Introduction

Malaria is a parasitic infection, transmitted through the bite of the infected female Anopheles mosquito. Five types of plasmodia cause disease to humans: Plasmodium falciparum, Plasmodium vivax, Plasmodium ovale, Plasmodium malariae and Plasmodium knowlesi. The most common symptoms of malaria (chills, high fever, sweating, malaise, headache and muscle aches) manifest 1-4 weeks after infection with the parasite, while relapses of the disease are usually observed in short intervals but up to 5 and in extreme cases even up to 8 years after P. vivax infections. A number of effective anti-malarial drugs are available to treat the infection; starting the treatment promptly is essential in avoiding complications.

Malaria is endemic in more than 100 countries around the world, mainly in sub-Saharan Africa and Asia. Greece was declared malaria-free in 1974, after an intense malaria eradication program (1946-1960). Until 2010, approximately 20-50 cases were reported annually to the Hellenic CDC, the majority of which were travel related. Until 2010, sporadic malaria cases without reported travel history were recorded in 1991, 1999, 2000, 2009 and 2010.

Epidemiologic surveillance data

This data is derived from the reports of each laboratory-confirmed malaria case to the Hellenic CDC. The Department of Epidemiologic Surveillance and Intervention undertakes a verification procedure through communication with the treating physicians, the hospital and the reference laboratories for Malaria. Single case investigation is undertaken by the staff of the Department of Epidemiologic Surveillance for malaria cases without reported travel history and for all malaria cases in Evrotas, Lakonia, where a cluster of malaria cases was detected in 2011. This involves communication with the patient and/or their relatives using a semi-structured questionnaire on possible risk factors for transmission and recording of detailed travel history for the last 5 years before the onset of symptoms. In addition, for the same cases the staff undertakes a focus investigation, which involves active case detection in an area of 100 meters around each case’s place of residence or place of exposure. All residents in that area (Greek and immigrants) are followed up for fever in weekly intervals for a total of one month and in addition, all immigrants are screened with one-round blood sample. Areas where sporadic malaria cases without travel history to a malaria endemic country are detected are immediately elevated to risk level 2 (according to the national risk assessment scheme) and are going to be closely monitored for the following three years.
Epidemiologic data, 2011

In 2011, a total of 96 laboratory confirmed cases of malaria were recorded in Greece, of which 54 imported (9 in returning travelers and 45 cases in migrants from malaria-endemic countries, classified based on their arrival date in Greece and/or past history of malaria) and 42 without reported travel history to malaria-endemic areas (34 Greeks and 8 immigrants from non-endemic countries). A cluster of 36 P. vivax malaria cases with no travel history to malaria-endemic areas was reported in the Municipality of Evrotas (Lakonia District) along with 6 P. vivax sporadic cases in 4 other Regional Units (Evia, Larissa, East Attiki and Viotia) (Epidemiological Surveillance Report- Malaria in Greece, 2011).

More specifically in Evrotas, Lakonia 28 cases of P. vivax malaria were recorded in Greek citizens and 8 in migrant farm workers from non-endemic countries (Morocco (2), Poland (1) and Romania (5, 2 of which were diagnosed in Romania). In addition, 23 P. vivax cases were reported from the same area in migrant farm workers from malaria-endemic countries (Pakistan (21), Afghanistan (2)) with unclear travel history.

Epidemiologic data, 2012

In 2012, a total of 92 laboratory confirmed cases of malaria were reported in Greece, of which 73 have been classified as imported (9 in returning travelers and 64 in migrants from malaria-endemic countries based on their arrival date in Greece and/or past history of malaria). Of the 70 imported cases with known Plasmodium species, 54 cases are confirmed P.vivax infections, 15 P. falciparum (8 in migrants from malaria-endemic countries and 7 in returning travelers) and 1 case is a P. vivax and P. falciparum co-infection. For the immigrants from endemic countries, P. vivax infections most likely represent relapses of past malaria infection from their country of origin.

The remaining nineteen (19) cases refer to patients with no history of travel to a malaria endemic country (13 Greek, 2 Moroccan, 3 Romanian, 1 Albanian) with evidence that they have acquired the infection locally during transmission period 2012. All locally acquired cases were confirmed with Plasmodium vivax infection.

Four additional malaria cases reported in 2012 were attributed to previous transmission periods and are not included in the analysis of this report. Specifically, 2 P. vivax cases were attributed to the 2011 transmission periods: one case referred to a Moroccan migrant (diagnosed in April 2012), resident of the Municipality of Evrotas (Lakonia District), and the other referred to a 7 year old Greek girl with onset of symptoms in August 2012 and a history of 4-week stay in Evrotas, Lakonia during the transmission period 2011. Moreover, 2 P. malariae cases were also reported in elderly patients, attributed to exposure many years ago. Finally five relapse cases of P. vivax were recorded in malaria cases diagnosed during 2011, who had received inadequate radical treatment.

The case classification by place of residence/exposure of all the malaria cases reported to the Hellenic CDC in 2012 is presented in Table 1.

The place of residence/exposure of the 19 locally acquired malaria cases without travel history is presented in Figure 1. Ten (10) of those patients are considered to be exposed in Evrotas (Lakonia), 2 in Marathon and 2 in Markopoulo (East Attiki), one in the Municipality of Avdira (Xanthi), 1 in the Municipality of Tanagra (Viotia), for one case the place of exposure was determined as the lake Paralimni (Viotia), while the remaining two (2) cases were residing in the Municipality of Sofades, Karditsa (Region of Thessaly). The last two cases are classified as introduced with direct epidemiological link to 9 imported cases of malaria, which
were registered in the same locality. The cluster was discovered in an active case detection mission of the Hellenic CDC in the area.

The patient considered to be exposed in the Municipality of Tanagra (Viotia) was diagnosed in Albania.

*Figure 2* presents the distribution of the locally acquired malaria cases in Greece by week of reported onset of symptoms.

Specifically in the Municipality of Evrotas, Lakonia, in 2012, a total of 17 malaria cases in migrant workers from malaria endemic countries (Pakistan (13), Afghanistan (4)) were also reported, which are classified as imported (based on recent entry date to Greece and/or history of malaria in the past). The place of residence/exposure of all malaria cases in Lakonia is shown in *Figure 3*, while *Figure 4* presents the distribution of the malaria cases in the same area by week of reported onset of symptoms.

The age range of the locally acquired cases without travel history to a malaria endemic country in the transmission period 2012, is between 23 – 82 years (median age: 52 years), while 63% of the cases are male.

### Table 1. Place of residence/exposure and classification of malaria cases, Greece, 2012 (n=92)

<table>
<thead>
<tr>
<th>District of Residence</th>
<th>Status of malaria cases</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Immigrants from malaria endemic countries</td>
<td>Travelers from malaria endemic countries</td>
</tr>
<tr>
<td></td>
<td>Imported cases</td>
<td>Locally acquired cases</td>
</tr>
<tr>
<td>Argolida</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>Attiki</td>
<td>24</td>
<td>6</td>
</tr>
<tr>
<td>Chania</td>
<td>2</td>
<td>1</td>
</tr>
<tr>
<td>Corfu</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>Chania</td>
<td>2</td>
<td>0</td>
</tr>
<tr>
<td>Ioannina</td>
<td>3</td>
<td>0</td>
</tr>
<tr>
<td>Karditsa</td>
<td>9</td>
<td>1</td>
</tr>
<tr>
<td>Korinth</td>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td>Lakonia</td>
<td>17</td>
<td>0</td>
</tr>
<tr>
<td>Rethimno</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>Thessaloniki</td>
<td>2</td>
<td>0</td>
</tr>
<tr>
<td>Viotia</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>Xanthi</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td><strong>64</strong></td>
<td><strong>9</strong></td>
</tr>
</tbody>
</table>
Figure 1: Place of residence/exposure of the malaria cases without reported travel history to malaria-endemic areas, Greece, 2012 (n=19).
Figure 2: Distribution of locally acquired malaria cases by week of reported onset of symptoms, Greece, 2012 (n=19)

Figure 3. Place of residence/exposure of the malaria cases, Municipality of Evrotas, Lakonia, 2012 (n=27)
Figure 4. Distribution of malaria cases by week of reported onset of symptoms, Municipality of Evrotas, Lakonia, 2012 (n=26*)

*One case in a migrant from malaria endemic country, which was diagnosed in week 12/2012 is not included in the above figure.

Hellenic CDC activities for the management of malaria- 2012

During spring 2012 the Hellenic CDC developed an Action Plan for the Management of Malaria 2012-2015, where the risk assessment for re-emergence of malaria in the different areas of Greece was included. Based on this risk assessment all areas (Regions, Municipalities) in Greece were assigned a risk level from 0-3, taking into consideration the malaria cases reported in the last three years, the size and place of origin of migrant population in the area and the ecological parameters in each area.

After the reporting of each locally-acquired malaria case to the Hellenic CDC a series of response activities are implemented:

- Communication to the hierarchy of the Ministry of Health
- Communication to the relevant regional department of public health
- Communication to the National Centre for Blood Donation, responsible for the relevant blood safety measures.
- Enhancement of early detection of cases and focus investigation: Hellenic CDC investigation teams are deployed after the detection of each malaria case to perform a “focus investigation” covering all residents in an area with radius 100m around the case’s residence, according to advice provided by the ECDC and WHO during their mission in 2011. In this activity, all migrants from malaria endemic countries
in this area are tested for malaria, while Greek citizens and migrants from non-endemic countries are screened for malaria compatible symptoms and/or tested for malaria accordingly.

In addition, the Hellenic CDC has supported and/or developed during 2012 a series of activities to prevent the re-establishment of malaria in Greece:

I. Enhance malaria surveillance:

• Active malaria case detection in the general and the migrant populations

The Hellenic CDC has deployed a field team in the area of Evrotas, Lakonia (epi-centre of the 2011 cluster), since the end of September 2011, which has been working in the area since then. A report on the local activities can be accessed here in Greek. The Hellenic CDC field team collaborated from April to October 2012 with MSF-Greece for the prevention and investigation activities in the area, while support is also provided by the Municipality of Evrotas and local volunteers.

A significant number of migrants from malaria endemic countries (Pakistan and Afghanistan, etc) live and work in Evrotas. During the field visits a registry of all residences and residents was created, health promotion information was provided for protection against mosquitoes and fever screening and/or testing for malaria was performed. During the 2012 transmission period 16 out of 17 malaria cases in migrants were actively detected, all of whom were also treated with antimalarials under directly observed therapy (DOT).

Of note is also the fact that in the framework of our active case detection activity in the area of Evrotas Lakonia, the median time from onset of malaria symptoms to diagnosis for both migrants from endemic countries and Greeks was 3 days (range: 0-15 days for migrants and 0-8 days for Greeks respectively), while in 2011 it was calculated at 5 days (range: 2-12) for migrants and 7 days (range: 2-17) for Greeks. This improvement in timeliness of diagnosis is mainly attributed to the active case detection activities and the increased awareness of local clinicians for malaria and contributes significantly in decreasing the risk of local onward transmission.

• Screening of migrants for malaria

Protocols for screening of asymptomatic migrants for malaria have been implemented in the framework of the partnership to implement the national project: “Integrated Surveillance and control programme for West Nile Virus and malaria in Greece” in:

- 759 migrants from malaria endemic countries from the area of Evrotas, Lakonia
- 499 migrants from malaria endemic countries from the area of Marathon, East Attiki
- 132 migrants from malaria endemic countries from the area of Markopoulo, East Attiki
- 60 migrants from malaria endemic countries from the area of Thiva, Viotia
- Over 1,000 migrants held at Reception Centres in Korinth, Drama, Komotini, Xanthi and Evros.

• A geographical information system (GIS) tool was created for risk assessment (mapping of vectors, their breeding sites and malaria cases) in the framework of the above project.
II. **Enhancing laboratory diagnosis of malaria** through a training programme for microbiologists and laboratory technicians, according to the risk assessment of each geographic area. In addition, the Hellenic CDC has imported 15,000 Rapid Diagnostic Tests (RDTs) for malaria, which are currently in use by the field teams, and have also been distributed to health centres and hospitals around the country depending on the above mentioned risk assessment. Another 10,000 RDTs for malaria have been procured by MSF-Greece for the same reason. The use of malaria RDTs in 2012 has contributed significantly in early diagnosis of cases in symptomatic patients.

III. **Standardization of the malaria treatment:** according to treatment guidelines, developed by the Hellenic CDC. A protocol for following up the antimalarial treatment efficacy was developed and was in place in 2012. In addition, all malaria cases treated in 2011 were followed up in 2012 with a 2nd antimalarial treatment course with chloroquine x 2d and primaquine x 14d, as per the national guidelines.

IV. **Increase awareness amongst health professionals** for the diagnosis of malaria. In collaboration with the National School of Public Health (NSPH) and the University of Thessaly, 41 seminars were delivered to health professionals (hospitalists and nursing personnel, primary care physicians, private practitioners, laboratory personnel, intensivists) all over the country.

V. **Communication to the public** on malaria and personal protection measures against mosquitoes: through public meetings and educational material developed by the Hellenic CDC and available through the Centre’s website: www.keelpno.gr. In addition a video with information on protection measures against mosquito bites was disseminated throughout the summer months. A total of 29 public meetings have been organized with the assistance of local communities, along with 48 presentations to primary schools (6,932 students) and 34 presentations in secondary schools (6,311 students).

VI. **Vector control activities - Entomologic Surveillance**
Vector control activities in Greece belong to the mandate of the municipal and regional governments. A Working Group of experts on vectorborne diseases supported by the Hellenic CDC developed guidance for local authorities for organizing vector control activities and entomologic surveillance. This guidance was communicated early in the season for the planning of 2012 vector control activities. In addition, the Hellenic CDC financed three mosquito mapping projects targeting the breeding sites of mosquitoes around the country and including all geographic areas that have reported malaria cases since 2009.
In the framework of the project "**Integrated Surveillance and control programme for West Nile Virus and malaria in Greece**", a number of entomological activities were also carried out:

- identification of mosquitoes collected through entomological surveillance (NSPH, University of Thessaly, Benaki Phytopathological Institute)
- genetic identification of mosquitoes
- testing of mosquitoes for biocide resistance (Benaki Phytopathological Institute)
- mosquito overwintering study (in-vitro and in-vivo)
- systematic mosquito traps effectiveness study.
Communication to the local level: the Hellenic CDC in collaboration with the Ministry of Agriculture and an expert entomologist from the US-CDC/WHO organized training seminars for the regional staff that supervises vector control activities in risk areas level 2 and 3.

VII. Communication with international public health stakeholders: The Hellenic CDC communicates frequently for exchange of knowhow and information on malaria cases and activities with the European CDC and the World Health Organization, as well as with a number of European and international agencies and networks. A number of foreign experts have visited our country repeatedly for this reason.

Advice for travelers to areas in Greece with reported locally-acquired malaria cases:
The Hellenic CDC, based on the surveillance data available until now and the implemented control measures in the areas where locally-acquired malaria cases have been reported, maintains that the risk to travelers for malaria infection in Greece is very low. For this reason, chemoprophylaxis for malaria is not recommended for visitors to the areas of Lakonia, East Attiki, Xanthi, Viotia or Karditsa.

Discussion
Greece has been malaria-free since 1974, but a number of significant factors may lead to the re-establishment of the disease, mainly:

(i) the large number of immigrants from malaria-endemic countries, who work mostly in the farming sector

combined with

(ii) the circulation of Anopheles mosquitoes, the competent vector of the disease, in many areas of Greece.

All the above underlines the urgent need for an effective multi-sector control strategy for the management of malaria reintroduction and the prevention of its re-establishment in Greece.

Despite the increased sensitivity of the malaria surveillance (active case detection, increased awareness of health professionals) in 2012 fewer locally-acquired malaria cases were recorded, compared with 2011. An overall 55% decrease is noted in the number of locally acquired malaria cases from all over Greece; 72% decrease in locally-acquired cases in Evrotas, Lakonia. Furthermore, active case detection in Evrotas improved significantly the timeliness of diagnosis of malaria in the area.

Early detection, appropriate investigation and appropriate treatment of malaria cases combined with effective vector control (larviciding and IRS) represent the main components of the public health strategy to prevent further transmission and re-establishment of malaria in Greece.