factors are favourable there.
  - Severity. With the introduction of a new serotype, people who are already infected with DENV-1 are potentially at risk to present with severe disease.
  - Vulnerable groups: entire population (except people previously infected) is vulnerable to DENV-1, including tourists.

- Objectives of the plan
    - To prevent/limit the occurrence of an outbreak of dengue in the Autonomous Region of Madeira
    - To limit the public health/socio-economic impact of an outbreak of dengue on the population (residents and visitors)
    - To prevent the exportation of *Aedes aegypti*

- Operational plan
    - Identification of the main outbreak phases and transition criteria
    - Identification of main partners and agreement on intersectoral coordination (Annex 14)
    - Identification of main tasks according to the different outbreak phases (Annex 15)

- Others topics
    - Identification of resource requirements and capacities (gap analysis)
    - Standard operating procedures
    - Simulation exercise to test and improve the contingency plan
    - How to be best prepared (capacity building, training, etc.)

SWOT analysis contingency plan

	Helpful	Harmful
Internal	**Strengths** • Intersectoral approach • Process ongoing • Capitalisation on experience • Communication • Realistic scenario	**Weaknesses** • Challenge: to be ready before the next increase of mosquitoes activity • Need to be updated every year
External	**Opportunities** • Collaboration (DGS, experts, etc.) • Example for response to an emerging vector-borne disease in Europe • Experience can be shared with areas with similar experiences (e.g. southern France)	**Threats** • Mobilization of resources and cooperation

7 Key recommendations

Recommendations for the surveillance, prevention and control of dengue in Madeira are divided into four main sections: epidemiological surveillance, contingency plan, and short- and mid-term activities for vector surveillance and control.

Epidemiological surveillance

The importation of pathogens transmitted by *Aedes aegypti* remains a probability. The presence of the vector in Madeira Island already led to the 2012–2013 dengue outbreak and shows that the area is suitable for outbreaks of other vector-borne diseases. From a public health point of view it is essential to monitor the potential re-emergence of the virus, the introduction of others serotypes, and the importation of others pathogens carried by *Ae. aegypti* (such as chikungunya virus and, to a lesser extent, yellow fever virus). The early detection of human cases of local transmission remains a key element of epidemiological surveillance in Madeira. Early case detection is also critical for a prompt and efficient response effort. An integrated geographic information system would be an important information tool for public health management and vector control activities.

People entering Madeira, particularly if they originate from regions with an ongoing dengue epidemic, should receive disease-specific information right at their port of entry. The specifics should be covered in a long-term communication plan. It should also be considered to make yellow fever vaccination mandatory for new arrivals from endemic countries.

Multi-disciplinary collaboration at the national and local level would help to implement the following actions:

- Environmental monitoring data (landscape, temperature and rainfall) and vector surveillance data should be regularly analysed to prepare for and anticipate the risk period.
- ECDC data on epidemic intelligence on dengue and other vector-borne diseases transmitted by *Ae. aegypti* should be easily accessible.
- Regular training should be implemented to ensure that healthcare professionals are able to detect even the early stages of dengue.
- Laboratory capacities: Laboratories should test all suspected cases, with a focus on imported cases; methods should include serotype identification and analysis (genotyping); the storage period for specimens should be extended to one year (for serum), so that a retrospective analysis is possible; finally, the collaboration between INSA (Portugal) and the central laboratory in Funchal should be strengthened, for example by sending pre-notifications of impending sample shipments to INSA.

Contingency plan

At the local level, the roles of all partners should be described in a contingency plan which lists all response activities necessary during an outbreak. The following recommendations focus on specific issues to be addressed in the plan.

Gap analysis and preparation

Major gaps should be addressed well ahead of the dengue transmission season. Some of the issues that should be included in a gap analysis have already been identified:

- Maintain communication activities at the community level: provide information on vector threat and vector control in order to significantly reduce vector breeding sites and subsequently control the vector population before the transmission season starts.
- Prepare communication items for outbreaks; take into account different audiences, for example medical officers on cruise ships, travellers, dengue patients.
- Evaluate electronic methods of communication such as SMS, social media (Twitter, RSS feed) and e-mail newsletters.
- Encourage the retrospective analysis and dissemination of outbreak information to local and national authorities, healthcare providers, partners, and to the public in order to keep awareness.
- Capacity building and external collaboration:
    – Provide training for severe case management in municipal healthcare centres, regardless of *Ae. aegypti* establishment.
    – Provide complementary training for biostatisticians and GIS teams.
    – Improve the detection of pathogens transmitted through *Ae. aegypti* in human samples and blood donations.

    –   Offer training on vector surveillance and control for personnel in all municipalities.
    –   Identify experts who can provide technical support and confirm findings.

Human and financial resource analysis

The analysis should be conducted for the each scenario/epidemic phase described in the contingency plan.

- All tasks should be defined, and competent staff should be available.
- Clarify coordination of vector surveillance and control activities.
- Define tasks and workload for the healthcare facilities and the vector control staff.
- Estimate costs and supplies for laboratory work.
- Identify complementary support from outside the Autonomous Region of Madeira.

Detailed tasks and standard operating procedures (SOPs)

The analysis should be conducted for each scenario/epidemic phase described in the contingency plan.

- Define activities and responsibilities of the intersectoral team in charge of the epidemic phases.
- Adapt a decision tree for patient management for hospitals and healthcare centres according to the hospital emergency plan and the epidemic phases.
- Develop SOPs/logistics for the deployment of temporary healthcare and day-care facilities.
- Develop SOPs for activities aimed at breeding site reduction.

Simulation exercise for the contingency plan

- Conduct a table-top simulation exercise.
- Consider a command-post exercise to test operational aspects of the contingency plan.

Vector surveillance and control and risk of vector-borne diseases

There is a significant risk that *Ae. aegypti* will be introduced through the shipping of goods or incoming travellers. Hence, the flux from endemic areas to Madeira and the flux from Madeira to mainland Portugal and other EU countries should be evaluated in detail. Complementary activities could cover:

- enhanced surveillance of airports which have direct flights to or from Madeira, of harbours and ports, but also in places where containers are closed or opened;
- surveillance of the vector population to detect the multiple introduction of *Ae. aegypti* and assess the genetic structure of mosquitoes population;
- and the identification of relevant vector control strategies (short- and medium-term) in order to reduce the probability of emergence and the impact of vector-borne diseases.

General recommendations are presented below:

Short-term actions

- Organise a workshop in Madeira with vector control experts to identify accurate mid- and long-term strategies and support a rapid decision process for vector control.
- Find a coordinator with experience in dengue surveillance and control to organise and coordinate the surveillance and control of mosquito vectors.
- Integrate epidemiological and entomological information to analyse the typology of the main affected area (analyse potential evolution into vector-suitable areas) and inform surveillance and control activities (see Figure 14 and Annex 9). A detailed spatial analysis would be helpful to delineate vector habitat suitability and seasonality drivers.
- Redefine vector surveillance activities under Scenario 3 of the 'Guidelines for the surveillance of invasive mosquitoes in Europe'[11]:
  - Reset traps placed during the outbreak in order to cover almost all areas favourable to *Ae. aegypti* establishment and strategic settings (airport, harbour).
  - Define a clear strategy for timely vector control (private contractors, equipment purchases, etc.).
- Recruit expertise for insecticide testing.
- Monitor the utilisation of the dengue hotline *Saúde24*: 808 24 24 24 (number of calls per day and location as well as topic, e.g. *Ae. aegypti* presence, nuisance report, etc.)
- Update information on insecticide resistance in *Ae. aegypti* (perform insecticide tests in Madeira, both for the larval and adult stages).

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[11] http://ecdc.europa.eu/en/publications/publications/ter-mosquito-surveillance-guidelines.pdf

Medium-term actions

- Implement entomological surveillance in a sustainable way to ensure the accurate analysis and monitoring of mosquito distribution, support early detection and risk assessment, and evaluate the impact of vector control measures.
- Monitor insecticide resistance of the local *Ae. aegypti* population.
- Encourage applied research projects to monitor the impact of vector control measures, e.g. modifications to buildings (such as screen doors and windows) or piloting innovative field studies.
- Identify main issues to be addressed in order to develop a mid- and long-term strategy to control diseases transmitted by *Ae. aegypti*.
- Identify and evaluate the different strategies for the long-term control of *Ae. aegypti*. Innovative approaches, e.g. the release of *Wolbachia*-infected mosquitoes and genetically modified mosquitoes, should be considered.
- Reinforce collaboration and benefit from lessons learnt and experiences from other vector control initiatives.
- Other European countries should take advantage of the lessons learnt in Madeira to limit the impact of possible outbreaks by identifying long-term vector control strategies.

References

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[7] Bivand RS, Pebesma E, Gómez-Rubio V. Applied spatial data analysis with R. UseR! Series. 2nd edition. Heidelberg: Springer; 2013)

Annex 1. Summary of ECDC team activities

At the request of the health authorities of Portugal and the Autonomous Region of Madeira, an ECDC team stayed in Maderia from 10 March 2013 to 16 March 2013, with a final meeting in Lisbon on 17 March 2013.

The ECDC mission team collaborated with the IASAÚDE, IP-RAM staff, and the public health authority of the Autonomous Region of Madeira.

ECDC team: Bertrand Sudre, environmental determinants of infectious disease; Laurence Marrama, emerging and vector-borne diseases; Joana Vaz, trainee, microbiology section.

Activities were focused on:

- data management of the outbreak, including clinical, laboratory and GIS data; introduction of an automatic system for timely analysis of epidemiological features of the outbreak, and capacity building of the local team;
- entomological situation and vector control activities: evaluation and support for the best evidence-based strategy for vector control activities and proposals for vector monitoring;
- planning technical, logistic and normative aspects;
- collaboration on the response plan and vector control activities;
- intersectoral approach with other stakeholders in Madeira; and
- collaboration on the integrated response plan with expert consultations and input from ECDC experts.

Annex 2. Key stakeholder meetings

General Directorate for Health (Lisbon)

Director of the Department of Disease Prevention and Health Promotion: Ana Leça; Head of Division for European Affairs and International Cooperation: Paula Vasconcelos; Public Health Emergencies Unit (UESP): Cristina Abreu Santos; Biocide expert: Cesaltina Ramos; National Institute of Health (INSA): Dr Ricardo Jorge; Centro de Estudos de Vectores e Doenças Infecciosas: Maria João Alves.

IASAÚDE, IP-RAM

President: Ana Nunes; Vice President: Ana Clara Silva; Coordinator of Sanitary Engineering Unit: Dores Vacas; Technicians/biostatisticians and GIS experts: Catarina Valente, Márcia Baptista, Marco Magalhães, Margarida Clairouin, Luís Antunes, Duarte Araújo; Coordinator of the Information System Unit: João César; Cabinet Counsellor: Marta Gouveia; health delegate of the Funchal municipality: Maurício Melim; health delegate of the Santa Cruz municipality: Alice Romão.

SESARAM, E.P.E.

Advisor of the Clinical Board and Director of the Emergency Unit: Pedro Ramos; Advisor of the Clinical Board and Coordinator of Primary Healthcare: João Araújo; Coordinator of the Infectious Disease Unit: Ana Paula Reis; Director of the Pathology Unit: Graça Andrade; Director of the Blood Safety Unit: José Bruno Freitas; Director of the Nursing Board: Maria Conceição Vieira; Head of the ICT service: João Abreu.

Stakeholders and policymakers

Regional Secretary for Social Affairs: Francisco Ramos; Regional Secretary for Culture, Tourism and Transport: Conceição Estudante; Regional Secretary for Environmental Affairs and Events of Nature: Manuel Correia; Regional Director of Tourism and President of the Madeira Promotion Bureau: Bruno Freitas; Regional Director of Agriculture and Rural Development: Bernardo Araújo; Regional Director of Environment: João Correia.

Annex 3. Daily schedule and main activities

Day	Activities undertaken
Monday, 11 March 2013	09:00 - Welcome from Director and Vice Director of IASAÚDE, Ana Nunes and Ana Clara Silva
	10:00 – Tour de table and mission objectives presentation (Ana Clara Silva, Dores Vacas, Luis Antunes, Marco Magalhaes, Carla Sousa, Margarida Clairouin, Laurence Marrama, Bertrand Sudre and Joana Vaz)
	11:00 – Presentation of coordination (command and control) structure in the Autonomous Region of Madeira (Ana Clara Silva, Laurence Marrama, Bertrand Sudre, Joana Vaz, Carla Sousa and Dores Vacas)
	12:00 to 13:00 – Discussion; overview of patients flow in the health system and clinical management: conclusions, lessons, questions. Discussion about retrospective study of clinical characteristics of cases and a sero-survey. (Pedro Ramos, Maria da Luz Reis, Joao Araujo, Pedro Freitas, Graca Andrade, Ana Clara Silva, Ana Nunes, Dores Vacas, Carla Sousa , Laurence Marrama, Bertrand Sudre and Joana Vaz)
	14:30 to 16:00 – Geographical system and analysis discussion (Bertrand Sudre, Laurence Marrama, Luis Antunes , Carla Sousa and Marco Magalhaes)
	15:00 to 18:00 – Overview of vector control activities (Laurence Marrama and Carla Sousa)
	16:00 to 17:00 – Visit to the hospital laboratory and meeting with Graca Andrade (Joana Vaz)
	18:00 to 19:00 – Overview of contingency plan main topics (Ana Clara Silva, Ana Nunes , Carla Sousa, Laurence Marrama, Bertrand Sudre and Joana Vaz)
Tuesday, 12 March 2013	09:00 – Review of the laboratory and blood safety questionnaire (Bertrand Sudre and Joana Vaz)
	11:00 – Presentation of the school project for vector control (Luis Antunes, Carla Sousa and Laurence Marrama)
	10:30 to 13:00 – Meeting with Dr Bruno Freitas at the blood bank (Bertrand Sudre and Joana Vaz)
	12:00 – Visit to the meteorological centre (Laurence Marrama and Carla Sousa)
	14:00 to 18:30 – Field visit Funchal and Madeira to assess the environmental profile (Laurence Marrama and Carla Sousa)
	14:00 to 18:00 – Synthesis of biological results of the dengue outbreak and data management issues. Data checking and analysis (Bertrand Sudre and Joana Vaz)
	18:00 to 19:30 – Debriefing: Ana Clara Silva, Dr Ana Nunes, Dr Bertrand Sudre and Joana Vaz with the following topics: integration of laboratory results in the follow-up of an outbreak, review of blood donation results, improved laboratory confirmation and formalisation of SOPs on suspicion of dengue among returning travellers with dengue symptoms, planning of meeting between IASAÚDE and tourism sector, discussion about the concept of 'risk = vulnerability x hazard' for dengue in the Madeira setting.
Wednesday, 13 March 2013	9:00 to 10:00 – Meeting to review proposal for contingency plan to be presented in the afternoon (Laurence Marrama, Bertrand Sudre, Joana Vaz and Carla Sousa)
	10:00 to 13:00 – Meeting with director of clinical pathology laboratory (Main hospital Funchal; Graca Andrade) to clarify remaining questions; laboratory database extraction (Bertrand Sudre and Joana Vaz)
	11:00 to 12:00 – Meeting with municipality; vector control activities (Laurence Marrama)
	14:30 – Teleconference with DGS (Cristina Abreu Santos, Ana Leca, Isabel Falcao, Cesaltina Ramos, Paula Vasconcelos), ECDC (Herve Zeller, Josep Jansa), IASAÚDE Ana Clara Silva Ana Nunes)
	15:00 – Intersectoral meeting to present and discuss the proposed contingency plan framework (Dr Gil Camacho, Eng. Manuel Ara Oliveira, Dr Marcos Teixeira, Dr Gonçalo Olim, Dr Graca Andrade, Dr Pedro Ramos, Ana Clara Silva , CS, Bertrand Sudre, Laurence Marrama, and Joana Vaz)
	16:00 to 18:00 – Exploratory analysis of epidemiological data; data quality issues (Bertrand Sudre)
	16:30 – Review of entomological surveillance activities (Laurence Marrama and Carla Sousa)
	17:30 to 19:30 – Summary of the daily activities and planning of next day (all)
Thursday, 14 March 2013	8:00 to 10:00 – Overview of the vector surveillance and discussion about long-term vector control strategies (Laurence Marrama, Bertrand Sudre and Carla Sousa)
	9:00 to 10:00 – Overview of the activities during the outbreak (Bertrand Sudre and Ana Clara Silva)
	11:00 to 13:00 – Meeting in the blood bank and dataset for RT-PCR positive cases created. (Bruno

Day	Activities undertaken
	Freitas and Joana Vaz)
	10:30 to 12:30 – Preparation of mission de-briefing in Madeira and DGS, Lisbon (all); SWAT analysis
	14:30 to 16:30 – Presentation of SWAT analysis to IASAÚDE; contingency plan and integration of scenario; review of the topic for the DGS meeting, Lisbon (all)
	17:00 to 19:00: Epidemiological analysis, guidance to biostatisticians and GIS experts for further analysis
	17:30 to 18:30 – Discussion about control measures to prevent exportation of *Ae. aegypti* from Madeira and long-term strategy for vector control (Laurence Marrama and Ana Clara Silva)
	18:30 to 20:00 – Preparation of mission documents (all)
Friday, 15 March 2013	10:15 – Flight to Lisbon
	15:00 to 18:00 – Debriefing at DGS; SWOT analysis and summary of main activities (Paula Vasconcelos, Ana Leca, Cristina Abreu Santos, Isabel Falcao, Cesaltina Ramos, Maria Joao Alves, Maria Sofia Nuncio, Kamal Mansinho, Isabel Castelao, Isabel Pires, Sofia Ferreira, Carla Sousa , Bertrand Sudre, Laurence Marrama and Joana Vaz).

Annex 4. Temperature profile in Funchal

The figure below shows the daily mean temperature and long-term trend combined with a seasonal component derived from a time series analysis of daily temperatures in Funchal (January 1999 to December 2012). According to the time series decomposition, there is a small temperature increase in the long-term trend and a marked seasonality in temperature patterns, which justifies higher vigilance against mosquitoes between July and October. The brown arrows in Figure 10 indicate anomalies (higher-than-normal temperatures) for 2012, but also for 2003 and 2004.

Madeira has a rainy season in late summer, leading to a significant increase in the number of breeding sites (field observation, first mission). However, late spring can also be characterised by frequent rainfall, and even if temperatures are usually lower than in summer, vector surveillance data show that the vector population can temporarily increase during this period (data not shown).

Figure 10: **Daily mean temperature and long-term trend combined with seasonal component of time series analysis of daily temperature in Funchal, January 1999 to December 2012**
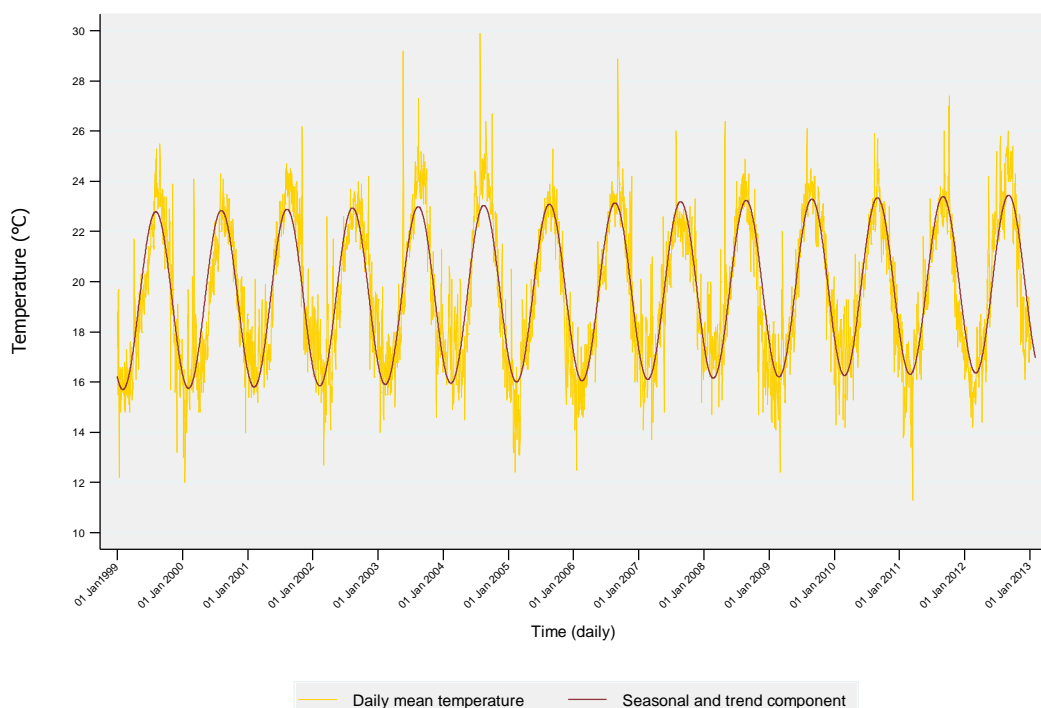
Annex 5. Laboratory confirmation, National Institute of Health, Portugal

Figure 11: **Flow chart of laboratory confirmation of dengue at INSA**
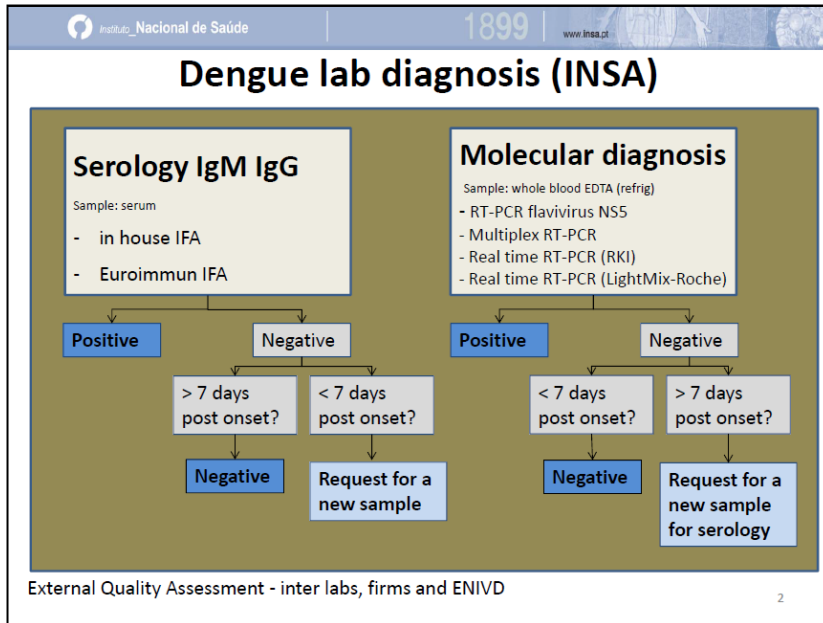
Source: National Institute of Health, Dr Ricardo Jorge; Centro de Estudos de Vectores e Doenças Infecciosas, Dr Maria João Alves.

Annex 6. Statistical methods

To investigate whether a probable case of dengue (residence location) is randomly distributed over space and/or time, the free software *SaTScan*™ was used (http://www.satscan.org). A space–time scan analysis was conducted for three municipalities together (Funchal, Câmara de Lobos and Santa Cruz). The spatial unit corresponded to the lowest unit for the last population census (Base Cartográfica dos Censos (BGRI 2011); for more information, please refer to: http://www.ine.pt/xportal/xmain?xpid=INE&xpgid=censos2011_asp_org_cartografia).

The geographical data analyses and thematic mapping were performed with the open source geographic information system (GIS) *Quantum GIS 1.8* (http://www.qgis.org), notably the geolocation of probable cases and the subsequent spatial aggregation at block level (Subsecção Estatística). Spatial analysis and thematic outputs were performed with *Quantum GIS* in close collaboration with IASAÚDE, IP-RAM. The standardised incidence ratio was calculated with the free software environment *R for Statistical Computing* (http://www.r-project.org), following Bivand et al. [7] and using an indirect standardisation method.

The time series decomposition (extraction of seasonal component and anomalies) was conducted with the Time Series Tool support by ECDC under STATA 12 (data period: January 1999 to December 2012).

Annex 7. Population density in 2011, Madeira

Figure 12: **Population density, Madeira Island, 2011**

Source: Censos 2011, Base Cartográfica dos Censos (BGRI 2011); discretisation method: natural breaks (Jenks); map projection: EPSG:3061– Porto Santo/UTM zone 28N; software: Quantum GIS 1.8; map reference: ECDC_Pop_Density_Madeira.

Annex 8. Estimated population dengue immunity in Funchal

Figure 13: Simulation of dengue population immunity in Funchal municipality
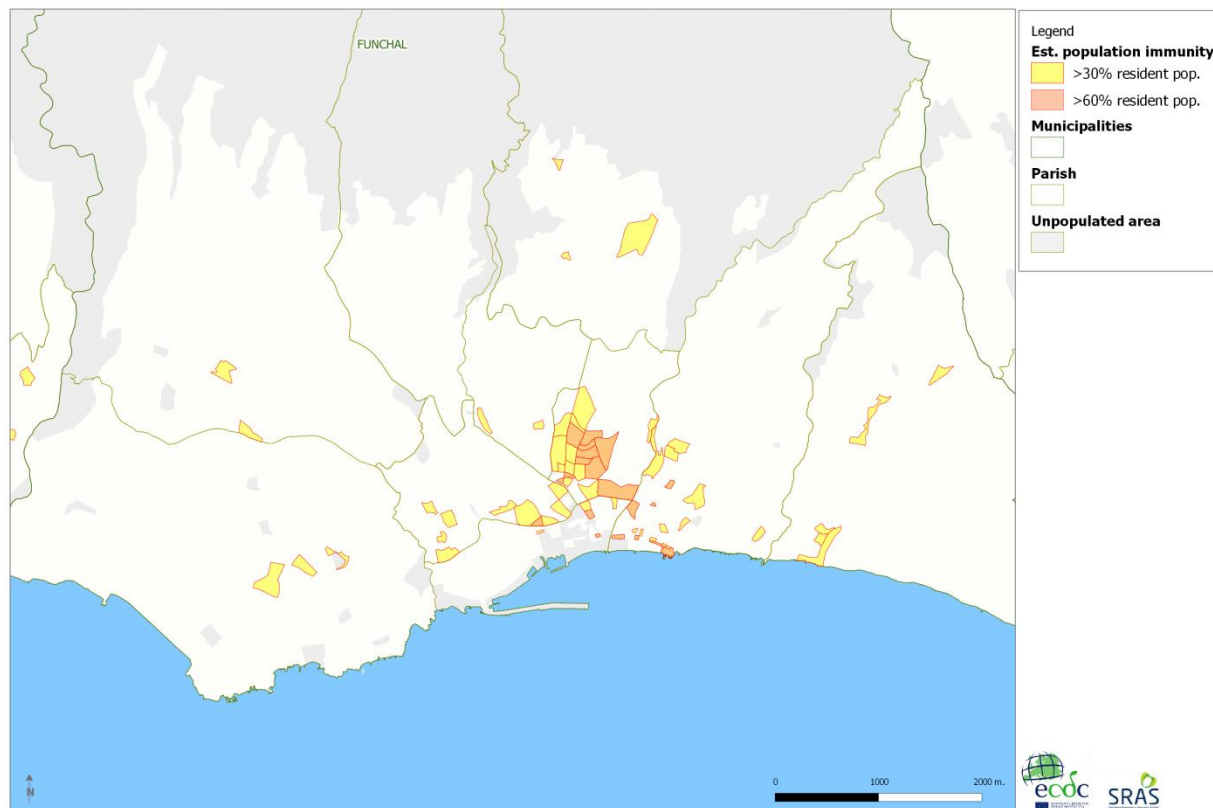
Source: IASAUDE/ECDC; population data: Censos 2011, Base Cartográfica dos Censos (BGRI 2011); dengue population immunity scenario based one geolocation of place of residence; ratio symtomatic/asymptomatic: 20/80; map projection: EPSG:3061 – Porto Santo/UTM zone 28N; software: Quantum GIS 1.8; map reference: ECDC_Pop_Immunity_Madeira.

The figure above represents the estimated percentage of immunity in the resident population based on the geolocation of probable cases and the symtomatic/asymptomatic ratio (20:80).

Annex 9. Example of GIS application

Figure 14: **Standardised incidence ratio of dengue cases (probable and confirmed), by block of residence and secondary cluster (Number 3)**
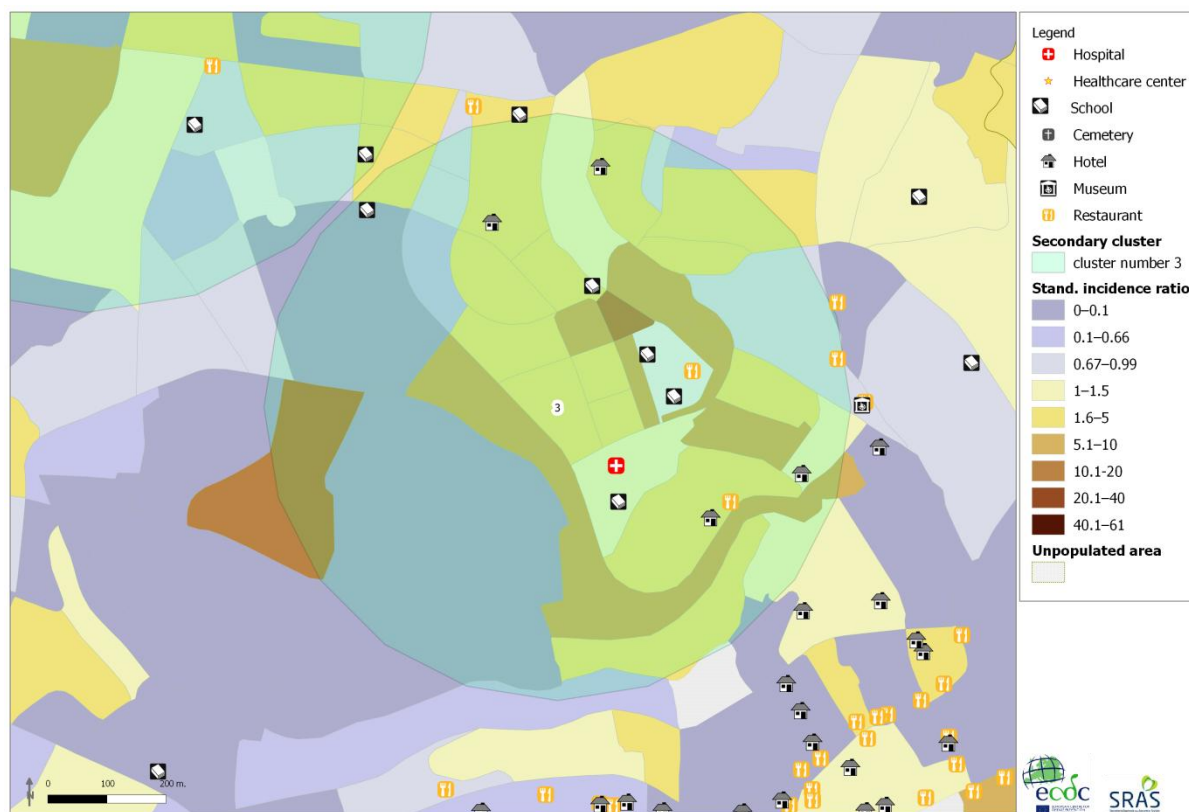
Source: IASAUDE/ECDC; discretisation method: pretty breaks; scale: 1/5000; map projection: EPSG:3061- Porto Santo/UTM zone 28N; software: Quantum GIS 1.8; map reference: ECDC_GIS_example_Madeira.

The above map demonstrates the potential of GIS for the operational responses during a vector-borne disease outbreak in Madeira. (Please note that this figure is for illustration purposes only and only uses a subset of data).

The map facilitates various aspects of vector bite prevention (e.g. the distribution of posters or leaflets in restaurants, hotels, museums; community awareness measures through door-to-door campaigns) and active vector control at potential places of exposure (e.g. disinsection of hotels, restaurants and schools).

Please note that the geolocation of cases is aggregated to the lowest administrative level in order to protect privacy and confidentiality. However, geolocation of vector-borne disease (place of residence and/or place of work) can be used for a cluster analysis by the health authorities and combined with vector surveillance data (e.g. geotagged breeding sites) to define areas of intervention during an outbreak.

Newly detected cases of vector-borne disease should be analysed by taking into account not only vector surveillance data but also features such as water drainage systems, water reservoirs, vegetation, agricultural use (e.g. banana plants) and parks in order to optimise field interventions.

Annex 10. Blood donor population characteristics

Donor population characteristics

- Population size (N): around 267 000
- Cumulative infections reported (Ip): 2168
- Duration of epidemic (D): 122 days
- Duration of infectivity for acute (Ta) infection: 5 days
- Proportion of chronic infection (%C): 0%
- Proportion of undetected cases (%U): 60%
- Donor relative risk (RR): 100%
- Prevalence of infection in the donor population (Pd): 82.73 per 100 000.

Around 6000 blood donations were collected in 2012, with about 2500 regular donors and 400 new donors. This means that on average each donor donates blood 3.5 times a year (men can donate every three months and women every four months).

The average number of donors per month is 400–500, and the number of deferred donors was 591. The male-female ration among donors is 3:1. The age structure is given in Table 5.

Blood donors gain an additional two vacation days per donation, which might be a strong incentive to donate blood.

The software used to store blood donors' details at Dr Nélio Mendonça Hospital does not allow the extraction of datasets which correlate a donor's age group and the geographical location of their residence. According to information from the blood bank, donors are geographically distributed across the entire island.

Table 5: **Age structure of blood donors, Autonomous Region of Madeira, 2012**

Age group	Percentage
18–25	7.1
26–35	20.8
36–45	30.8
46–55	26.1
56–66	13.2

Source: Blood bank, Dr Nélio Mendonça Hospital, Funchal, Autonomous Region of Madeira

Annex 11. Outline of a vector-borne disease contingency plan

The introductory section of should briefly present the rationale behind the contingency plan and present its objectives: integrated surveillance and response framework. The outline below is based on a vector-borne disease outbreak (notably dengue).

Section 1: Background information and analysis of the situation

- Health: epidemiology (time – place – person; clinical presentation/immunity); case management (clinical, laboratory, blood safety issues)
- Virus: dengue serotype
- Vector: spatial distribution, genetic studies, insecticide resistance

Section 2: Scenarios

- Health: immunity (naïve and immune population; population in areas with confirmed vector presence)
- Virus: re-emergence and circulation in inter-epidemic period/re-introduction of identical or different serotypes
- Vector: scenario of mosquito activities (climate, vector typology, background information from vector network surveillance)

Section 3: Strategies and key activities in function of scenarios and epidemics phases

Elements for scenarios

- Low mosquito activity AND low number of human cases (limited outbreak)
- High mosquito activity AND high number of cases (large outbreak)
- Early re-emergence during late spring versus mid-summer emergence
- Geographical extent: Funchal and/or other municipalities
- Epidemic phases

Activities: include all stakeholders in the scenario planning to ensure their involvement

- Health system activities (preparedness and response)
- Integrated vector management: control activities (adult, larvae); list and procedure for ordering insecticides and EU derogations.
- Plan of implementation: workflow of actions and activities matrix
- Gap analysis
- Synthesis: scenario versus i) indicator, ii) prevention and control activities, iii) surveillance activities, iv) budget.

Section 4: Multisectoral key partners, tasks and responsibilities

- Coordination and intersectoral mechanisms for collaboration on vector control interventions and their coordination
- Tasks and responsibilities by partners (focal points, key actors)
- Description of interactions between administrative entities and operational levels
- Financial support: assessment conducted by the intersectoral committee (financial planning)

Section 5: Communication strategy

- Communication plan for various scenarios (local/national authorities and international partners)

Section 6: Monitoring

- Prior to outbreak: simulation exercise (table-top exercise, e.g. emergence of ten new case with items to be evaluated during the exercise: alert procedure, field coordination of initial intervention, laboratory confirmation, local and national workflow, blood bank quarantine, etc.)
- During an outbreak: tools should already be in place (objective indicators: SMART)
- Conduct an external review after an outbreak
- Research to monitor impact of intervention might be considered in the specific context of Madeira.
- Budget monitoring (for further cost–benefit analysis)

Conclusions

Annexes

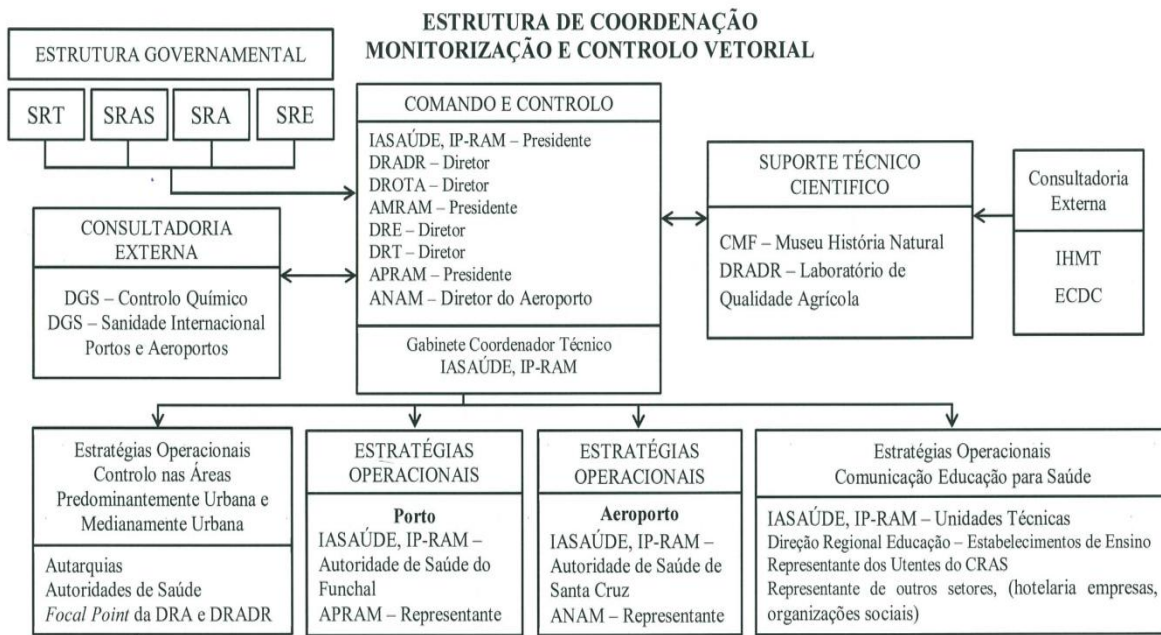Scenarios; involved sectors: key stakeholders with main competences and responsibilities; organisational chart of sectors involved in the intersectoral committee; contact list; capacity and resource assessment versus scenarios; technical standard operational procedure by activities (check list, flow chart, objectives/tasks/indicators, focal points and contacts details, schedule for reporting of activities [diffusion list]).

Annex 12. Main activities and products developed in the communication plan during the outbreak

Activities	Quantity
Community health education sessions	49
Community services health education sessions	18
Sessions for health professionals (at health centres)	48
Radio programmes	1
Radio spots	11 spots: 21 daily broadcasts over seven different local radio stations (since 6 November 2012)
TV spots	Three daily broadcasts (since 11 October 2012)
Intersectoral information distribution (letters, emails, informative bulletins, faxes, technical guidelines)	485

Type	Designation	Quantity
Pamphlet	Medidas de prevenção nas doenças transmitidas por mosquitos – Measures to prevent mosquito-transmitted diseases	11.557
Poster	Medidas de prevenção nas doenças transmitidas por mosquitos – Measures to prevent mosquito-transmitted diseases	234
Flyer	Recomendações a viajantes – Recommendations for travellers (in Portuguese and English)	1.200
Pamphlet	Recommendations for travellers (multilingual) [at points of entry]	2.600
Flyer	Recomendações a viajantes (multilingual) [at points of departure]	3.700
Flyer	Recommendations for travellers (in Russian and Chinese)	242
Flyer	Saiba distinguir sintomas de uma gripe sazonal e da dengue – Know who to distinguish seasonal flu symptoms from dengue	2.965
Poster	Saiba distinguir sintomas de uma gripe sazonal e da dengue – Know who to distinguish seasonal flu symptoms from dengue	12
Poster	Eliminar o mosquito *Aedes aegypti* e controlar a dengue depende de todos – Mosquito control and dengue prevention depends on all of us	366
Poster	Dengue: principais sintomas. O que fazer? (Dengue: main symptoms. What to do?)	210
Pamphlet	Eliminar o mosquito *Aedes aegypti* e controlar a dengue depende de todos – Mosquito control and dengue prevention depends on all of us	7.375
Flyer	Eliminar o mosquito *Aedes aegypti* e controlar a dengue depende de todos – Mosquito control and dengue prevention depends on all of us	5.000
Pamphlet	Inventário – criadouros de mosquitos *Aedes aegypti* – Overview: breeding sites of *Aedes aegypti*)	12.466

Annex 13. Sectors involved in the intersectoral committee

ESTRUTURA DE COORDENAÇÃO MONITORIZAÇÃO E CONTROLO VETORIAL

ESTRUTURA GOVERNAMENTAL

SRT | SRAS | SRA | SRE

COMANDO E CONTROLO
- IASAÚDE, IP-RAM – Presidente
- DRADR – Diretor
- DROTA – Diretor
- AMRAM – Presidente
- DRE – Diretor
- DRT – Diretor
- APRAM – Presidente
- ANAM – Diretor do Aeroporto

Gabinete Coordenador Técnico
IASAÚDE, IP-RAM

CONSULTADORIA EXTERNA
- DGS – Controlo Químico
- DGS – Sanidade Internacional Portos e Aeroportos

SUPORTE TÉCNICO CIENTIFICO
- CMF – Museu História Natural
- DRADR – Laboratório de Qualidade Agrícola

Consultadoria Externa
- IHMT
- ECDC

Estratégias Operacionais Controlo nas Áreas Predominantemente Urbana e Medianamente Urbana
- Autarquias
- Autoridades de Saúde
- *Focal Point* da DRA e DRADR

ESTRATÉGIAS OPERACIONAIS
Porto
- IASAÚDE, IP-RAM – Autoridade de Saúde do Funchal
- APRAM – Representante

ESTRATÉGIAS OPERACIONAIS
Aeroporto
- IASAÚDE, IP-RAM – Autoridade de Saúde de Santa Cruz
- ANAM – Representante

Estratégias Operacionais Comunicação Educação para Saúde
- IASAÚDE, IP-RAM – Unidades Técnicas
- Direção Regional Educação – Estabelecimentos de Ensino
- Representante dos Utentes do CRAS
- Representante de outros setores, (hotelaria empresas, organizações sociais)

Siglas:
- AMRAM – Associação de Municípios da RAM
- ANAM – Aeroportos e Navegação Aérea da Madeira
- APRAM – Administração dos Portos da Região Autónoma da Madeira, SA
- DGS – Direção-Geral da Saúde
- DROTA – Direção Regional do Ordenamento do Território e Ambiente
- DRADR – Direção Regional de Agricultura e Desenvolvimento Rural
- DRE – Direção Regional de Educação
- DRT – Direção Regional do Turismo

- ECDC – European Centre for Disease Prevention and Control
- CMF – Câmara Municipal do Funchal
- CRAS – Conselho Regional dos Assuntos Sociais
- IASAÚDE, IP-RAM – Instituto de Administração da Saúde e Assuntos Socias, IP-RAM
- UES – Unidade de Engenharia Sanitária
- IHMT – Instituto de Higiene e Medicina Tropical
- SRT – Secretaria Regional da Cultura Turismo e Transportes
- SRA – Secretaria Regional do Ambiente e Recursos Naturais
- SRE – Secretaria Regional da Educação e Recursos Humanos

Annex 14. Contingency plan – identification of the main phases and transition criteria

Phases	Description	Indicators	Activities
Inter-epidemic phase	• Absence of cases • Sporadic cases • Small clusters of cases • No evidence of spread of the disease	• No. of probable cases • No. of confirmed cases low • % positive tests low • No. of hospitalisations low • No spread around clusters • No new serotype	• Actions to be prepared ahead of time Identification and investigation of: • all confirmed cases; • clusters of probable cases. • Early vector control in affected areas
Epidemic alert phase	Signs of worsening of the situation	• No. of probable cases ↗ • No. of confirmed case ↗ • % positive tests ↗ • No. of hospitalisations ↗ • No spread in clusters • New serotype detected • Favourable weather conditions	• Identification and investigation of all cases and clusters • Vector control in the affected area • Serotype analysis for all cases • Communication about prevention and clinical signs • Communication on next steps
Onset of the outbreak phase (transition)		Increased transmission/spread of the disease for two weeks in a row	Declaration of an outbreak
Outbreak phase	Occurrence of an outbreak	• No. of probable cases high • No. of confirmed case high • % positive tests ≥ 10% of probable cases • No. of hospitalisations high • Spread around clusters • New serotype detected	Confirmation of: • 10% of ambulatory cases • 100% of hospitalised cases • 100% of imported cases • Vector control in the affected area • Communication about prevention and signs
End of the acute outbreak phase (transition)		No. probable cases ↘ for three successive weeks (/ < 20) Hospitalisations ↘ Transmission ↘	Declaration of the end of the outbreak

Annex 15. Contingency plan – identification of main tasks by phase

Phases	Activities: Clinical management and epidemiological surveillance	Activities: Vector surveillance
Pre-/inter-outbreak phase	• Identify and investigate all probable cases in a laboratory setting • Study and geographically delimit all clusters • Compare the standards of clinical and laboratory-confirmed cases with sporadic cases found from a retrospective study • Weekly monitoring of international epidemic intelligence for dengue (e.g. CDTR, dengue health map) • Serotyping of all imported suspected cases and protection measures against mosquito bites • Investigate all unconfirmed cases • Review the algorithms and protocols in the health units for dengue cases • Review the emergency plan for hospitals for dengue fever (attack rate and scenarios, percentage of hospitalisation and severe cases) • Training and updating of professionals for the clinical management of dengue, in particular for the management of severe cases and complications • Alert doctors and nurses of vector activity and dengue • Estimate population immunity by using the blood donor database, georeferencing dengue cases, and calculating the ratio of asymptomatic cases • Revise allocation of human resources in health centres dedicated to dengue case treatment and follow-up • Continue with the screening of blood donors • Implement the European Risk Assessment Tool to model the potential risk associated with blood donations	• Network maintenance (vector surveillance for immature and adult mosquitoes) • Relocation of ovitraps ('emergency ovitrap') in order to better understand vector distribution • Maintain vector surveillance at all points of entry/departure: harbours, airports, container terminals • Conduct entomological research • Assess resistance in the larval and adult stages of the mosquito (testing of larvicides and insecticides) • Testing the effectiveness of disinsecting • Intersectoral coordination: ensure the implementation of the various activities to prevent and control the vector, through the structure of • Align the flow of information to intersectoral coordination • Strengthen partnerships in social mobilisation campaigns against the vector (breeding reduction) • Encourage the establishment of a vector surveillance network around high-density settings (hotels, other lodging, company grounds) • Ensure data sharing • Continue with the development of the various sectoral plans for vector prevention and control • Develop a joint measures approach to diminish high vulnerability (empty houses, vacant land, buildings for demolition, etc.) • Maintain links with international structures for the study of alternative and long-term strategies for mosquito control
Outbreak alert phase	• Identify, investigate and confirm all probable cases • Study and geographically delimit all cases and clusters (home, work, and travel) • Ensure serotyping of all investigated cases • Strengthen guidance, protection and information of confirmed cases • Produce and disseminate guidance for treatment/hospitalisation and follow-up of severe cases • Increase activities in health education and social mobilisation (detect signs of illness and complications)	• Implement early vector control measures in the affected areas • Promote community participation in activities to reduce breeding sites at home and in peridomestic areas • Delimit the size for implementation of control measures • Maintain and enhance partnership activities for awareness and environmental sanitation • Maintain and enhance partnership activities for environmental sanitation, inspection; evaluate communication channels to the community in general
Outbreak phase	• Follow and update algorithms for clinical management • Disseminate standardised guidelines and updates for the entire healthcare network • Confirm 10% of all probable cases • Check 100% of all hospitalised cases • Introduce serotyping to confirm all severe cases • Ensure the flow of information and the monitoring of the epidemic curve	• Vector control measures in the affected areas • Promote community participation in all activities to reduce breeding site number at home and peridomestic areas • Maintain and enhance partnership activities in measures of environmental sanitation, • Inspection and survey information • Communication to the various sectors on the entomological situation

Annex 16: Possible approaches to *Ae. aegypti* control in combination with the implemented strategies

The release of *Wolbachia*-infected mosquitoes would significantly reduce the transmission of dengue virus. The infection of the mosquito population by *Wolbachia* would not modify the mosquito's population dynamic but strongly reduce the dengue transmission to humans. This approach can be very successful in tropical dengue-endemic countries where the overall eradication of the vector is difficult.

Several scientific research projects are currently focusing on the reduction of the mosquito population by releasing non-biting male mosquitoes. The application of the Sterile Insect Technique (SIT) calls for the sterilisation (chemosterilisation or ionizing radiation) of insect. RIDL (release of insects carrying a dominant lethal technology) genetically modifies mosquito strains, which are then released. Through RIDL, non-sterile males pass on a genetic defect which kills female offspring before they reach maturity.

Sterilisation by irradiation remains the most frequently used method.

Annex 17. Web links of interest

Direção-Geral da Saúde (DGS): www.dgs.pt

Instituto de Administração da Saúde e Assuntos Sociais (IASAÚDE, IP-RAM): http://IASAÚDE,IP-RAM.sras.gov-madeira.pt/

World Health Organization: http://www.who.int/topics/dengue/en/

Dengue haemorrhagic fever: diagnosis, treatment, prevention and control. 2nd edition. Geneva: World Health Organization; 1997. Available from:
http://www.who.int/csr/resources/publications/dengue/Denguepublication/en/print.html

Manual for Indoor Residual Spraying: Application of Residual Sprays for Vector Control:
http://www.paho.org/English/AD/DPC/CD/mal-who-insecticide-manual.htm

Guidelines for Integrated Vector Management: http://www.afro.who.int/vbc/framework-guidelines/guide_integrated_vector_management.pdf

Planning Social Mobilization and Communication for Dengue Fever Prevention and Control: A Step-by-Step Guide:
http://www.who.int/tdr/publications/publications/pdf/planning_dengue.pdf

Dengue haemorrhagic fever: early recognition, diagnosis and hospital management. An audiovisual guide for healthcare workers responding to outbreaks:
Video http://terrance.who.int:85/streaming/dhf.wmv
DHF video transcript http://www.who.int/csr/don/archive/disease/dengue_fever/dengue.pdf

Residual spraying on surfaces, many options possible according to WHO guidelines (p. 30):
http://whqlibdoc.who.int/hq/2006/WHO_CDS_NTD_WHOPES_GCDPP_2006.1_eng.pdf

Aerial spraying: http://www.who.int/whopes/Insecticides_for_space_spraying_Jul_2012.pdf ; see also
http://whqlibdoc.who.int/publications/2009/9789241547871_eng.pdf

ECDC: http://ecdc.europa.eu/en/Pages/home.aspx

Guidelines for the surveillance of invasive mosquitoes in Europe:
http://www.ecdc.europa.eu/en/publications/Publications/TER-Mosquito-surveillance-guidelines.pdf