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Using global maps to predict the risk of dengue in Europe

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ABSTRACT

This article attempts to quantify the risk to Europe of dengue, following the arrival and spread there of one of dengue's vector species *Aedes (Stegomyia) albopictus*. A global risk map for dengue is presented, based on a global database of the occurrence of this disease, derived from electronic literature searches. Remotely sensed satellite data (from NASA's MODIS series), interpolated meteorological data, predicted distribution maps of dengue's two main vector species, *Aedes aegypti* and *Aedes albopictus*, a digital elevation surface and human population density data were all used as potential predictor variables in a non-linear discriminant analysis modelling framework. One hundred bootstrap models were produced by randomly sub-sampling three different training sets for dengue fever, severe dengue (i.e. dengue haemorrhagic fever, DHF) and all-dengue, and output predictions were averaged to produce a single global risk map for each type of dengue. This paper concentrates on the all-dengue models. Key predictor variables were various thermal data layers, including both day- and night-time Land Surface Temperature, human population density, and a variety of rainfall variables. The relative importance of each may be shown visually using rainbow files and quantitatively using a ranking system. Vegetation Index variables (a common proxy for humidity or saturation deficit) were rarely chosen in the models. The kappa index of agreement indicated an excellent (dengue haemorrhagic fever, Cohen's kappa = 0.79 ± 0.028 , AUC = 0.96 ± 0.007) or good fit of the top ten models in each series to the data (Cohen's kappa = 0.73 ± 0.018 , AUC = 0.94 ± 0.007 for dengue fever and 0.74 ± 0.017 , AUC = 0.95 ± 0.005 for all dengue). The global risk map predicts widespread dengue risk in SE Asia and India, in Central America and parts of coastal South America, but in relatively few regions of Africa. In many cases these are less extensive predictions than those of other published dengue risk maps and arise because of the key importance of high human population density for the all-dengue risk maps produced here. Three published dengue risk maps are compared using the Fleiss kappa index, and are shown to have only fair agreement globally (Fleiss kappa = 0.377). Regionally the maps show greater (but still only moderate) agreement in SE Asia (Fleiss kappa = 0.566), fair agreement in the Americas (Fleiss kappa = 0.325) and only poor to fair agreement in Africa (Fleiss kappa = 0.095). The global dengue risk maps show that very few areas of rural Europe are presently suitable for dengue, but several major cities appear to be at some degree of risk, probably due to a combination of thermal conditions and high human population density, the top two variables in many models. Mahalanobis distance images were produced of Europe and the southern United States showing the distance in environmental rather than geographical space of each site from any site where dengue currently occurs. Parts of Europe are quite similar in Mahalanobis distance terms to parts of the southern United States, where dengue occurred in the recent past and which remain environmentally suitable for it. High standards of living rather than a changed environmental suitability keep dengue out of the USA. The threat of dengue to Europe at present is considered to be low but sufficiently uncertain to warrant monitoring in those areas of greatest predicted environmental suitability, especially in northern Italy and parts of Austria, Slovenia and Croatia, Bosnia and Herzegovina, Serbia and Montenegro, Albania, Greece and in south-eastern France, parts of Germany and Switzerland, and in smaller regions elsewhere.

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1. Introduction

Approximately one third of the world's human population are exposed to the risk of dengue (Rogers et al., 2006). Each year there are between 50 and 100 million recorded cases of dengue fever, 500,000 cases of severe dengue (usually referred to as dengue haemorrhagic fever, DHF) requiring hospitalisation and between 20,000 and 25,000 deaths, mostly of children (Gubler, 2006). Although today dengue is mostly a tropical disease, historically it occurred as far North as Philadelphia in the USA and, less than 100 years' ago, caused 1000 deaths amongst one million infected people in Greece (Reiter, 2010). Development of public health services, environmental sanitation and improvement of construction methods have removed dengue from most temperate areas, but increased international trade and tourism currently increase the risk of introduction or re-introduction of one or more of dengue's vectors, and of the disease itself in travellers returning from dengue infected areas. Whilst dengue's major vector species, *Aedes aegypti*, which once had a range that extended into temperate Europe (Reiter, 2010), is now restricted mostly to the tropics, the alternative vector species *Aedes (Stegomyia) albopictus* – the Asian tiger mosquito – now occurs on all the world's populated continents, with relatively recent successful introductions into Europe. The global distribution and spread of this vector has been analysed in a number of recent publications (Benedict et al., 2007; Tatem et al., 2006a,b), including in the twin contexts of the environmental suitability of the destination areas and the volume of international (mostly sea) traffic going to those areas. Concern over the arrival of *Aedes albopictus* in Europe was shown to be justified by the later arrival and transmission by it in Europe of both the alphavirus chikungunya, following a large outbreak of this disease in the Indian Ocean (Pialoux et al., 2007), and dengue in mainland France (La Roche et al., 2010) and Croatia (Gjenero-Margan et al., 2011). An outbreak of dengue in Madeira in late 2012 (transmitted by *A. aegypti*) involved over 2000 cases, the majority residents of the island, but with a minority of cases in tourist visitors to the island, diagnosed after they had returned to their home countries in the rest of Europe (<http://ecdc.europa.eu/en/press/news/Lists/News/ECDC.DispForm.aspx?List=32e43ee8%2De230%2D4424%2Da783%2D85742124029a&ID=809>).

Another trend that may favour the spread of vectors and diseases is climate and environmental change. Much has been written on the impacts of climate change on vector-borne diseases, but careful analysis suggests that many examples of such changes can also be explained by alternative causes, from better reporting (e.g. in the case of Lyme disease in some parts of Europe) to drug resistance (e.g. malaria in East Africa) (Rogers et al., 2006). Several examples of the arrival establishment and spread of a number of vector-borne diseases, and what we may learn from them, are reviewed by (Randolph and Rogers, 2010). Undoubtedly climate change and other environmental changes will eventually affect vector-borne and other diseases, if such changes are large enough to affect important demographic rates and transmission processes. Vector-borne diseases are particularly sensitive to climate and it is therefore among this group of diseases that we might expect to detect first the impacts of climate change. Whether such diseases will increase or decrease in distribution and severity depends on the relative impacts of the climatic changes on factors that increase or decrease transmission.

The present work arose from the desire of the European Centre for Disease Prevention and Control (ECDC) to assess the possibility of dengue establishing within Europe, or on its fringes. Currently, most dengue cases reported in Europe are of travellers returning with infections contracted in exotic destinations, mostly India, Thailand, Indonesia, Mexico and Brazil. A few cases have also been observed in patients from EU overseas territories. Bearing in mind

the recent spread of *A. albopictus* in Europe, and of disease events attributable to this species, the potential for the re-establishment of dengue in Europe appeared to warrant further study.

The objective of this study was therefore to obtain a better understanding of the various factors that contribute to the determination of the risk of dengue in continental Europe. This was achieved by developing global risk maps for dengue, based on and extending previous work on this topic (Rogers et al., 2006), and examining the predictions of such maps for Europe.

A variety of global predictions now exist for dengue (Degallier et al., 2010; Hales et al., 2002; Jetten and Focks, 1997; Patz et al., 1998; Rogers et al., 2006; Simmons et al., 2012; Bhatt et al., 2013), developed from different databases and using different modelling approaches. Model outputs are rarely compared to see whether or not there is any consensus in areas predicted to be at risk of this disease. Here we compare three different predictions, based on non-linear discriminant analysis (this study), logistic regression (Hales et al., 2002) or boosted regression tree (Bhatt et al., 2013) modelling approaches. Considerable differences are found between pairs of models, and the consensus of all three models is classed as only 'fair' (Landis and Koch, 1977), with disagreement around the edges of dengue's predicted distributions, or in Africa where dengue is considered to be under-reported.

2. Materials and methods

2.1. Disease and vector data

The search strategy to produce the disease and vector database was an extended version of that described elsewhere (Rogers et al., 2006). Briefly, searches were made in PubMed, Web of Science and Promed databases using the search terms '*Aedes aegypti*', '*Aedes albopictus*', 'dengue fever' and 'dengue haemorrhagic fever'. Searches were restricted to publications that appeared between 1960 and the end of 2009, the retrieval of which was considerably easier (electronically or by direct library searches) than of articles published before this time. All search Abstracts were read and all papers were acquired and read in full if the Abstracts suggested they might contain geographical information about the vectors or disease. Data were extracted from these into an electronic database, and place names were geolocated using gazetteers, including the GEOnet Names Server (GNS) of the National Geospatial-Intelligence Agency's (NGA) and the U.S. Board on Geographic Names' (US BGN) database of foreign geographic feature names (<http://earth-info.nga.mil/gns/html/>, last accessed December 2012), Encarta, (Microsoft Corporation, WA, USA), the Alexandria Digital Library Gazetteer (URL: <http://middleware.alexandria.ucsb.edu/client/gaz/adl/index.jsp>, last accessed November 2012) and the Getty Thesaurus of geographic names online, (URL: http://www.getty.edu/research/conducting_research/vocabularies/tgn/index.html, last accessed December 2012).

An improved version of the dengue database used in this study has recently been developed by (Brady et al., 2012) as part of a project to estimate the global burden of dengue (Bhatt et al., 2013).

One common feature of disease and vector data is that location names frequently refer to polygons (usually administrative units) rather than to precise points. This information was also stored in the database, and administrative unit geolocations (i.e. of polygon centres) were later extracted from the SALB (<http://www.unsalb.org/>, last accessed November 2012) or GAUL (<http://www.fao.org/giews/english/shortnews/sdrngiewsgaul.htm>, last accessed November 2012) databases. Totals of 2736 unique dengue fever and 736 unique dengue haemorrhagic fever records were recorded in the database (points and polygons, resolved to the 1/6th degree resolution of all the models). When combined,

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