Environmental drivers, climate change and emergent diseases transmitted by mosquitoes and their vectors in southern Europe: A systematic review

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Review article

Environmental drivers, climate change and emergent diseases transmitted by mosquitoes and their vectors in southern Europe: A systematic review

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ABSTRACT

Mosquito borne diseases are a group of infections that affect humans. Emerging or reemerging diseases are those that (re)occur in regions, groups or hosts that were previously free from these diseases: dengue virus; chikungunya virus; Zika virus; West Nile fever and malaria. In Europe, these infections are mostly imported; however, due to the presence of competent mosquitoes and the number of trips both to and from endemic areas, these pathogens are potentially emergent or re-emergent. Present and future climatic conditions, as well as meteorological, environmental and demographic aspects are risk factors for the distribution of different vectors and/or diseases. This review aimed to identify and analyze the existing literature on the transmission of mosquito borne diseases and those factors potentially affecting their transmission risk of them in six southern European countries with similar environmental conditions: Croatia, France, Greece, Italy, Portugal and Spain. In addition, we would identify those factors potentially affecting the (re)introduction or spread of mosquito vectors. This task has been undertaken with a focus on the environmental and climatic factors, including the effects of climate change. We undertook a systematic review of the vectors, diseases and their associations with climactic and environmental factors in European countries of the Mediterranean region. We followed the PRISMA guidelines and used explicit and systematic methods to identify, select and critically evaluate the studies which were relevant to the topic. We identified 1302 articles in the first search of the databases. Of those, 160 were selected for full-text review. The final data set included 61 articles published between 2000 and 2017.39.3% of the papers were related with dengue, chikungunya and Zika virus or their vectors. Temperature, precipitation and population density were key factors among others. 32.8% studied West Nile virus and its vectors, being temperature, precipitation and NDVI the most frequently used variables. Malaria have been studied in 23% of the articles, with temperature, precipitation and presence of water indexes as the most used variables. The number of publications focused on mosquito borne diseases is increasing in recent years, reflecting the increased interest in that diseases in southern European countries. Climatic and environmental variables are key factors on mosquitoes' distribution and to show the risk of emergence and/or spread of emergent diseases and to study the spatial changes in that distributions.

1. Introduction

Mosquito borne diseases (MBDs) are a group of infections that affect humans, as well as wildlife and livestock – which may then act as a reservoir for the disease. For a MBD to be present and be propagated in a specific environment, an interaction between the infectious agent, reservoir, vector and susceptible population is necessary. MBDs represent a public health concern causing hundreds of thousands deaths every

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year. For instance, *Plasmodium* parasites, the causative agent of malaria, were responsible for an estimated 219 million cases worldwide and 435,000 fatalities in 2017 (WHO, 2018).

Emerging or reemerging diseases are those that (re)occur in regions, groups or hosts that were previously free from these diseases or that show unexpected increases in their incidence or changes in their previous distribution patterns. Many MBDs are considered to be emerging or reemerging, as it is the case of dengue virus (DENV) fever, which has dramatically increased its incidence during the last few decades and has expanded towards previously unaffected areas of Africa, America, Asia and Oceania (WHO, 2012). Similarly, chikungunya virus (CHIKV) was first described in 1952, but outbreaks were confined to Africa and Asia until 1973. Since 1999/2000 it has produced sizeable outbreaks in tropical and sub-tropic regions of Africa, Asia and Oceania. In 2013, the disease emerged on the island of Saint Martin in the Caribbean and has spread since them to many parts of the WHO Region of the Americas (PAHO) (Pettersson et al., 2016). In addition, Zika virus (ZIKV) was discovered in 1947 but only 14 cases were reported across Africa and Asia until 2007, when the first substantial outbreak was identified on the Island of Yap (Duffy et al., 2009). Between 2013 and 2014 a major Zika virus outbreak was identified in French Polynesia and in other Oceanic and Pacific islands. In 2015 the disease appeared in Brazil and subsequently spread across Americas (Gubler et al., 2017). Finally, West Nile virus (WNV), discovered in 1937, is widespread and naturally circulating between mosquitoes and birds, who determines its mobility into other areas with favourable environments. Since the mid-90s its frequency and severity have intensified, and its geographic range has broadened, especially since their introduction in America in 1999 (ECDC, 2018). At this moment, the virus is considered the principal cause of viral encephalitis worldwide (Chancey et al., 2015).

In Europe, infections by DENV, CHIKV and ZIKV are mostly imported due to the high number of humans travelling both to and from endemic areas. The spread of invasive mosquito species has created novel epidemiological scenarios that may result in the local circulation of exotic diseases in the area. This may be specially the case of *Aedes albopictus*, a competent vector for dengue, chikungunya and Zika diseases (Ruche et al., 2010). In Europe, this mosquito species was first detected in Albania in 1979, and has since expanded its range rapidly across numerous countries. It is currently distributed across all the Mediterranean regions of Europe and is expanding into other more northerly territories ("Aedes albopictus - Factsheet for experts," n. d.). On the other hand the yellow fever mosquito, *Aedes aegypti*, was present in Europe up to the middle of the 20th century, especially across Mediterranean regions (Medlock et al., 2012). This mosquito species has reappeared on the island of Madeira, where it is now considered established (Almeida et al., 2007); it has also been discovered in isolated localities in the Netherlands. Records of additional invasive species in Europe include potential vectors of MBDs, such as *Aedes japonicus*, *A. (Ochlerotatus) atropalpus, and A. koreikus*. In addition to exotic, native mosquito species may also be involved in the transmission of MBDs in Europe. This is the case of West Nile fever (WNF), an emerging MBD in our context. It is mainly transmitted by widespread mosquitoes of the *Culex* genus, although species from other genera such as *Coquillettidiae* and *Aedes (Ochlerotatus) caspius* could be also involved in transmission. Finally, malaria has been eradicated in the greater part of continental Europe. However different species of the genus *Anopheles*, which are vectors of the human malaria are still present, with differences in distribution according to region (Piperaki and Daikos, 2016).

Diverse environmental factors determine the spread and incidence of MBDs, by affecting either directly the pathogen transmission or vector or infectious agent behaviour, or indirectly through changes in the mosquito or reservoirs life cycles and thus in its distribution and abundance. Temperature is one of the environmental factors potentially affected by climate change which may alter the transmission dynamics of MBDs. It can affects the cycles of the pathogens both in the mosquito, humans and in other hosts or reservoirs (e.g.: birds and WNF) (Chan and Johansson, 2012; Parham and Michael, 2010; Paz, 2015). It can also modify vectors' behaviour (biting rate and vector capacity). Furthermore, temperature may condition mosquitoes survival and distribution (including seasonal diapause for invasive species in temperate regions, necessary for its establishment in such climates), abundance (hatching rates and adult mortality), and seasonal range. Precipitation is also likely to affect mosquitoes' distribution and its abundance is usually positively associated to precipitation (Almeida et al., 2007; Bhatt et al., 2013; Cunze et al., 2016; Valdez et al., 2017). Other climatic factors (humidity, wind) seem to have a less important role or it have not been well stablished yet. Regarding climatic factors, to establish their thresholds for each mosquito vector (MV) species is very useful in order to know and predict the present and future seasonal and geographic distribution of those involved in human diseases. In addition, anthropogenic factors as population density, land use, travels, migrations and international trade may create new suitable habitats for some mosquito species (Derraik and Slaney, 2007; Medlock et al., 2012; Rochlin et al., 2016). Furthermore, other environmental factors such as host or reservoir presence, migratory bird routes or special habitats as wetlands contribute to mosquitoes or MBDs dynamics (Rizzoli et al., 2015).

The proliferation of the invasive *Ae. albopictus* mosquito in Europe, among other factors, have resulted in a number of locally transmitted MBD-outbreaks as well as isolated cases since 2007. Up to 2017, there had been two substantial outbreaks of locally transmitted chikungunya fever in Italy, and three in France (Calba et al., 2017; Tomasello and Schlagenhauf, 2013; Venturi et al., 2017). Additionally there was an outbreak of dengue in Croatia and various outbreaks and isolated cases of dengue transmission in France (Delisle et al., 2015; Succo et al., 2016; Tomasello and Schlagenhauf, 2013). Further afield, in 2012–2013 there was a sizeable dengue outbreak caused by *Ae. aegypti* (Lourenco and Recker, 2014). In Europe, WNF produced an important outbreak in Romania in 1996–1997 (Tsai et al., 1998), and the virus has continued circulating in the area (Chaskopoulou et al., 2016) causing over 2000 infections resulting in 180 fatalities in EU/EEA and EU enlargement countries during 2018 (ECDC, 2018). Additionally, there have been a number of documented cases or outbreaks of introduced malaria, generally self-limiting and small in size; however, Greece and other European countries has reported autochthonous transmission from 2009 up until the present day (*Epidemiological surveillance report Malaria in Greece, 2017*, 2017; Olaso et al., 2017; Velasco et al., 2017).

Present and future climatic conditions, as well as meteorological, environmental and demographic aspects are risk factors for the distribution of different vectors and/or diseases (Bouzid et al., 2014; Calzolari, 2016; Engler et al., 2013; Semenza and Suk, 2018). Thus, it is essential to identify those variables which could act as predictors of risk, both for the presence of each vector and for the introduction/transmission of each disease. These predictors, as well as their geographical distribution, are key elements for the development and implementation of strategies to reduce the impact of these emergent diseases.

For these reasons, the aim of this study is to review the existing literature on the transmission of MBDs and those factors potentially affecting their transmission risk in six southern European countries with similar environmental conditions: Croatia, France, Greece, Italy, Portugal and Spain. In addition, we will identify those factors potentially affecting the (re)introduction or spread of MVs. This task has been undertaken with a focus on the environmental and climatic factors, including the effects of climate change.

2. Material and methods

We undertook a systematic review of the literature on the association between climatic and environmental factors and vectors and MBDs presence in six European countries of the Mediterranean region: Croatia, France, Greece, Italy, Portugal and Spain. We followed the PRISMA guidelines and used explicit and systematic methods to identify, select and critically evaluate the studies which were relevant to the topic. In addition, we recompiled and analysed the data from the studies included in this review.

The diseases included in this study were infection by DENV, CHIKV, ZIKV, WNV and malaria. As a consequence, the mosquitoes which were the object of study were: *Aedes* spp (including *Ae. aegypti* and *Ae. albopictus*), *Anopheles* spp, *Coquillettidia* spp, *Culex* spp and *Ochletotatus* spp.

All of the articles published in the national or international journals indexed by PubMed, Embase, Scopus, Web of Science and the AHL Regional Portal were considered. The date range was from January 1, 2000 through to September 30, 2017. The languages considered were English, Spanish, French, Italian and Portuguese. We used the keywords: (dengue OR chikungunya OR Zika OR West Nile OR malaria) AND (Portugal OR Spain OR France OR Italy OR Greece OR Croatia) AND (climat* OR environment* OR temperature OR warm* OR meteo* OR rainfall OR humidity OR altitude) using the option 'all fields' to recover the articles in which the search terms appeared in the title, abstracts or keywords.

We included articles that referred to the presence of any of the diseases and/or vectors focus of the study, and those related to climate change presenting data regarding environmental or climatological variables. We excluded the case studies and literature reviews which included previously published data. We also excluded other reports and guides published by relevant organizations, manuscripts, summaries of and posters from conferences, 'grey' literature and historical reports. We discarded notification of outbreaks; prevalence studies; clinical descriptions of diseases, pathogenicity and diagnosis in humans or animals; purely descriptive studies; experimental laboratory studies; and entomological surveys. We also eliminated duplicate articles and those that were not accessible (either due to the language or lack of full-text access).

The recovered abstracts were read by two authors independently (double peer review), and we applied inclusion/exclusion criteria to produce the final list of publications to be read in full-text. This first filtering was carried out by responding to the following questions:

1. Did the study include any of these countries: Croatia, France, Greece, Portugal, or Spain?

   Yes No Not certain.

2. A. Does it study the vector's geographical distribution?

   Yes No Not certain.

   B. Does it study one of the target diseases in humans?

   Yes No Not certain.

3. A. Does the study consider climatic factors?

   Yes No Not certain.

   B. Does it study the relationship with environmental factors?

   Yes No Not certain.

   C. Does it study the relationship with geographical factors?

The article was discarded if the answer to Question 1 was no or, if in the second and third blocks of questions, the article did not receive at least one point per block.

Each reviewer read all of the selected articles and entered the information of interest and the variables into a database. During the second filtering, those articles which did not fit the criteria for inclusion in relation to the objectives of the study were also excluded. Once again, a third person revised both databases in order to compare the results and resolve any discrepancies.

Subsequently, we reviewed the bibliographies of the articles that has already been included in order to check for new articles which fitted the criteria but which had not been identified previously. We then repeated the process, beginning by reading the abstracts and then adding these new articles to the database, followed by revising them using the same methodology detailed above.

Excel tables were created to ensure systematic and consistent compilation of data; and were tested with the first 15 articles included in the revision process. Finally, tables were completed for all of the articles, and contained the following information:

1. Principal characteristics of the included article (i.e.: article ID, year of publication, year/period studied, analytical approaches/methodology of the study, use of maps, studies which describe associations (variables), studies that make predictions).
2. Climatic and/or environmental variables included in the articles
3. Countries included in the articles evaluated (for those studies including more than one country we created additional labels. We named them as 'Europe' when the articles dealt with data from more than one European country and 'Global' when one or more non-European country was included in addition to one or more of the target countries). The geographical area of the study was determined and represented on a map.
4. Quality assessment of the included articles. We created a tool to assess a number of quality criteria related to the types of studies included. The evaluated categories were:

- Potential selection bias comprising two categories, *source* and *data collection* of the disease and/or vector and of the climactic and/or environmental variables. Evaluate whether the methodology used for the collection of data and its sources is clearly described.
- Time period: Clear description of the period covered by the study.
- Analysis: description of the methodology used for the analysis of data and for obtaining the results.
- Results: well-described and presented, and coinciding with the objectives of the study.

We evaluated each of the categories, scoring with 1 when the criteria were met, and 0 in those cases where they were not. Scores assigned to each category were summed, ranging from 0 (minimum) to 5 (maximum quality value).

A flow diagram was created which specifies all of the steps taken and indicating which articles and reasons of inclusion/exclusion from this study, and for what reasons (see Fig. 1).

For the section on analytical methods (Table 1) we classified the articles due to the variability of the methodological proposal addressed by each according to the following categories:

- Transmission models (TM) included: Bayesian transmission models, dynamic transmission models, reproduction number, receptivity, and infectivity.
- Predictive models (PMo) including: maxent models, suitability models, generalized additive models (GAM), generalized linear models (GLM), negative binomial mixed models, ecological niche models, Mahalanobis distance, regional climate models, GIS-based weighted linear combination, multivariate predictive models, logistic regression models, dynamic multi-agent simulation, vulnerability models, host-vector spatial predictive models, non-linear discriminant analysis, remote vector models), multilayer perceptron with back propagation – artificial neural network, Gradient Model Risk Index and General Circulation Models.
- Association/correlation models (A/CM) included: linear regression models, logistic regression models, Pearson correlation, GAM, GLM, non-linear discriminant analysis (NLDA), Linear mixed model, linear mixed-effects models lag correlations, binary and multinomial

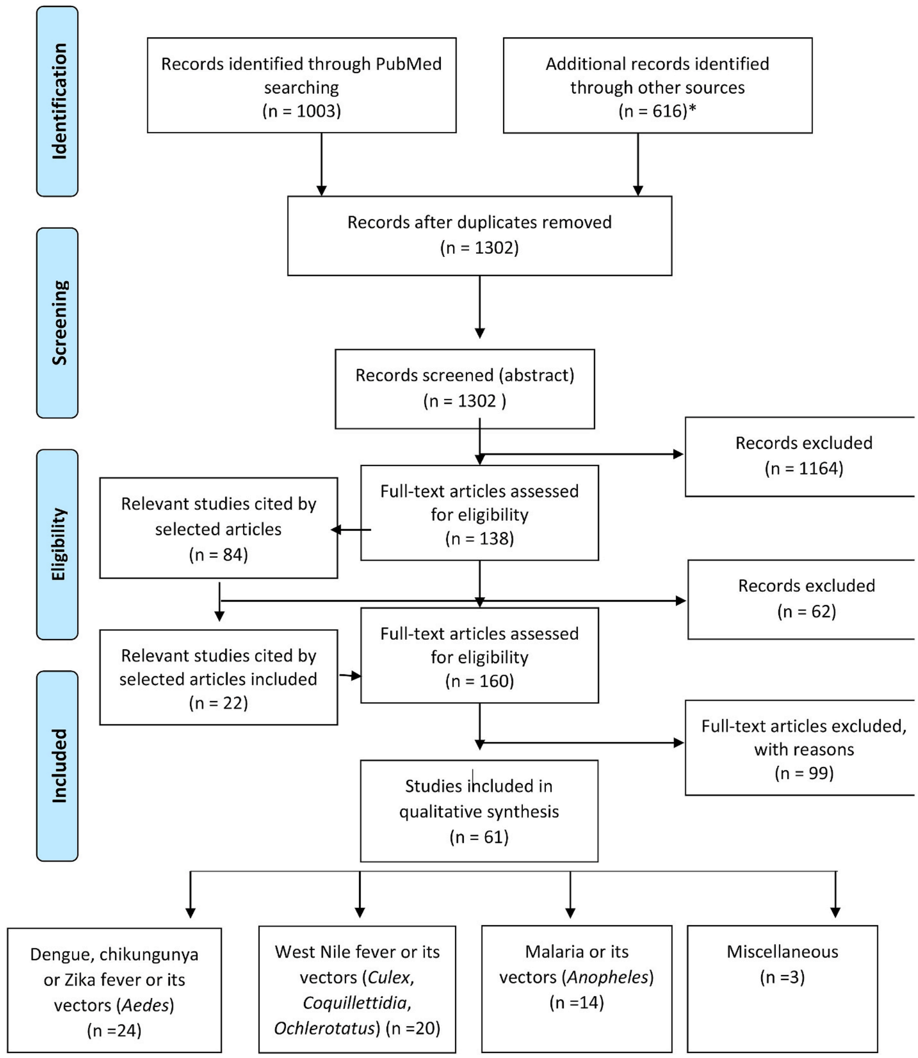

Fig. 1. PRISMA 2009 Flow * *Embase: 174; Scopus: 290; Web of science: 128; Portal Regional de la BVS: 24.*

logistic regressions, autoregressive time series models and autoregressive integrated moving average (ARIMA) models.

- Models of abundance/density/population dynamics (A/D/DPM) included: occurrence, hierarchical state-space structure, and GLM.
- Spatial models (SM) included: kriging, superimposing maps, cluster analysis, spatial point pattern analysis, and kernel density estimation

The ‘maps’ section in Table 1 indicates if the results of a study were presented via maps and these were classified as:

- Probability Maps (PM) which includes maps of risk and suitability maps.
- Climate change projection maps (CCP), which represent potential future situations in relation to different climate change scenarios.
- Abundance maps (AM) show the presence/absence or density of vectors and/or cases.

The ‘association’ section in Table 1 shows which articles describe an association between vector/diseases and climatic/environmental variables. Table 2 provides classifications by vector/disease, with the article number and the type of association (positive (+) or negative (−)).

Table 2 classifies the articles according to the presence of climatic/environmental variables* according to criteria laid out by the Spanish State Meteorological Office and the National Oceanic and Atmospheric Administration (“Glosario Meterologico Visual - AEMET,” n. d.; “Glossary - NOAA’s National Weather Service,” n. d.) and also provides classification by disease and vector studied – specifying if the study describes associations or makes predictions.

3. Results

We identified 1302 articles in the first search of the databases, and a further 84 articles via the bibliographies of the already-included articles. Of those, 160 were selected for full-text review (Fig. 1). After reading the full-texts we excluded 99 articles as they did not fulfil the pre-established criteria, thus the final data set included 61 articles published between 2000 and 2017 (see details in Table 1).

The distribution of the selected articles by year of publication and disease/vector group and country is shown in Fig. 2. The first article in the final selection was published in 2003. Until 2010 the number of articles per year was between 1 and 3, but from 2011 to 2013, this rose to between 4 and 5 reaching the maximum in 2014 (12 publications). Furthermore, 57.4% of the articles included in this review were published between 2014 and 2017. Most studies were carried out in the north of Italy, with 9 studies focused on WNV or *Culex pipiens* and 8 on dengue, chikungunya or *Ae. albopictus*. A good number of articles also focus on the Camargue (France) with 4 studies on malaria or its vectors, 1 on WNV and 1 on malaria and WNV (Fig. 3).

There are 8 articles specifically dealing with climate change (Bietolini et al., 2006; Bouzid et al., 2014; Caminade et al., 2012; Fischer et al.,

Table 1
Main characteristics of the articles included in the review.

Paper ID	Publication year	Analytical approaches	Maps	Association	Predictions	Quality
Dengue, chikungunya, Zika fever or *Aedes*						
Croatia						
52	2014	A/CM, SM	AM	X		5
France						
13	2015	A/CM		X		5
14	2015	A/CM, PMo	AM and PM	X	X	5
44	2015	PMo	PM		X	5
51	2013	A/D/DMP			X	5
Italy						
1	2017	TM			X	5
45	2017	PMo, A/CM	AM and PM	X	X	5
7	2016	TM	AM and PM	X	X	5
59	2016	A/CM		X		5
55	2011	Pmo	PM		X	5
57	2011	PMo	PM and CCP	X	X	5
33	2010	A/CM		X		5
53	2003	A/CM		X		5
Europe						
5	2016	TM	PM		X	5
6	2016	PMo	PM and CCP		X	5
60	2016	PMo	PM		X	5
61	2016	A/D/DPM	PM		X	4
16	2014	PMo	PM and CCP		X	5
22	2013	Pmo	PM and CCP		X	4
28	2012	PMo	PM and CCP		X	5
56	2011	PMo	PM and CCP		X	4
34	2009	SM,A/CM	PM		X	5
Global including Europe						
3	2017	PMo	AM and PM	X	X	5
24	2014	A/CM, PMo	PM		X	5
West Nile fever or *Culex* or *Ochlerotatus*						
France						
40	2007	A/D/DPM	PM		X	3
Greece						
4	2016	A/CM		X		5
19	2014	SM, A/CM	AM and PM	X	X	5
Italy						
8	2016	A/D/DPM		X	X	5
11	2015	SM,A/CM	AM and PM	X	X	5
18	2014	A/CM		X		5
20	2014	A/CM		X		5
21	2014	A/CM, A/D/DPM		X		5
23	2014	PMo	AM and PM		X	5
47	2014	A/D/DPM		X	X	5
27	2012	A/CM		X		5
29	2011	SM	Am and PM	X	X	5
Spain						
2	2017	PMo y A/CM	AM and PM	X	X	5
31	2012	PMo	PM		X	4
Europe						
9	2016	TM y PMo	PM		X	5
Global including Europe						
43	2017	A/CM		X		5
15	2015	A/CM		X		5
10	2015	PMo	AM and PM		X	5
50	2014	PMo y A/CM	AM and PM	X	X	5
49	2013	A/CM		X		5
Malaria or *Anopheles*						
Croatia						
41	2004	A/CM		X		5
France						
48	2012	A/D/DPM			X	5
35	2009	PMo	PM		X	5
37	2008	PMo	AM and PM		X	5
38	2008	SM, A/CM	AM	X	X	5
Greece						
42	2017	TM	PM		X	5
25	2013	Pmo	PM		X	5
Italy						
26	2012	A/CM		X		4
58	2006	PMo	AM and PM		X	5
Portugal						
54	2016	TM, Pmo	AM and PM		X	5

(*continued on next page*)

Table 1 (*continued*)

Paper ID	Publication year	Analytical approaches	Maps	Association	Predictions	Quality
Dengue, chikungunya, Zika fever or *Aedes*						
Croatia						
46	2014	SM, A/CM	PM	X	X	5
30	2011	A/CM, Pmo		X	X	5
36	2009	PMo	PM and CCP		X	5
Spain						
32	2010	TM			X	5
Various mosquito genera						
12	2015	A/D/DPM, A/CM	AM	X		5
17	2014	A/CM		X	X	5
39	2007	A/CM		X		5

A/CM: Association/correlation models. A/D/DMP: abundance/density/population dynamics models. PMo: predictive models. SM: spatial models. TM. Transmission models. AM: abundance maps. CCP: climate change projection maps. PM: probability maps. 1:(Erguler et al., 2017); 2(Sanchez-Gomez et al., 2017); 3:(Santos and Meneses, 2017); 4:(Stilianakis et al., 2016); 5:(Rocklov et al., 2016); 6:(Liu-Helmersson et al., 2016); 7:(Guzzetta et al., 2016); 8:(Marini et al., 2016); 9(Semenza et al., 2016):10:(Conte et al., 2015); 11:(Calzolari et al., 2015); 12:(Roiz et al., 2015b); 13:(Roiz et al., 2015a); 14:(Roche et al., 2015); 15:(Marcantonio et al., 2015); 16:(Bouzid et al., 2014); 17:(Roiz et al., 2014); 18:(Rosa et al., 2014); 19:(Valiakos et al., 2014); 20:(Carrieri et al., 2014); 21:(Mulatti et al., 2014); 22:(Fischer et al., 2013b); 23:(Mughini-Gras et al., 2014); 24:(Rogers et al., 2014); 25:(Sudre et al., 2013); 26:(Boccolini et al., 2012); 27:(Roiz et al., 2012); 28:(Caminade et al., 2012); 29:(Bisanzio et al., 2011); 30:(Lourenco et al., 2011); 31:(Rodriguez-Prieto et al., 2012); 32:(Sainz-Elipe et al., 2010); 33:(Roiz et al., 2010); 34:(Tilston et al., 2009); 35:(Linard et al., 2009); 36(Capinha et al., 2009); 37:(Ponçon et al., 2008); 38:(Tran et al., 2008); 39:(Poncon et al., 2007); 40:(Tran et al., 2007); 41:(Merdic and Boca, 2004); 42:(Pergantas et al., 2017); 43:(Trájer A..J, 2017); 44:(Moyne et al., 2015); 45:(Baldacchino et al., 2017); 46:(Benali et al., 2014); 47:(Jian et al., 2014); 48:(Cailly et al., 2012); 49:(Paz et al., 2013); 50:(Tran et al., 2014); 51:(Tran et al., 2013); 52:(Zitko and Merdić, 2014); 53:(Toma et al., 2003); 54:(Gomes et al., 2016); 55:(Neteler et al., 2011); 56:(Fischer et al., 2011); 57:(Roiz et al., 2011); 58:(Bietolini et al., 2006); 59:(Manica et al., 2016); 60:(Cunze et al., 2016); 61(Erguler et al., 2016).

2013a, 2011; Liu-Helmersson et al., 2016a; Roiz et al., 2011; Semenza et al., 2016) 6 of them related to dengue, chikungunya, Zika and/or their vector (Bouzid et al., 2014; Caminade et al., 2012; Fischer et al., 2013, 2011; Liu-Helmersson et al., 2016, p.; Roiz et al., 2011), one to WNF (Semenza et al., 2016) and other to *Anopheles maculipennis* complex (Bietolini et al., 2006). Among them, 1 were global (Fischer et al., 2011) 5 were about Europe (Bouzid et al., 2014; Caminade et al., 2012; Fischer et al., 2013; Liu-Helmersson et al., 2016; Semenza et al., 2016) and 2 were restricted to Italy (Bietolini et al., 2006) or an Italian region (Roiz et al., 2011).

We scored 55 studies (90.2%) with the maximum quality score (5 points), 8.2% (5) with 4 points and 1 study was rated at 3 points. The variation in quality scores between the studies was primarily related with difficulties when it came to identifying the study period or difficulties obtaining the data used (Table 1).

3.1. Dengue, chikungunya, Zika and/or their vectors

Of the 61 articles included in the study, 24 (39.3%) focused on DENV, CHIKV, ZIKV or their vectors, most of them (15; 62.5%) published after 2014 while a single study was published before 2009 (Fig. 2). Nine (37.5%) of them covered aspects regarding all of Europe, 8 (33.3%) from Italy, 4 (16.7%) from France and 1 from Croatia. Two additional studies were classified as global but with prominent reference to a part of Europe (Table 1).

Most of the studies used predictive models (PMo; n = 13) and association/correlation (A/CM; n = 9). Nine of the articles tested the possible association between the climatic and/or environmental variables and the disease or vector (Baldacchino et al., 2017; Guzzetta et al., 2016; Manica et al., 2016; Roche et al., 2015; Roiz et al., 2015a, 2011; 2010a; Toma et al., 2003; Zitko and Merdić, 2014), while 19 studies used different variables as predictors for the distribution of the vector and/or the MBD (Baldacchino et al., 2017; Bouzid et al., 2014; Caminade et al., 2012; Cunze et al., 2016; Erguler et al., 2017, 2016; Fischer et al., 2013, 2011; Guzzetta et al., 2016; Liu-Helmersson et al., 2016; Moyne et al., 2015; Neteler et al., 2011; Roche et al., 2015; Rocklov et al., 2016; Rogers et al., 2014; Roiz et al., 2011; Santos and Meneses, 2017; Tilston et al., 2009; Tran et al., 2013). The response variable was transmission of the disease in 11 of the articles (Bouzid et al., 2014; Erguler et al., 2017, 2016; Fischer et al., 2013; Guzzetta et al., 2016; Liu-Helmersson et al., 2016; Roche et al., 2015; Rocklov et al., 2016; Roiz et al., 2015a,b; Santos and Meneses, 2017; Tilston et al., 2009) measured as the abundance or population density of the vector, or considering imported cases (Erguler et al., 2017b, 2016b; Guzzetta et al., 2016b). In 6 articles the variable was the suitability of the vector (Caminade et al., 2012; Cunze et al., 2016; Fischer et al., 2011; Moyne et al., 2015; Neteler et al., 2011; Roiz et al., 2011). In other cases, the dependent variable was the dynamic and/or distribution of the vector (Baldacchino et al., 2017; Manica et al., 2016; Roche et al., 2015; Roiz et al., 2010; Tran et al., 2013) or its eggs and larvae (Toma et al., 2003; Zitko and Merdić, 2014).

Temperature was a key factor in all of these studies with 8 of them reporting a positive association with the transmission of the disease or dynamics of the vector (Baldacchino et al., 2017; Guzzetta et al., 2016; Manica et al., 2016; Roiz et al., 2015a, 2011; 2010; Toma et al., 2003; Zitko and Merdić, 2014). Only one article found a negative association with temperature (Roche et al., 2015) of the coldest month of the second half of the year and *Ae. albopictus* presence. In 19 of the studies, temperature was used as a driver for the accurate prediction of the vector's dynamics or the transmission of the MBD (Baldacchino et al., 2017; Bouzid et al., 2014; Caminade et al., 2012; Cunze et al., 2016; Erguler et al., 2017, 2016; Fischer et al., 2013, 2011; Guzzetta et al., 2016; Liu-Helmersson et al., 2016; Moyne et al., 2015; Neteler et al., 2011; Rocklov et al., 2016; Rogers et al., 2014; Santos and Meneses, 2017; Tilston et al., 2009; Tran et al., 2013). Temperature variables included: mean, máximum and minimal daily temperature (Erguler et al., 2017b; Guzzetta et al., 2016b; Liu-Helmersson et al., 2016; Manica et al., 2016; Neteler et al., 2011; Rocklov et al., 2016; Roiz et al., 2015a, 2011, 2010; Tran et al., 2013), weekly (Toma et al., 2003; Zitko and Merdić, 2014), monthly (Bouzid et al., 2014; Fischer et al., 2013; Roche et al., 2015), annual (Caminade et al., 2012; Erguler et al., 2017; Roche et al., 2015; Rogers et al., 2014), seasonal (Santos and Meneses, 2017) and annual mean temperature, mean diurnal range, maximum temperature of the warmest month, minimum temperature of the coldest month, mean temperature of the wettest, driest, warmest and coldest quarter based on BIOCLIM (Baldacchino et al., 2017; Cunze et al., 2016; Fischer et al., 2011; Moyne et al., 2015; Roche et al., 2015; Tilston et al., 2009).

Other meteorological conditions like precipitation also had a key role in the transmission and dynamics of the MBDs and/or their vectors. Of the articles, 19 (80%) used accumulated precipitation over a concrete

Table 2
Climatic and environmental features of the articles included in the review.

	Malaria and/or *Anopheles*			Dengue, chigungunya or Zika viruses and/or their vectors			West Nile virus and/or their vectors		
Variables	Studies which include these variables	Association	Prediction	Studies which include these variables	Association	Prediction	Studies which include these variables	Association	Prediction
Climatic variables									
Temperature	25, 26, 30, 32, 36, 37, 42, 46, 48, 54, 58	30(+), 46 (±)	25, 30, 32, 36, 37, 42, 46, 48, 54, 58	1, 3, 5, 6, 7, 13, 14, 16, 22, 24, 28, 33, 34, 44, 45, 51, 52, 53, 55, 56, 57, 59, 60, 61	3(+), 7(+), 14 (−), 33(+), 45 (+), 52(+), 53 (+), 57(+), 59 (+)	1,3,5,6,7,14,16,22,24,28,34,44,45,51,55,56,57,60,61	2, 4, 8, 9, 10, 11, 15, 18, 19, 20, 21, 23, 27, 29, 31, 43, 47, 49, 50	2 (+), 4(+), 8(+) (−), 11(+), 15(+), 18(+) (−), 20(+) (−), 21 (+), 27(+), 29(+), 43 (+), 49(+), 50(+)	2, 8, 9, 10, 11, 23, 29, 31, 50
Precipitation	26, 30, 32, 36, 48, 54, 58		32, 36, 54, 58	1, 3, 7, 13, 14, 16, 22, 24, 28, 33, 34, 44, 45, 51, 52, 53, 56, 59, 60, 61	7(+), 13(+), 14 (−), 59(+)	1,3,7,16,24,28,34,44,45,51,52,53,56,59,60,61	4, 8, 11, 15, 18, 19, 20, 21, 23, 27, 29, 31, 43, 49	8(+), 11(−), 15(+), 18(+) (−), 20(+), 27 (+), 29(+), 43(−)	8, 11, 23, 29, 31
Humidity	26, 32, 37		32, 37	16, 52			4, 20, 21, 47, 49	4(−), 20(+), 47(−), 49(−)	
Wind speed	32		32				4, 20, 47	4(−), 20(−)	
Evapotranspiration	32		32				11, 20	11(+), 20(+)	11
Daytime length				13, 52, 53, 60, 61	13(+), 52(+), 53 (+)	60,61	8, 10, 21, 47	21(+), 47(+)	8, 10
Other: vapor pressure, radiation, hydroclimatic balance	32		32				20, 47	20 (+)	
Environmental variables									
Vegetation/NDVI	25, 30, 32, 46	30(+), 46 (+)	25, 30, 32, 46	24			9, 10, 11, 15, 18, 19, 29, 47, 50	11(+), 29(+), 47(+)	10, 11, 29
Presence of standing water, wetlands or water bodies	35, 36, 38, 41, 46, 54	41 (+)	35, 36, 38, 54				2, 9, 15, 50	2(+), 50(+)	2, 9, 50
NDWI	46	46 (+)					9, 15, 18, 50	18(+), 50(+)	9, 50
Altitude	25, 42		25, 42	3, 7, 14, 24, 55, 56	7 (+)	3,7,14,24, 55, 56	10, 11, 15, 19, 20, 23, 29	19(−), 29(−)	10, 19, 23, 29
Land use	26, 32, 35, 36, 38, 46, 54	26(+), 38 (+), 46(+)	32, 35,36, 38, 46, 54	14, 44, 45, 59	14(+),45(+),59 (+)	14,44,45	15, 18, 19, 23, 29, 40, 47	15 (+), 18 (+), 47 (−)	23
Animal reservoirs/ migratory routes/animal density and/or protected areas (existence)							2, 9, 15, 23, 31, 50	50 (+)	9, 23, 31, 50
Distance to areas (protected, breeding sites, urban or aquatic)	38, 46	38(−), 46 (−)	38, 46				18, 19, 29, 31	19 (+)	19, 31
Population density	42			1, 3, 7, 14,16, 24, 57, 59, 61	3(+), 14(+), 61 (+)	1,3,7,14,16,24,61	9, 15, 19, 23, 50		9

(*continued on next page*)

Table 2 (*continued*)

	Malaria and/or *Anopheles*		Dengue, chigungunya or Zika viruses and/or their vectors		West Nile virus and/or their vectors	
Miscelaneous: tourism, contac with vector/ insect bites, migrants from endemic countries	26, 35, 37, 42	35, 37, 42	5, 34	5,34	4, 10, 19, 37, 40	10, 40
Climate change						
	58	58	6, 16, 22,28, 56, 57	6, 16, 22,28, 56, 57	9	9

1:(Erguler et al., 2017); 2(Sanchez-Gomez et al., 2017); 3:(Santos and Meneses, 2017); 4:(Stilianakis et al., 2016); 5:(Rocklov et al., 2016); 6:(Liu-Helmersson et al., 2016); 7:(Guzzetta et al., 2016); 8:(Marini et al., 2016); 9(Semenza et al., 2016):10:(Conte et al., 2015); 11:(Calzolari et al., 2015);;13:Roiz et al. (2015a); 14:(Roche et al., 2015); 15:(Marcantonio et al., 2015); 16:(Bouzid et al., 2014); 17:(Roiz et al., 2014); 18:(Rosa et al., 2014); 19:(Valiakos et al., 2014); 20:(Carrieri et al., 2014); 21:(Mulatti et al., 2014); 22:(Fischer et al., 2013); 23:(Mughini-Gras et al., 2014); 24:(Rogers et al., 2014); 25:(Sudre et al., 2013); 26:(Boccolini et al., 2012); 27:(Roiz et al., 2012); 28:(Caminade et al., 2012); 29:(Bisanzio et al., 2011); 30:(Lourenco et al., 2011); 31:(Rodriguez-Prieto et al., 2012); 32:(Sainz-Elipe et al., 2010); 33:(Roiz et al., 2010); 34:(Tilston et al., 2009); 35:(Linard et al., 2009); 36:(Capinha et al., 2009); 37:(Ponçon et al., 2008); 38:(Tran et al., 2008); 39:(Poncon et al., 2007); 40:(Tran et al., 2007); 41:(Merdic and Boca, 2004); 42:(Pergantas et al., 2017); 43:(Trájer A..J, 2017); 44:(Moyne et al., 2015); 45:(Baldacchino et al., 2017); 46:(Benali et al., 2014); 47:(Jian et al., 2014); 48:(Cailly et al., 2012); 49:(Paz et al., 2013); 50:(Tran et al., 2014); 51:(Tran et al., 2013); 52:(Zitko and Merdić, 2014); 53:(Toma et al., 2003); 54:(Gomes et al., 2016); 55:(Neteler et al., 2011); 56:(Fischer et al., 2011); 57:(Roiz et al., 2011); 58:(Bietolini et al., 2006); 59:(Manica et al., 2016); 60:(Cunze et al., 2016); 61 (Erguler et al., 2016).

period (Baldacchino et al., 2017; Bouzid et al., 2014; Caminade et al., 2012; Cunze et al., 2016; Erguler et al., 2017, 2016; Fischer et al., 2011; Guzzetta et al., 2016; Manica et al., 2016; Moyne et al., 2015; Roche et al., 2015; Rogers et al., 2014; Roiz et al., 2015a, 2010; Santos and Meneses, 2017; Tilston et al., 2009; Toma et al., 2003; Tran et al., 2013; Zitko and Merdić, 2014). Two of them found positive associations (Manica et al., 2016; Roiz et al., 2015a). In one article (Roiz et al., 2015a) heavy rain was associated with an increase in the abundance of the MV and consequently, on the risk of transmission of MBDs. In the other (Manica et al., 2016), the accumulation of rain in the previous weeks was associated with an increase in the abundance of the vector. One of the articles found a negative association with the levels of rainfall at the end of spring (Guzzetta et al., 2016). Another study found a negative association between the abundance of female *Ae. albopictus* and the rainfall accumulated in the previous 1 up to 4 weeks (Roche et al., 2015). In the remaining articles rain was a driver of the dynamics of the vector, as well as for the transmission of the disease (Baldacchino et al., 2017; Bouzid et al., 2014; Cunze et al., 2016; Erguler et al., 2017, 2016; Fischer et al., 2011; Guzzetta et al., 2016; Manica et al., 2016; Moyne et al., 2015; Rogers et al., 2014; Santos and Meneses, 2017; Tilston et al., 2009; Toma et al., 2003; Tran et al., 2013; Zitko and Merdić, 2014). The precipitation variables used were: accumulated precipitation, weekly (Roiz et al., 2010; Toma et al., 2003; Zitko and Merdić, 2014), daily (Erguler et al., 2016; Guzzetta et al., 2016; Manica et al., 2016; Tran et al., 2013), monthly (Bouzid et al., 2014; Fischer et al., 2013, 2011; Tilston et al., 2009), seasonal (Santos and Meneses, 2017), annual (Baldacchino et al., 2017; Caminade et al., 2012; Cunze et al., 2016; Erguler et al., 2017; Moyne et al., 2015; Roche et al., 2015; Rogers et al., 2014) or precipitation of wettest and driest month, precipitation of wettest, driest, warmest and coldest quarter, precipitation seasonality (Baldacchino et al., 2017; Cunze et al., 2016). Daytime length is another environmental variable used in 5 of the studies (Cunze et al., 2016; Erguler et al., 2016; Roiz et al., 2015a,b; Toma et al., 2003; Zitko and Merdić, 2014). In three of these it had a positive association with the dynamic of the vector and the transmission of the disease was reported (Roiz et al., 2015a; Toma et al., 2003; Zitko and Merdić, 2014), while in the others this variable was used as a driver (61,60). In one of these articles, the calculated photoperiod appeared to have a fairly limited role in the distribution of *Ae. albopictus* (Cunze et al., 2016). Land use has also been employed as a factor to determine the transmission of MBD and abundance of mosquitoes (Baldacchino et al., 2017; Manica et al., 2016; Moyne et al., 2015; Roche et al., 2015), with agricultural areas, semi-urban and urban areas proving the most suitable conditions for transmission (Roche et al., 2015), as well as artificial areas (Baldacchino et al., 2017) or small green islands (Manica et al., 2016). Human activity, measured by population density is also a key factor (Erguler et al., 2016; Roche et al., 2015; Santos and Meneses, 2017). Human activity is very important for the distribution of mosquitoes, and land use is an important factor for mosquitoes to become established (Roche et al., 2015). Other variables such as the number of commercial airplane flights from endemic countries (Rocklov et al., 2016) or the volume of passengers from those countries (Tilston et al., 2009) have also been used as determinants for the transmission of the disease (Table 2).

There were 6 articles that specifically addressed climate change and future *Ae. albopictus* presence in Europe (Caminade et al., 2012; Fischer et al., 2013), worldwide including Europe (Fischer et al., 2011) and the Region of Trentino-Alto Adige in Italy (Roiz et al., 2011) or both *Ae. albopictus* and *Ae. aegypti* in several European cities (Liu-Helmersson et al., 2016). Other study showed future of dengue incidence in Europe (Bouzid et al., 2014). They find a strong seasonality in dengue epidemic with a possible increase in epidemic potential with a south to north gradient by the end of 21st century (Liu-Helmersson et al., 2016), an increase in climatically suitable areas for the establishment of *Ae. albopictus* northward in Italy in 2040–50 (Roiz et al., 2011) and in western, central and eastern Europe, while decline in southern Europe by 2050 (Caminade et al., 2012) and until 2100 (Fischer et al., 2011).

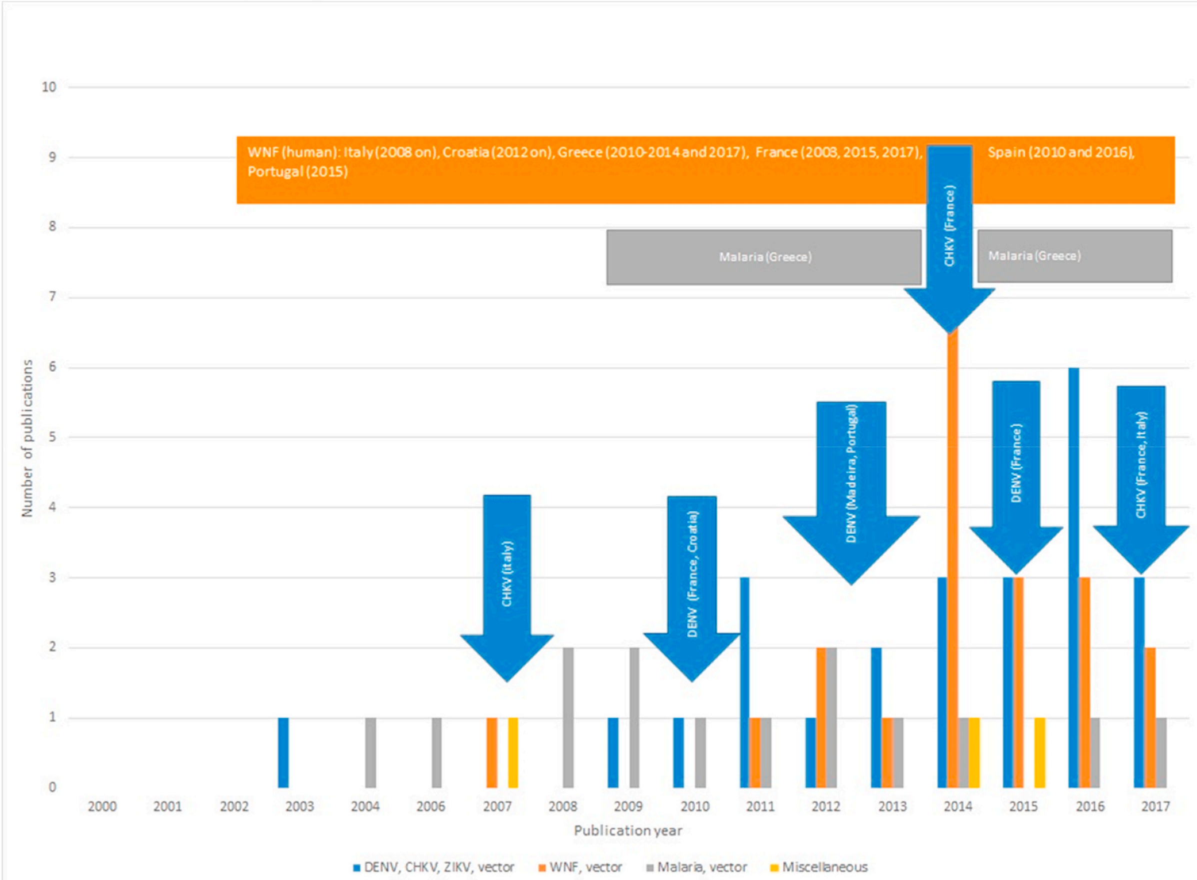

Fig. 2. Temporal distribution of articles included in the revision (n = 61) according to publication date, and outbreaks of chikungunya and dengue, and/or transmission of Malaria and West Nile fever in humans by country.

Finally, an increasing risk for DENV and CHIKV is predicted, especially around Mediterranean and Adriatic coasts or new areas and towards the end of 21st century (Bouzid et al., 2014; Fischer et al., 2013).

3.2. West Nile virus and its vectors

Twenty (32.8%) out of the 61 studies were about WNV and/or its vectors. Of these, 15 (75%) have been published since 2014, and none before 2007 (Fig. 2). Among the 20 studies, 9 (45%) were from Italy, 2 (10%) from Greece, 2 from Spain and 1 from France. A single article made predictions for the whole of Europe, and 5 (25%) included other countries from the Mediterranean basin from Asia and Africa, in addition to European countries (Table 1). Of them, 15 analysed associations (of which 7 made predictions), while the 5 remaining studies provided predictions. Association/correlation models (A/CM) were the most frequently used (n = 13) ((Calzolari et al., 2015; Carrieri et al., 2014; Manica et al., 2016; Marcantonio et al., 2015; Mughini-Gras et al., 2014; Mulatti et al., 2014; Paz et al., 2013; Roiz et al., 2012; Rosa et al., 2014; Sanchez-Gomez et al., 2017; Stilianakis et al., 2016; Trájer A..J, 2017; Tran et al., 2014, 2007; Valiakos et al., 2014) followed by predictive models (PMo) in 5 (Conte et al., 2015b; Mughini-Gras et al., 2014; Rodriguez-Prieto et al., 2012; Sanchez-Gomez et al., 2017; Tran et al., 2014) (Table 1).

Temperature (Table 2) was the most frequently used environmental variable, appearing in 19 of the 20 publications that dealt with WNF or its vectors (Bisanzio et al., 2011; Calzolari et al., 2015, 2015; Carrieri et al., 2014; Conte et al., 2015b; Jian et al., 2014; Marcantonio et al., 2015; Marini et al., 2016; Mughini-Gras et al., 2014; Mulatti et al., 2014; Paz et al., 2013; Rodriguez-Prieto et al., 2012; Roiz et al., 2012; Rosa et al., 2014; Sanchez-Gomez et al., 2017; Semenza et al., 2016; Stilianakis et al., 2016; Trájer A..J, 2017; Tran et al., 2014; Valiakos et al., 2014). In 13 of these articles, a positive association was found between an increase in temperature and the circulation of WNV or with the presence, abundance or rate of increase of the mosquito populations (Bisanzio et al., 2011; Calzolari et al., 2015; Marcantonio et al., 2015; Marini et al., 2016; Mulatti et al., 2014; Paz et al., 2013; Rodriguez--Prieto et al., 2012; Roiz et al., 2012; Stilianakis et al., 2016; Trájer A..J, 2017; Tran et al., 2014). Higher temperatures (increase of 1.5–2.5 °C respect to average T^a 18.5–21.5 °C from mid-April to June) can lengthen the vector's season and produce high population densities of adult mosquitoes, while overly low temperatures (decrease of 1.5–2.5 °C respect to average T^a 9.6–13.4 °C from mid-February to May) can reduce the season length and *Culex* adults density (Marini et al., 2016). Furthermore, an early increase in temperatures (weeks 8–19) is associated with an earlier start and a longer duration of the vector's activity season, and with a longer duration (Marini et al., 2016; Rosa et al., 2014). By contrast, a late (weeks 16–27) increase in temperatures (Rosa et al., 2014) or an increase in the month of July (Carrieri et al., 2014) can be associated with a decrease in the population density of mosquitoes. Of the 11 studies which made predictions, 9 included temperature as a key predictor (Bisanzio et al., 2011; Calzolari et al., 2015; Conte et al., 2015; Marini et al., 2016; Mughini-Gras et al., 2014; Rodriguez-Prieto et al., 2012; Sanchez-Gomez et al., 2017; Semenza et al., 2016; Tran et al., 2014)). Temperature variables included: minimum and maximum temperatures (Carrieri et al., 2014; Roiz et al., 2012) as well as any anomalies (Marcantonio et al., 2015; Paz et al., 2013; Semenza et al., 2016; Stilianakis et al., 2016; Tran et al., 2014), the 'growing degree days' during 15 days before (GDD: an indicator which is calculated

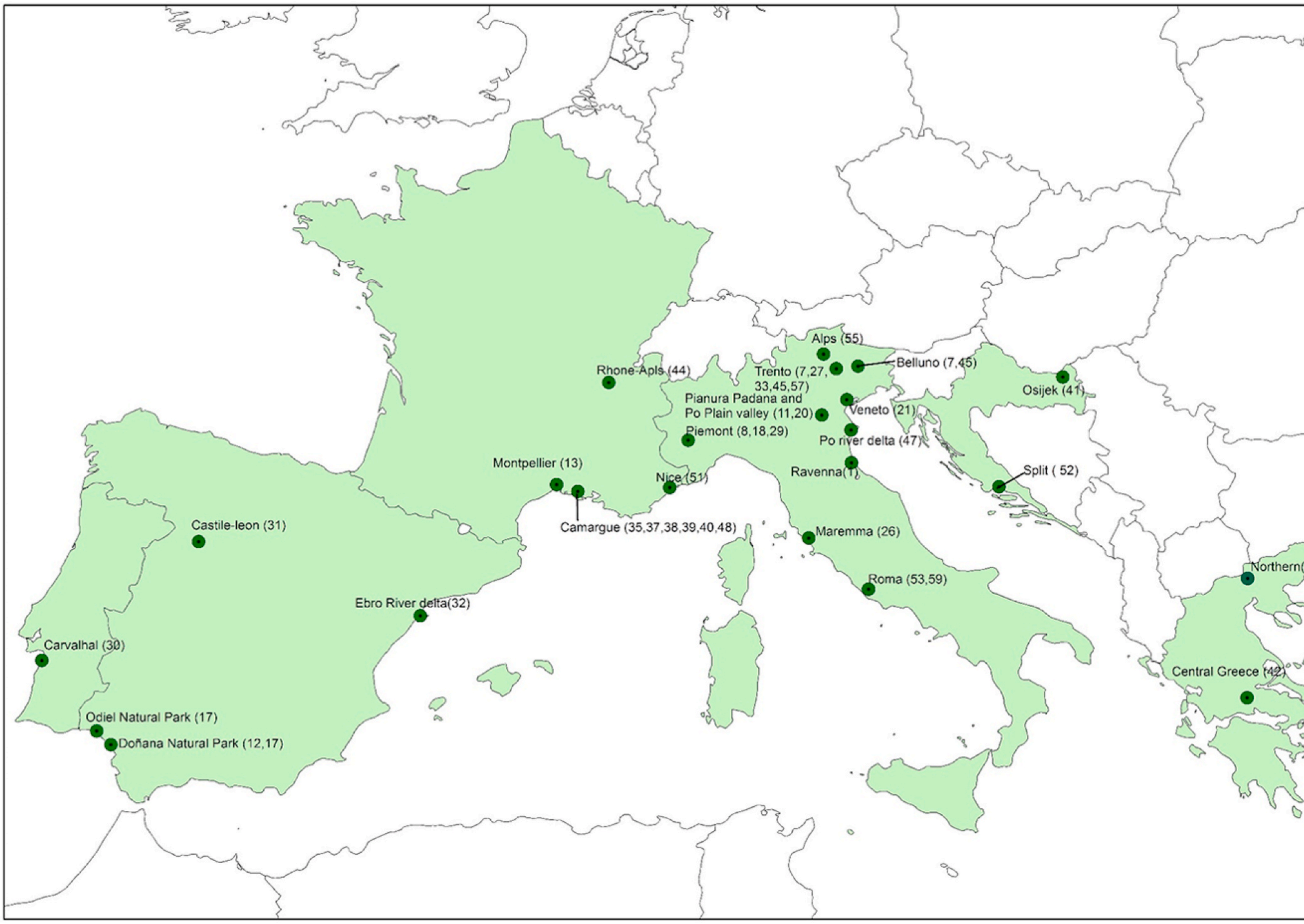

Fig. 3. Spatial distribution of articles by area*Multi-country papers are not included.

based on the temperature range within which mosquitos develop best: 13–33 °C) (Mulatti et al., 2014), mean daily temperature (Carrieri et al., 2014; Conte et al., 2015b; Marini et al., 2016; Roiz et al., 2012), weekly (Bisanzio et al., 2011; Rosa et al., 2014), monthly (Calzolari et al., 2015; Rodriguez-Prieto et al., 2012; Trájer A..J, 2017) or by season (Marcantonio et al., 2015; Sanchez-Gomez et al., 2017) and daily temperature range (Conte et al., 2015b), 'Growing degree weeks' (Rosa et al., 2014), annual mean temperature, mean diurnal range, maximum temperature of the warmest month, minimum temperature of the coldest month, mean temperature of the wettest, driest, warmest and coldest quarter (Mughini-Gras et al., 2014).

Precipitation was used in 14 out of 20 articles (Bisanzio et al., 2011; Calzolari et al., 2015; Carrieri et al., 2014; Marcantonio et al., 2015; Marini et al., 2016; Mughini-Gras et al., 2014; Mulatti et al., 2014; Paz et al., 2013; Rodriguez-Prieto et al., 2012; Roiz et al., 2012; Rosa et al., 2014; Stilianakis et al., 2016; Trájer A..J, 2017; Valiakos et al., 2014). Six articles found an association between precipitation and the population density of the vector or circulation of WNV (Bisanzio et al., 2011; Carrieri et al., 2014; Marcantonio et al., 2015; Marini et al., 2016; Roiz et al., 2012; Rosa et al., 2014). Precipitation in spring (Marcantonio et al., 2015; Marini et al., 2016), at the end of winter (Marcantonio et al., 2015), from May to September (Carrieri et al., 2014) or in a period prior to capturing the mosquitoes (Bisanzio et al., 2011; Roiz et al., 2012) was associated with an increase in adult mosquito population density or in the incidence of WNF. Early precipitation was related to a later start and shorter duration of the vector's season. By contrast, the mosquito season lasted longer when rain was late (Rosa et al., 2014). Other studies also found higher mosquito densities in the months with lower precipitation (April to October) (Calzolari et al., 2015) or a negative association between accumulated monthly precipitation and the number of WNF cases (Trájer A.J, 2017). Five of the 11 studies made predictions which used precipitation as a key predictor (Bisanzio et al., 2011; Calzolari et al., 2015; Marini et al., 2016; Mughini-Gras et al., 2014; Rodriguez-Prieto et al., 2012). The precipitation variables used were: accumulated precipitation some in previous days or weeks (Bisanzio et al., 2011; Mulatti et al., 2014; Roiz et al., 2012), anomalies in weekly (Stilianakis et al., 2016), monthly (Calzolari et al., 2015), or seasonal precipitation (Marcantonio et al., 2015) total seasonal precipitation (Marcantonio et al., 2015; Rodriguez-Prieto et al., 2012; Rosa et al., 2014), number of days with rain (Marini et al., 2016; Rosa et al., 2014), annual precipitation, precipitation of wettest and driest month, precipitation of wettest, driest, warmest and coldest quarter, precipitation seasonality (Mughini-Gras et al., 2014) and precipitation rate (Paz et al., 2013).

Nine studies used the normalized difference vegetation index (NDVI), a variable related to vegetation presence and photosynthetic activity (Bisanzio et al., 2011; Calzolari et al., 2015; Conte et al., 2015b; Jian et al., 2014; Marcantonio et al., 2015; Rosa et al., 2014; Semenza et al., 2016; Tran et al., 2014; Valiakos et al., 2014). Three studies found a positive relationship between NDVI and vector density (Bisanzio et al., 2011; Calzolari et al., 2015; Jian et al., 2014). Three of the 7 studies that made predictions used it as a key predictor (Bisanzio et al., 2011; Calzolari et al., 2015; Conte et al., 2015b). Altitude was considered in 7 studies (Bisanzio et al., 2011; Calzolari et al., 2015; Carrieri et al., 2014; Conte et al., 2015b; Marcantonio et al., 2015; Mughini-Gras et al., 2014; Valiakos et al., 2014). Low altitude was associated with WNF cases in both humans and birds (Valiakos et al., 2014), while an increase in altitude presented a negative association with the number of mosquitoes captured (Bisanzio et al., 2011). Altitude was a key predictor in 4 studies (Bisanzio et al., 2011; Conte et al., 2015b; Mughini-Gras et al., 2014; Valiakos et al., 2014). Seven studies used land use variables (Bisanzio et al., 2011; Jian et al., 2014; Marcantonio et al., 2015; Mughini-Gras et al., 2014; Rosa et al., 2014; Tran et al., 2007; Valiakos et al., 2014), of which 2 found a positive association between the percentage of irrigated land and/or forests (Marcantonio et al., 2015), or the proximity of rice paddies with the vector's population density (Rosa et al., 2014), another found a negative association with the distance to rice paddies (Jian et al., 2014) and 1 used this as a key predictor (Mughini-Gras et al., 2014). Five studies used humidity (Carrieri et al., 2014; Jian et al., 2014; Mulatti et al., 2014; Paz et al., 2013; Stilianakis et al., 2016) with divergent results as to whether the association was positive (Carrieri et al., 2014) or negative (Jian et al., 2014) with the density of the local mosquito population or with the circulation of WNV (Stilianakis et al., 2016). In a study that was carried out across 8 Mediterranean counties, this negative association was only found in specific regions (Paz et al., 2013). The presence of wetlands or marshes was used in 4 articles (Carrieri et al., 2014; Marcantonio et al., 2015; Sanchez-Gomez et al., 2017; Semenza et al., 2016), 2 of which found a positive association with the circulation of the virus (birds, mosquitoes, mammals) (Sanchez-Gomez et al., 2017), or with WNF cases in humans (Tran et al., 2014), and in 3 it was a key predictor (Sanchez-Gomez et al., 2017; Semenza et al., 2016; Tran et al., 2014). Normalized Difference Water Index (NDWI) was used in 4 studies (Marcantonio et al., 2015; Rosa et al., 2014; Semenza et al., 2016; Tran et al., 2014) of which 2 found positive association between high NDWI in the early part of the year and an early start to and prolonged duration of the vector's season (Rosa et al., 2014) or with the presence of WNF cases (Tran et al., 2014), and one found a negative association with case incidence (a reduction in NDWI in spring and the start of summer was associated with an increase in cases (Marcantonio et al., 2015). NDWI was used as a key predictor in 2 studies (Semenza et al., 2016; Tran et al., 2014). The number of daylight hours was used in 4 studies (Conte et al., 2015b; Jian et al., 2014; Marini et al., 2016; Mulatti et al., 2014) of which two found a positive association with the growth rate (Mulatti et al., 2014) or population density of the mosquito (Jian et al., 2014) In the other two studies, the variable was used as a key predictor (Conte et al., 2015b; Marini et al., 2016). Wind speed was used in 3 studies (Carrieri et al., 2014; Jian et al., 2014; Stilianakis et al., 2016), of which two found a negative association with the number of human cases of WNF and the presence of mosquitoes infected with WNV or with the mosquito population density (Carrieri et al., 2014; Stilianakis et al., 2016). Evapotranspiration was used in 2 studies, which found positive associations with the density of the vector (Calzolari et al., 2015; Carrieri et al., 2014). Hydroclimatic balance was used in one study (Carrieri et al., 2014) which found an association with the dynamic of the vector.

In addition, other studies considered variables related to populations or migratory habits of vertebrate animals: protected areas for birds (Marcantonio et al., 2015; Sanchez-Gomez et al., 2017), an east or west pattern for the routes used by migratory birds (Semenza et al., 2016; Tran et al., 2014), animal population density: birds, horses and others (Mughini-Gras et al., 2014; Rodriguez-Prieto et al., 2012). A positive association was found between birds' eastward migratory routes and the presence of human cases in Mediterranean countries (Tran et al., 2014). Furthermore, some studies used migratory routes as key predictors (Semenza et al., 2016; Tran et al., 2014) as well as horse and bird populations (Mughini-Gras et al., 2014; Rodriguez-Prieto et al., 2012). Distances from points where mosquitoes or infected birds have been captured to urban (Bisanzio et al., 2011; Rosa et al., 2014; Valiakos et al., 2014) or aquatic areas (Rodriguez-Prieto et al., 2012; Valiakos et al., 2014) have also been used. A positive association was found between infected birds and distance to aquatic areas (Valiakos et al., 2014), which was a key predictor in 2 studies (Rodriguez-Prieto et al., 2012; Valiakos et al., 2014). Although no association was found, population density was used in 5 articles (Marcantonio et al., 2015; Mughini-Gras et al., 2014; Semenza et al., 2016; Tran et al., 2014; Valiakos et al., 2014) and it was used as a key predictor in one study (Semenza et al., 2016). Other variables such as 'slope aspect' (Conte et al., 2015b; Stilianakis et al., 2016; Valiakos et al., 2014) or flood-prone areas (Tran et al., 2007) were considered key predictors in some studies (Conte et al., 2015a; Tran et al., 2007).

There was only one article that specifically addressed climate change and future WNV transmission (Semenza et al., 2016), which modelled and projected prevalence of infection for 2025 and 2050 in Europe. It revealed a progressive expansion of areas with elevated probability for WNV infections, particularly at the edges of the transmission areas (e.g.: northern Serbia, central Hungary, north-eastern Greece, eastern and western Romania and north-western Turkey).

3.3. Malaria and/or its vectors

14 (23.0%) of the articles studied malaria or *Anopheles* spp. at a local scale, including studies from France (4), Portugal (4), Greece (2), Italy (2), Spain (1) and Croatia (1). We did not find any articles at a global scale, nor at European level (Table 1). Of them, 5 articles searched for associations/correlations (A/CM) between environmental or climatic variables and the disease or its vectors (Benali et al., 2014; Boccolini et al., 2012; Lourenco et al., 2011; Merdic and Boca, 2004a; Tran et al., 2008) and 9 produced predictive models (PMo) (Bietolini et al., 2006; Capinha et al., 2009; Gomes et al., 2016; Linard et al., 2009; Lourenco et al., 2011; Ponçon et al., 2008; Sudre et al., 2013) and/or for transmission risk (TM, A/D/DPM, SM)) (Benali et al., 2014; Cailly et al., 2012; Gomes et al., 2016; Pergantas et al., 2017; Sainz-Elipe et al., 2010), (Table 1).

In 6 of the articles the response variable was the risk/suitability of malaria reemergence/transmission (Gomes et al., 2016; Linard et al., 2009; Pergantas et al., 2017; Ponçon et al., 2008; Sainz-Elipe et al., 2010; Sudre et al., 2013) while 8 used variables related to the vector: abundance/density of *Anopheles* (Benali et al., 2014; Boccolini et al., 2012; Cailly et al., 2012; Lourenco et al., 2011; Merdic and Boca, 2004), and presence/absence of the vector (Bietolini et al., 2006; Capinha et al., 2009; Tran et al., 2008).

All but one of the articles (Sudre et al., 2013) used data related to the vector. Species considered in these studies varied according to the geographical distribution of the *Anopheles* vectors: *Anopheles labranchiae* (Boccolini et al., 2012) in Italy, *Anopheles atroparvus* (Benali et al., 2014; Capinha et al., 2009; Gomes et al., 2016; Lourenco et al., 2011; Sainz-Elipe et al., 2010) in Portugal and Spain, *Anopheles hyrcanus* (Linard et al., 2009; Ponçon et al., 2008; Tran et al., 2008) in France and *Anopheles maculipennis complex* (Bietolini et al., 2006; Cailly et al., 2012; Merdic and Boca, 2004a; Pergantas et al., 2017) in Croatia, France, Greece, and Italy.

The most used variable in the studies of malaria and its vectors was temperature (n = 10; 71.4%), being in all cases used as a predictive variable (Benali et al., 2014; Bietolini et al., 2006; Cailly et al., 2012; Capinha et al., 2009; Gomes et al., 2016; Lourenco et al., 2011; Pergantas et al., 2017; Ponçon et al., 2008; Sainz-Elipe et al., 2010; Sudre et al., 2013). Relationships reported varied among studies, with one article showing a positive association between temperature and mosquito density (Lourenco et al., 2011) and another one showing both negative and positive associations. In this last case, these contrasting results were found when considering the upper and lower limits, finding an optimum temperature range for the vector ranging from 19 to 25 °C (Benali et al., 2014). Temperature variables used were: daily temperature (Cailly et al., 2012; Lourenco et al., 2011; Ponçon et al., 2008; Sudre et al., 2013), average temperatures (Pergantas et al., 2017; Ponçon et al., 2008), annual variation (Sudre et al., 2013), annual mean temperature, maximum temperature of the warmest month/trimester/quarter, and minimum temperature of the coldest month/trimester/quarter (Benali et al., 2014; Bietolini et al., 2006; Capinha et al., 2009; Gomes et al., 2016; Sainz-Elipe et al., 2010). Land use was used as a variable in 7 articles, using it to infer predictions in 4 articles (Capinha et al., 2009; Gomes et al., 2016; Linard et al., 2009; Sainz-Elipe et al., 2010). In 2 of these they found an association between land use and the presence of vectors (Benali et al., 2014; Tran et al., 2008), but only one found a positive association between the area used for rice cultivation and the distribution and abundance of the vector (Boccolini et al., 2012). Presence of still water or bodies of water was used as a variable in 5 articles. This was employed in 4 in order to make predictions (Capinha et al., 2009; Gomes et al., 2016; Linard et al., 2009; Tran et al., 2008), and the 1 remaining article found a correlation between water levels and *Anopheles* abundance (Merdic and Boca, 2004). Furthermore, 4 articles used vegetation or normalized difference vegetation index (NDVI) in order to make predictions (Benali et al., 2014; Lourenco et al., 2011; Sainz-Elipe et al., 2010a; Sudre et al., 2013); two of these found a positive association between this variable and the density of *An. atroparvus* (Benali et al., 2014; Lourenco et al., 2011). On the other hand, we found 4 articles that used precipitation as a variable to make predictions (Benali et al., 2014; Lourenco et al., 2011; Sainz-Elipe et al., 2010; Sudre et al., 2013). For precipitation, the variables used were: annual precipitation, precipitation during wettest month, precipitation during driest month (Bietolini et al., 2006), mean total annual precipitation (Capinha et al., 2009; Gomes et al., 2016), and monthly and annual precipitation (Sainz-Elipe et al., 2010. Relative humidity (%) was used as a predictor of malaria re-emergence risk in two specific areas of Spain (Ebro Delta) (Sainz-Elipe et al., 2010) and France (The Camargue) (Poncon et al., 2007) (37). Other variables used in the articles were humidity (Boccolini et al., 2012; Poncon et al., 2007; Sainz-Elipe et al., 2010) NDWI, positively associated to vector density, altitude (Pergantas et al., 2017; Sudre et al., 2013), wind speed (Sainz-Elipe et al., 2010), evapotranspiration (Sainz-Elipe et al., 2010), vapor pressure (Sainz-Elipe et al., 2010), radiation (Sainz-Elipe et al., 2010), distance to the nearest rice field (Tran et al., 2008), population density (Pergantas et al., 2017), tourism and people-vector contacts (Linard et al., 2009), bites (Ponçon et al., 2008), number of migrants from malaria endemic countries (Pergantas et al., 2017), and distance to breeding sites (Benali et al., 2014).

The 4 articles from France were focused on the Camargue and found that the risk of malaria re-emergence is low (Linard et al., 2009), although possible, with the highest risk during August (Cailly et al., 2012; Ponçon et al., 2008). The variables associated with the presence of the vector were temperature (Ponçon et al., 2008) and land use (Tran et al., 2008). In the two articles from Greece, they found that the risk of malaria transmission in Greece is potentially substantial, both in rural and urban areas, highlighting coastal regions, and areas close to lakes and rice paddies (Pergantas et al., 2017). The areas which are ideal for transmission are characterized by low altitudes, warmer temperatures and intensive agriculture which is irrigated throughout the year (Sudre et al., 2013). With respect to Portugal, the results suggest that there is already a risk of transmission, and that the current environmental conditions are suitable for the vectors' development (Benali et al., 2014; Capinha et al., 2009; Gomes et al., 2016; Lourenco et al., 2011). This suggests that the distribution of the vector in this area is still similar to the last endemic period (Benali et al., 2014; Capinha et al., 2009). Vegetation indices are associated with the presence of the vector (Benali et al., 2014; Lourenco et al., 2011). In Italy, there has been a reduction in the prevalence of the vector. However, in the coastal rice production areas there are high levels of vector reproduction during the warm season, and the population levels of the vectors continues to be epidemiologically significant (Boccolini et al., 2012). In Spain the current transmission risk of malaria covers from May to September for *P. falciparum*, and from May to October for *P. vivax*. The Ebro Delta have appropriate environmental conditions allowing malaria transmission (Collantes et al., 2014). Finally, in Croatia high water levels across a long time period were found to provide conditions that helped maintain continuous mosquito reproduction (Caminade et al., 2012).

There was one article that specifically addressed climate change and future suitability areas for *An. maculipennis* complex in Italy (Bietolini et al., 2006). They found a general decrease in its distribution for 2041–2060, with *An. atroparvus* moving towards north-east locations, *An. labranchiae* conquering central sites and a likely extinction of *An. sacharovi*.

3.4. Various mosquito genera

Three articles (Poncon et al., 2007; Roiz et al., 2015b, 2014) found associations between climatic and environmental variables and different genera of mosquitoes. In one of them, developed in Southern Spain, authors used as response variables the presence, abundance and diversity (yearly and annual) of 7 mosquito species potential vectors of WNV and other pathogens (Roiz et al., 2015b). The environmental variables they analysed were hydroperiod (annual), normalized difference vegetation index (NVDI), and area of inundation (monthly). The study found both positive and negative associations between these variables, depending on the mosquito species analysed and concluded that environmental variables significantly affect the distribution and abundance of mosquitoes, and potentially the risk of MBD transmission. An additional study conducted in the same area in Spain (Roiz et al., 2014) analysed the seasonal and annual abundance of mosquitoes of 7 species. The climatic variables associated were temperature (mean, maximum, minimum; mean weekly temperature), precipitation (weekly total), tide height (mean weekly values), relative humidity (mean, maximum and minimum; weekly mean values) and photoperiod (hours of daylight during the study period; mean weekly values). In addition, they made predictions using the temperature and precipitation values projected for the next century. The last study was conducted in Camargue (France) (Poncon et al., 2007) where authors found correlations between the abundance of different mosquito species and the temperature and precipitation (daily averages).

4. Discussion

This study presents the first systematic review to identify the possible relations between MBDs, their vectors and climatic or environmental factors in six countries from southern Europe. We focused on countries which share similar climatic characteristics. This review provides complete information about the data published between 2000 and 2017 which may well be essential for the control and prevention of these diseases.

The number of studies conducted during the last years has increased, probably because we are dealing with emerging diseases that have produced outbreaks in all the studied countries since 2000. The colonization by invasive mosquito species have made possible many of such outbreaks (Calba et al., 2017; Delisle et al., 2015; ECDC, 2014; Monge et al., 2020; Succo et al., 2016; Tomasello and Schlagenhauf, 2013; Venturi et al., 2017). This appears to correspond to the publication years of the included articles – mostly since 2014 – which deal with *Aedes* or the diseases which it transmits. The six countries included in this review have reported human WNF cases, with small self-limiting events or more extensive outbreaks, like in Italy, Croatia and Greece. All of the countries have produced studies which have been included in this review, except Portugal. This is probably because, until now, Portugal is the country which has the lowest number of WNF cases in humans. At the other extreme is Italy, particularly the northern regions, which have had a great number of cases; consequently, there are studies that relate the disease and its vectors with environmental factors. There have also been cases of introduced malaria in Italy, France and Spain ("Rapid risk assessment," 2017; Romi et al., 2012; Velasco et al., 2017). Greece is the more worrying case, with transmission occurring each year since 2009, with the exception of 2014 (*Epidemiological surveillance report Malaria in Greece, 2017*, 2017).

The southern European countries included in this review share some climatic characteristics, although there is still great diversity in conditions between regions. According to Koppen (AEMET, n. d.), these countries share middle latitude or temperate climates (warm temperate) although within each country clear differences occurs according to seasonal rainfall levels, and summer temperatures (Peel et al., 2007). In this respect, the meteorological changes and variations in parameters like temperature, humidity and precipitation can affect the spatio-temporal distribution of many climate-sensitive infectious diseases. This is the case of MBDs, which have different impacts and spatio-temporal scales. According to the technical document from the European Centre for Disease Prevention and Control (ECDC), 'Climate Change and communicable diseases in the EU member States', the diseases transmitted by vectors have their mode of transmission linked to, or sensible to, climate changes and meteorological oscillations. These factors can change their geographical pattern, their seasonality, incidence or prevalence, should there be climate changes or extreme meteorological or environmental events. ("Contribution of Working Group I to the Fourth Assessment Report of the Intergovernmental Panel on Climate Change, 2007," n. d.). In addition, the World Meteorological Organization has confirmed a warming climate in Europe and Eurasia (Paz et al., 2013). For this reason, it is crucial to quantify the association between meteorological factors and the risk of transmission in order to build predictive models based on the meteorological forecasts. One of the key results of this study is that temperature is a key factor to be able to understand MVs' abundance and expansion in the territory studied. Altogether, these studies support the importance of temperature affecting the population dynamics of both invasive and native MV of MBDs. Furthermore, in the case of the articles which did not include temperature, have included other factors that directly depend on temperature or have a high level of correlation with it (Linard et al., 2009; Merdic and Boca, 2004a; Tran et al., 2008, 2007), vegetation indices (Roiz et al., 2015b) or rainfall (Caminade et al., 2012). In fact, the studies analysed confirm that rainfall is another key factor for explaining vector abundance due to its impact on the reproduction and survival of the mosquitoes. Other environmental factors identified as related to the distribution and abundance of the vectors include land use – obtained from the Corine Land Cover database for 2000 and 2012 – as well as vegetation indices generated from satellite imagery – such as the Normalized Difference Vegetation Index (NVDI). Human population density, although not the focus of this review, also seems to be a determining factor in the distribution of the vectors. Epidemiological studies consider that geographical variables play an essential role in the transmission of these diseases, as they depend on the spatial density of both humans and vectors (Chevalier et al., 2014).

With regards to the quality of the studies, we have already seen that all of the articles rated well against the pre-established quality criteria. This is almost certainly due to the fact that the criteria for inclusion in the review were restrictive at the onset, and aimed at finding high quality original articles about the topic of this study.

4.1. Dengue, chikungunya, Zika and/or their vectors

Environmental characteristics are known to play a key role in the expansion of *Ae. albopictus*. Given the diverse climatic conditions in Europe and the climate changes that are occurring, it is very important to know the current limits of the mosquitoes' spread in order to predict their future expansion. For these reasons, most studies focus on analysing the potential distribution of the vector based on suitability of the climatic conditions. Almost 80% of the articles on *Ae. albopictus* or the diseases transmitted by this mosquito species make predictions about its future spatial distribution. This may be because the vector is already established in the countries of southern Europe and it is probably only a matter of time before they expand into bordering countries. Temperature seems to be the most important factor for the establishment and dynamics of *Ae. albopictus.* Winter temperatures limit its distribution range to areas with temperatures above 0 °C to allow egg survival and the emergence of adults from diapause eggs after the winter (Thomas et al., 2012). In addition, it is required an average annual temperature above 11 °C for adults to survive and be active (Caminade et al., 2012), while the optimal summer temperature for vector establishment ranges from 25 to 30 °C (Cunze et al., 2016), which are common conditions found in countries in the Mediterranean basin. *Ae. aegypti* requires warmer climates than *Ae. albopictus*; however, it can establish itself in regions of Europe that have a humid sub-tropical climate ("*Aedes aegypti* - Factsheet for experts," n. d.). Not only temperature but also precipitation is closely related to mosquito establishment and abundance. A minimum of 500 mm of rain annually is necessary to maintain the aquifers that facilitate the mosquitoes' reproduction (Caminade et al., 2012), but also during the summer, as a guarantee for aquatic habitats maintenance. Its high intensity has also been associated with the increasing in mosquito abundance (Manica et al., 2016; Roiz et al., 2015a) and, furthermore, with a higher risk of transmission of CHIKV following flooding (Roiz et al., 2015a). In this case accumulated rain before captures was found to be more important than temperature for the abundance of the *Aedes* mosquitoes. On the other hand, rainfall at the end of spring is negatively associated with vectors abundance, which indicates a possible washing effect on the larvae (Guzzetta et al., 2016). Daytime length, which is a variable related with the development of the mosquito and a key factor for the eggs' survival showed a positive association with vector dynamics and MBDs transmission. Different variables related to land use have been proved to be suitable habitats for mosquito development, as they provide humidity and temperature favourable conditions (Baldacchino et al., 2017; Manica et al., 2016; Moyne et al., 2015; Roche et al., 2015). The most likely scenario for the late 21st century seems to be a movement of *Ae. albopictus* towards future suitable areas that are currently free and an increasing risk for *Aedes*-borne diseases in some areas.

4.2. West Nile fever

WNF is an emerging disease in Europe and Mediterranean countries, mainly transmitted by widely distributed mosquitoes of the genus *Culex*. In the European Union it has been a notifiable disease since 2008, and it is monitored in both humans and horses. It appears to have been expanding during the last few years in the area (Chancey et al., 2015). Until 2017, the countries with the highest numbers of cases were Greece, Italy, Romania and Hungary (ECDC, n. d.). Almost half out of the 20 articles included in this review were from Italy, mostly from northern regions. Six of the studies included a number of Mediterranean countries, not just European, with active WNV circulation, mainly focused on humans. This probably reflects a greater concern in some of the most affected areas along with the perception of the need for an integrative approach to address the management of this disease beyond the borders of the countries and continents.

It is of great concern the vector's distribution and abundance (suitability, density, vector dynamics), as all the articles focus on studying them. Temperature is one of the most important variables and determines both the start-point and the duration of the vector's season (Carrieri et al., 2014; Marini et al., 2016; Rosa et al., 2014) and also is associated with mosquitoes' population density (Marini et al., 2016). There is an optimal known range of temperatures (25–35 °C) for the mosquitoes to develop (Mulatti et al., 2014), and *Culex pipiens* embryonic development cannot be completed below 7 °C. Both larval development and adult survival are shorter at higher temperatures (Conte et al., 2015; Loetti et al., 2011; Marini et al., 2016), being the highest survival at 25 °C. These are important aspects to make predictions of mosquitoes and disease dynamics, seasonality and new suitable areas, useful to establish risk assessment. On the other hand, the presence and density of the vector are essential for the virus's transmission between reservoirs (birds) and horses or humans (Martinez de la Puente et al., 2018). The temperature, therefore, exerts an indirect effect on the intensity and duration of the outbreaks (Marcantonio et al., 2015) and might be a good predictor of its occurrence. Variables associated to the presence of a suitable aquatic habitat required for the reproduction of the mosquitoes are also important determinants. This includes rainfall at the appropriate time (Bisanzio et al., 2011; Carrieri et al., 2014; Marcantonio et al., 2015; Marini et al., 2016; Roiz et al., 2012; Rosa et al., 2014), the Normalized Difference Water Index (Bisanzio et al., 2011; Calzolari et al., 2015; Jian et al., 2014), humidity (Carrieri et al., 2014; Jian et al., 2014), presence of wetlands or certain land uses (rice paddies, irrigated land) (Jian et al., 2014; Marcantonio et al., 2015; Rosa et al., 2014; Sanchez-Gomez et al., 2017; Tran et al., 2008) which may be related not only with MV presence but also with suitable habitats for birds and create ideal areas to maintain enzootic cycles of WNV transmission. Additional environmental factors, including land use and urbanization may have also major effects on the vector abundance and community composition (Ferraguti et al., 2016). These variables are also indicators of an appropriate ecosystem for mosquitoes to interact with their blood meal sources, which include birds, the main reservoirs of WNV, and dead-end hosts such as human or horses. In this context, the presence of WNV closes the circle and provides the necessary conditions to establish the WNF cycle, where infected mosquitoes may enter in contact to humans. The differences of WNF incidence rates among European Mediterranean countries with similar weather conditions could be explained by differences in the human interaction with suitable habitats such as wetlands or flooded fields. There are other local factors which could intervene. For instance, regional differences in mosquito species distribution and vector competence might be crucial. The paper of ornithophilic mosquitoes play an important role in maintaining and amplifying the zoonotic presence of VNV, as the so-called “bridge” mosquitoes play a role in the human WNF, as they can feed on both birds and mammals (Brugman et al., 2018) The occurrence and rate of hybrid populations of *Cx pipiens* complex has also been associated to different risk transmission in Europe (Vogels et al., 2017, 2016). Furthermore, migratory birds in important not only by the fact of being a reservoir but also for the possibility of introducing new virus lineages or strains.

WNF is likely to spread in the future, increasing the size of the current areas with greatest risk.

4.3. Malaria and its vectors

With regard to malaria, factors such as the presence of appropriate vectors and climatic conditions, and high frequency of human movements from malaria endemic countries may favour the reintroduction of the disease in the studies countries. In the last decade autochthonous vector-borne cases have been reported in several European countries, mainly in Greece due to *P. vivax* (Piperaki and Daikos, 2016). One of the determinant variables to estimate the presence of the vector and the possible re-emergence is temperature. This is because of temperature’s influence on the physiology, behaviour and lifecycle of *Anopheles* mosquitoes. (Cambournac and Hill, 1938; Hutchinson, 2004; Kuhn et al., 2002; Sandholt et al., 2002). Temperature is also known to limit *Plasmodium* sporogony, being the optimal temperature ranges 16 or 18–33 °C for *P. vivax* and *P. falciparum*, respectively. Regarding *Anopheles,* there are different species in Europe, varying by location, which have undergone changes during the last century (Piperaki and Daikos, 2016), so that their optimal environmental conditions might be species dependent and regionally studied. On the other hand, precipitation correlates with the productivity of mosquito breeding sites, affecting the availability and characteristics of the habitats of *An. atroparvus* in the aquatic phase of its life cycle (Paaijmans et al., 2007). In addition, the presence of vectors is linked to the presence of water or the existence of rice paddies. The variable presence of still water or bodies of water has also been associated with the aquatic lifecycle of *Anopheles* mosquitoes and land use also plays an important role in the development of these species (Dale and Knight, 2008; Minakawa et al., 2005; Pope et al., 1994; Sainz-Elipe et al., 2010; Shililu et al., 2003). The Normalized Difference Vegetation Index (NDVI), which is closely related to land use and still water, was used in 4 articles – which considered it as a proxy for suitable conditions for the insects’ habitat.

4.4. Model

Geographical Information Systems, spatial analysis and spatial modelling, as well as satellite imaging to obtain environmental and climatic variables are key for being able to make predictions related to specific territories. The rapid advance in these technologies during the last few years has allowed the development of new models. This has provided opportunities to represent spatial data in different ways, in particular enabling researchers to combine and superimpose different geographical layers; these relate to fundamental elements of the transmission process (Chevalier et al., 2014). 75% of articles included in this study presented the results of their models on maps. These included maps of probability, risk or habitat suitability for the presence of the vector or the disease; maps of risk under different future climate change scenarios; or maps of mosquito abundance and density.

The models used were very diverse, so they have been classified into 4 broad groups. Association and correlation models (A/CM) were the most frequently used, followed by predictive models (PMo), for their capacity to evaluate the risk associated with ecological variables in an area, and their ability to identify relevant niches for different species (Guisan and Zimmermann, 2000). The results of the applied models in the articles studied help to identify the principal factors that are related to the vector or the disease; this enables the integration of these factors into predictive spatial models as well as dynamic models. In all of the studies, although they do not generally provide a statistical value, they consider these factors as predictive variables, and measure statistically to what extent each contributes to an explanation of the spatial distribution of risk. Among these 4 general groups in which we classified the models, there is a wide variability of statistical and methodological approaches. The majority of them are ecological models using environmental variables or drivers for the mosquitoes’ or diseases’ distribution. Regarding climate change studies, the methodology proposed use different climate change scenarios (from the most conservative to most catastrophists taking into account different greenhouse gas emission pathways) with diverse approach and temporal windows, making them difficult to compare.

4.5. Limitations

In spite that summarise valuable information on MBDs research in southern Europe, this study has some limitations. The inclusion criteria may have resulted in an underestimation in the number of articles, particularly in specific areas. On the one hand, the language criteria may exclude studies published in Greek or Croatian. On the other hand, the non-inclusion of some European countries with WNV circulation may also have excluded relevant literature on this disease and its vectors. However we accessed the full text of almost all the articles via subscriptions to universities and scientific platforms, limiting the potential loose of relevant references. We consider that the number and representativeness of articles in the non-included languages is likely to be small, and that those countries where WNV is currently endemic circulation do not share environmental, climatic and geographical characteristics with the countries included in this review. With respect to the search strategy, its complexity – including a variety of different diseases and mosquito species – could have resulted in a failure to identify some articles. However, as the principles and guidelines established by PRISMA were strictly followed, using a systematic and explicit methodology, the number should be low. Lastly, it was necessary to produce criteria to evaluate the methodological quality of the articles; this was because there are not available tools to determine the quality of these kinds of studies, many of which are not observational. The majority of studies included in the review are ecological studies and their main weakness is that of their approach: it cannot be stablished a cause-effect relationship between mosquito (presence or dynamics) or disease and environmental variables. Another important point is that is not easy to make long-term reliable predictions. On the other hand experimental studies are not feasible to understand environmental factors in relation to distribution of mosquitoes or diseases. They are easy to carry on, there are multiple organizations working and providing data and they may provide useful information.

5. Conclusion

The number of publications focused on MBDs is increasing in recent years, reflecting the increased interest in MBD in southern European countries. Climatic variables, like temperature and rainfall, and environmental variables like land use, and vegetation, among others, are key factors related to determine mosquitoes' presence, abundance and dynamics and also for incidence of MBDs in the studied area. As a consequence, they also are a proxy for the risk of emergence and/or spread of emergent diseases, and allow to quantify potential spatial distribution of the vector and/or disease. Spatial models appear to be those most used to analyze the problem.

The variations in vector presence and abundance and seasonality associated with meteorological factors and climate change highlights the need to extreme surveillance and vector control in the years and regions with positive temperature anomalies.

The results of this review can be useful for future studies related to MBDs and/or their vectors, and can be of use when making public health related decisions, as well as when carrying out interventions aimed at controlling these diseases. This study represent a starting point for future investigation into MBDs in the countries studied. This could include both targeting resources and efforts to reduce disease burden and the presence of the vector, as well as improving public health measures in relation to emerging diseases.

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Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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