Trends in Parasitology

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Review

Mosquito-Borne Diseases: Advances in Modelling Climate-Change Impacts

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Vector-borne diseases are on the rise globally. As the consequences of climate change are becoming evident, climate-based models of disease risk are of growing importance. Here, we review the current state-of-the-art in both mechanistic and correlative disease modelling, the data driving these models, the vectors and diseases covered, and climate models applied to assess future risk. We find that modelling techniques have advanced considerably, especially in terms of using ensembles of climate models and scenarios. Effects of extreme events, precipitation regimes, and seasonality on diseases are still poorly studied. Thorough validation of models is still a challenge and is complicated by a lack of field and laboratory data. On a larger scale, the main challenges today lie in cross-disciplinary and cross-sectoral transfer of data and methods.

Highlights

The use of ensembles of different climate models for future projections, as well as multiple different mechanistic or correlative disease models per study, is increasing.

Communicating uncertainties related to disease models, different climate models, and emission and population pathways to end users is becoming a common thing to do.

Most models tend to project an increased risk for vector-borne disease (VBD) transmission at high latitudes and elevations during the upcoming century.

While mechanistic models typically cover the whole chain of infection by default, most environmental niche models (ENMs) still focus on vector distributions alone; they are increasingly applied to whole disease systems as well.

Spatiotemporal Models of Vector-Borne Diseases under Climate Change: An Overview

Modelling spatial patterns and temporal trends in **vector-borne diseases (VBDs**; see Glossary) has been done through a diversity of approaches. This field of research is very active and shows a rapid methodological development with regard to the inclusion of various drivers of diseases.

Models applied in this field are commonly divided into two groups. First, 'correlative' models predict a species' geographic distribution or support the understanding of why populations persist at a certain place. Thereby, both vector and pathogen occurrences can be used as response parameters. For this, various approaches, ranging from simple regression to advanced machine-learning techniques, are employed [1].

Secondly, 'mechanistic' or process-based models make explicit assumptions about the biological [2] and environmental mechanisms that drive species' distributions or infection dynamics. In epidemiology, these models are mainly derived from the Ross–MacDonald model (compare e.g., [3]). These models are based on a system of differential equations depicting each infectious stage for vectors and/or hosts. Important epidemiological parameters, such as vector biting rates, vector development, and mortality rates, and the **extrinsic incubation period (EIP)**, largely depend on rainfall and temperature. The empirical relationship between climate and these epidemiological parameters is derived from laboratory and, less frequently, field experiments.

The individual strengths and weaknesses, as well as the underlying paradigms, of these two approaches have led to heated discourse (compare [4] and [5]). However, both approaches

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exhibit specific qualities [2,6], and some authors explore promising hybrid approaches (e.g., [7–9]).

Model approaches for VBD risk assessment need to consider both positive and negative aspects of altered climatic conditions across different spatial and temporal scales. Global warming may shift climatically suitable regions for vector establishment and disease transmission to higher latitudes and higher elevations. Conversely, it may limit transmission of VBD in the warmest places, where temperature thresholds for vector or pathogen survival may be exceeded [10,11].

Expectations for long-term climatic trends are mostly robust, particularly as far as average conditions in air temperature are concerned. Projections on future development of medium-term variability [manifested in climatic phenomena such as the North Atlantic Oscillation (NAO) or the El Niño Southern Oscillation (ENSO)] are very uncertain [12]. This is a challenge, because interannual and even multidecadal climatic fluctuations are affecting VBD transmission in some parts of the world [13]. Furthermore, long-term climatic trends affect the probability of extreme temperature and rainfall events, making them less rare in occurrence and more elusive [14]. Even though heat or cold waves, drought, or flooding are important for disease emergence, vector abundance, and pathogen transmission dynamics, such events can hardly be predicted [15].

In this article we review recent advances in modelling the impacts of climate change (Box 1) on VBD, providing an overview of the literature published since 2014. We discuss primarily mosquito-borne diseases that are monitored by the European Centre for Disease Prevention and Control (ECDC), focusing on the applied models as well as on the data driving them.

Correlative Models

Environmental niche models (ENMs), and their spatial application as **species distribution models (SDMs)**, have become an integral tool in the fields of biogeography, ecology, and conservation biology. Different modelling tools and algorithms with individual strengths and weaknesses exist, but the general concept remains the same (Figure 1). First, locations of a target species are collected in the field or derived from existing data. Some modelling tools require knowledge of the locations where target species are truly absent, but as this is difficult to acquire for various reasons [1], pseudo-absence or background data are commonly generated instead [16]. The difficulty of finding high-quality presence/absence data of vectors or pathogens is an important limitation for correlative niche models. Spatial data representing environmental parameters relevant to the species in question (such as climate, land use, soil type etc.) are acquired, usually in the form of continuous grids covering the study area.

Box 1. Climate Change in Europe

During the 20th century, most of Europe experienced an increase in annual surface air temperature of about 0.8°C, mostly with a stronger warming in winter than in summer. At the same time, some parts of southern Europe have dried by as much as 20% while precipitation increased by 10–40% over northern Europe [114]. Warm night and daytime temperature extremes increased, cold temperature extremes decreased, and many regions are faced more frequently with heavy-rain days [115]. Expectations for the future vary by region and season. While temperatures are generally expected to increase across the continent, this will be more pronounced in the summer in southern Europe (Figure IA) and in the winter in northern and eastern Europe (Figure IB). Projections for changes in precipitation are subject to relatively high uncertainties. The general trends, however, are reduced rainfall in the south and increased precipitation in the north. At intermediate latitudes, there are opposing effects in the different seasons, with dryer summers and wetter winters (Figure IC,D).

Glossary

Area under the curve (AUC): the area under the ROC curve (see below) is commonly used for assessing a model's performance in distinguishing between (in this context) the presence or absence of a species. An AUC of 1 is considered a 'perfect' model, while a value of 0.5 indicates that the model is not better than a random guess.

Environmental niche model (ENM): a model that estimates the ecological niche (or aspects thereof) of a species based on the environmental conditions at locations where the species is known to exist. It can be used to examine species–environment relationships or as a species distribution model (SDM) in order to predict (changes in) species occurrences in space and time.

Extrinsic incubation period (EIP): the time that needs to pass after a vector's infectious blood meal before it can transmit the pathogen to another host.

Global climate models or general circulation models (GCMs): models that are used to simulate the earth's climate on a large scale (see Box 2 for details).

Intergovernmental Panel on Climate Change (IPCC): the IPCC defines itself as the 'international body for assessing the science related to climate change'. Its assessment reports aim to make the state-of-the-art in climate research accessible for policy makers and provide the scientific basis for the UN Climate Conferences.

Receiver operating characteristic (ROC): the ROC curve is used when a continuous model output (e.g., probability of presence of a species) is translated into binary information (e.g., presence/absence of the species). It illustrates how the ratio of true vs. false positives varies with different thresholds for the distinction between positive and negative.

Regional climate models (RCMs): models that can be seen as refinements of GCMs that are able to better reflect local conditions on smaller spatial scales (see Box 2 for details).

Representative concentration pathways (RCPs): RCPs succeed the older SRES scenarios (see below).

These climatic changes have an impact on vectors' habitats. Winter warming may promote overwintering of vectors. Increased precipitation could lead to increased habitat availability due to increased soil moisture, humidity, and availability of natural ponds. Extreme flooding can lead to the destruction of vectors' habitats, through flushing of stagnant water bodies, but at the same time it can create new breeding grounds when the water recedes [116]. Lower summer rainfall in the Mediterranean could make suitable breeding sites scarce – or have the opposite effect if it leads to more open containers being used for water supply and irrigation.

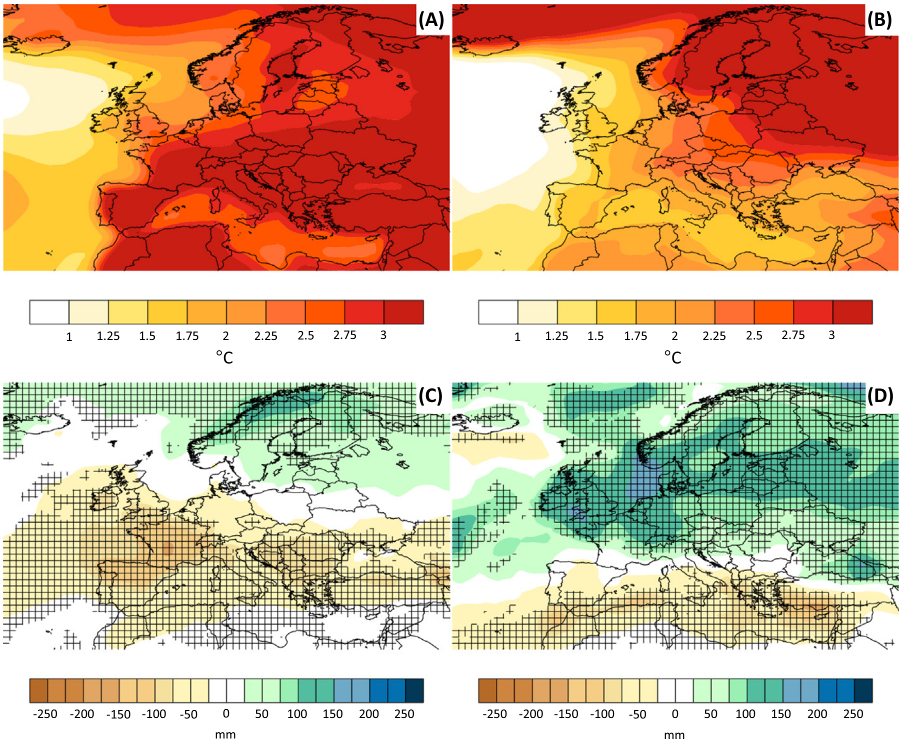

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Figure I. Climate Change in Europe. Simulated differences in temperature (A,B) and rainfall (C,D) between 2065 and 2085, and between 1961 and 1999, under the representative concentration pathway (RCP) 4.5 scenario based on 16 global climate model (GCM). A,C. Boreal summer (June–August). B,D. Boreal winter (December–February). Cross hatching indicates areas of high uncertainty due to low agreement of the different GCMs.

In the second step, a multivariate regression model is created. From an ecological perspective, loosely following the Hutchinsonian niche concept [17], this can be seen as constructing a virtual space representing all possible combinations of values of the chosen environmental parameters. From the location of the presence (and, when available, absence) of records within this environmental space, the environmental niche of the target species is constructed using methods ranging from simple multiple linear regression models to advanced machine-learning techniques. This model of the species' preferred environmental conditions is then projected back into geographical space, producing a map depicting how suitable the environmental conditions are for the species in each grid cell of the study area. Since functional features, such as dispersal barriers, cannot be directly included in this kind of model, environmental suitability cannot be easily translated into probability of occurrence. Instead, it should be perceived as an indicator for a particular species' ability to survive at a given location if some individuals were to reach this place. On

SEIR/SIR: susceptible, exposed, infectious and recovered are the stages of an infection an individual can typically go through. They make up the different compartments of a typical mechanistic disease model.

Special Report on Emissions Scenarios (SRES): this report, published by the IPCC, introduced a range of scenarios for how emissions of greenhouse gases may change in the future, depending on how mankind reacts to the challenges of climate change. These scenarios have been the basis for IPCC assessment reports, policy making, and climate modelling, but by now have been superseded by the representative concentration pathways (RCPs).

Species distribution model (SDM): SDMs are used to estimate the geographical distribution of a species (or other taxonomic rank). They are often, but not always, based on an environment niche model (ENM).

Vector-borne diseases (VBDs): illnesses in humans or other vertebrates that are mainly transmitted by other animals – often bloodsucking insects such as mosquitoes.

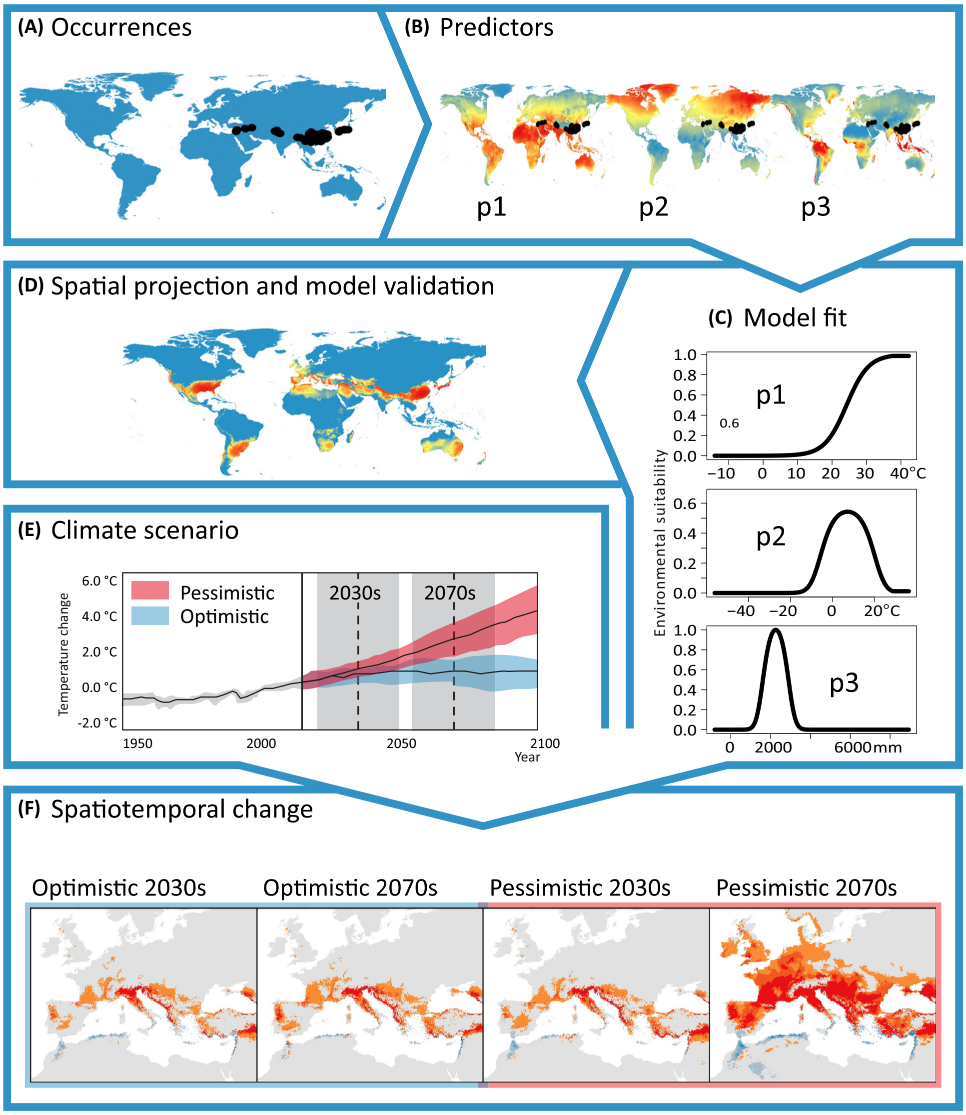

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Figure 1. Characteristic Workflow of an Environmental Niche Model (ENM). (A) Occurrence records for the vector, host, or disease in question are acquired. (B) A set of predictor variables selected (here exemplarily: p1 = summer temperature in °C, p2 = winter temperature in °C, p3 = annual precipitation in mm). (C) Based on these factors, the best fit model that describes the probability of occurrence of the species in (multivariate) dependence to its environmental conditions is developed (here simplified: environmental suitability in dependence of p1–3). Ideally, several different algorithms are utilized. (D) A spatial projection of the model is made based on the predictor variables. (E) A set of future climate change scenarios and relevant time frames is chosen. Shown here is the observed past and expected future average temperature change over time for an optimistic (blue) and a pessimistic (red) climate change scenario. Color shadings around the black lines show an estimate of the uncertainties. (F) Using data from global or regional climate models, further projections for the selected scenarios and time frames (grey vertical bars in panel E) are made. Ideally, different climate models are used to drive the ENM.

smaller spatial scales, it may be feasible to conduct extensive field collections of species that allow for an estimate of abundance rather than just simple presence or absence. Based on these data, species abundance models can be created in a very similar fashion (e.g., [18]).

In a third step, the prepared model can be used to identify the species' potential to become established in other parts of the world by using the same set of environmental predictors but for a different region as a reference for the projection. Similarly, projections over time can be made by using environmental data that follow historical emissions for the past or emission scenarios for the future [such as **global climate models (GCMs)** or **regional climate models** (**RCMs**); Box 2].

In epidemiology, ENMs are commonly used to map the potential distribution of vector species (Table 1). For simple disease systems, this alone can give a reasonably good estimate of regions that could be affected by pathogen transmission [1], although abundance models should be preferred whenever possible due to the more differentiated picture they provide. For more complex systems, such as those consisting of multiple different hosts, reservoirs and/or vectors, focusing on a single target species is often insufficient, as different species are likely to have different environmental requirements and competence to transmit diseases. In this particular case, the potential distributions of the different species involved can be modelled as separate components. The expected geographical ranges of these species can then be overlaid in order to derive areas of elevated risk of transmission [19]. For diseases where the involved species, their contribution to disease transmission, or their spatial distribution are unknown, the development of an ENM based on observed occurrence of the disease can be helpful [1]. In a way, this approach considers a pathogen and its transmission range as a species and its established populations. Regarding ectotherm arthropod vectors, this approach has the advantage of being able to additionally account for thermal impacts on the pathogen itself, such as the temperature-dependence of the EIP observed for several viral diseases [20].

While free and open-source software packages (like dismo[i] or biomod2[ii] for R; see https://www.r-project.org/) make the development of ENMs relatively easy from a technical point of view. There are several aspects that need to be considered carefully in order to gain meaningful results [1,21]. These include, for instance, sampling bias in the occurrence records [22], the regions where pseudo-absence locations are drawn from [23], potential niche-shifts of invasive species [24], and the choice of meaningful environmental predictors [25,26].

Thorough out-of-sample validation of a model is crucial; and there are numerous evaluation methods available for different kinds of ENM. While these evaluation methods have been reviewed elsewhere [27], it seems worth pointing out that the **area under the curve (AUC)** of the **receiver operating characteristic (ROC)**, one of the most widely applied evaluation metrics, has been criticized for being potentially misleading (e.g., [28]).

Among the techniques available, Maxent [29] has been by far the most popular choice for studies of climate change impact on vector-borne diseases over the past few years (Table 1). This is somewhat surprising as there are several other established methods available [such as Bioclim, Boosted Regression Trees (BRT), Random Forest (RF), Generalized Linear Models (GLM), Generalized Additive Models (GAM), or Genetic Algorithm for Rule-set Production (GARP)] and from the numerous studies comparing their performances (e.g., [30–32]) no preferential method has emerged so far. Consequently, there is a new trend towards using an ensemble of different ENMs to make up for the uncertainties inherent to the individual algorithms [31,33].

Box 2. Climate Models and Scenarios

General circulation models (GCMs), also called global climate models, are used to simulate the earth's climate at large spatial scales and estimate its long-term future development. They usually consist of several coupled components such as the atmosphere, ocean dynamics, sea ice, and vegetation. International efforts in climate modelling are coordinated through the Coupled Model Intercomparison Project (CMIP, http://pcmdi-cmip.llnl.gov), and GCM output data are made available through the various data nodes of the Earth System Grid Federation (ESGF, https://esgf.llnl.gov). Since running GCM simulations is computationally expensive, some finer-scale processes, such as convection, have to be heavily parameterized in global-scale models. However, regional climate models (RCMs) driven by a GCM can be used to make up for this on smaller spatial scales. The Coordinated Regional Downscaling Experiment (CORDEX, http://www.cordex.org) provides a common framework for such initiatives.

The Intergovernmental Panel on Climate Change (IPCC) provides the scientific basis to assess climate change, suggest adaptation and mitigation strategies, and highlight impacts and future risks for decision-makers. The IPCC assessments are compiled by hundreds of leading and volunteering scientists, they undergo multiple rounds of review to ensure objectivity, and underlie negotiations at the Conferences of the Parties (COP) of the United Nations Framework Convention on Climate Change (UNFCCC). In the latest assessment, the Fifth Assessment Report in 2013, new climate-change scenarios, so-called representative concentration pathways (RCPs), were developed. They describe a wide range of possible magnitudes of climate change by specifying concentrations and corresponding emissions. Although not directly based on socioeconomic storylines like the former IPCC **Special Report on Emissions Scenarios (SRES)**, they are additionally based on short-lived gases and land-use changes [117]. The start-point for all four RCP scenarios is 2006, with a baseline historical period from 1986 to 2005. These RCP*x* scenarios lead to a defined additional radiative forcing by 2100 (increase by xW/m^2), which can also be expressed as an increase in the global mean surface temperatures for 2081–2100. This increase for the different RCPs is expected to range between 0.3°C and 1.7°C (RCP2.6), 1.1°C and 2.6°C (RCP4.5), 1.4°C and 3.1°C (RCP6.0), 2.6°C and 4.8°C (RCP8.5) [118]. Both global and regional climate models rely on these pathways for future projections of climate change.

Most ENM-type models applied in disease modelling focus on vector distributions (Table 1). Among these, the most studied vector genus is *Aedes* (competent mosquito vector for diseases such as dengue, chikungunya, or Zika) followed by *Anopheles* (malaria mosquito vectors) and *Lutzomyia* (sand flies, vectors of leishmaniasis). While several ENM-type models for complete disease systems have been published recently [7,34–36], only a few of them feature future projections under climate-change scenarios [20]. The projected future changes in vector ranges vary among species and regions. However, there is a general trend of range expansion towards higher latitudes and altitudes, while some of the regions that are most affected by VBD today may benefit from a decline in environmental suitability under climate change (Table 1).

ENM-type models are commonly applied across all spatial scales. When it comes to future risk mapping, however, they are mostly used on larger global to continental scales (Table 1). Consequently, most studies use global rather than regional climate models. Almost half of the studies in Table 1 incorporate data from more than one climate model. This is good practice, as this leads to better estimates of uncertainty in final model output [37].

Regarding the predictors being used, most models rely mainly on various metrics applied to temperature and precipitation (and combinations thereof, such as 'precipitation of the warmest month'), both of which have been identified as important drivers of VBD transmission [38]. Some models additionally use other input parameters that may influence host or vector distribution, such as measures of air moisture [39–42], soil moisture [43], topography [42–45], or land cover/land use [42,43,46]. Socioeconomic factors, such as human population density or vulnerability indicators, can be included as well (e.g., [7]), but continuous future projections of these are often not available, and they are subject to large uncertainties.

One main advantage of ENMs compared to mechanistic approaches is the non-necessity of detailed knowledge about the complex interplay between environment, vectors, hosts, and

Table 1. Recent Studies Using Environmental Niche Models (ENMs) to Assess Vector-Borne Disease Risk under Climate Change

Vector/pathogen modelled	ENM	Climate model[a]/scenario[b]/ future time period[c]	Environmental variables	Country, region	Main findings	Refs
Aedes aegypti	MaxLike	NA[d]/RCP 4.5, RCP 8.5/ current, 2020s, 2080s	t[e], p[f]	Veracruz, Mexico	Data from the edges of the vector's distribution is valuable for - monitoring changes in distribution - understanding links between anthropogenic drivers and climate change	[97]
	Climate envelope	GCM: CCCma-CGCM2, CSIRO-MK2, NIES99, UKMO-HadCM3/A2a, B2b/2020s	t, p	Global	- macroclimate is the main driver of the species range limits - anthropogenic influence can help the species to survive in otherwise unsuitable climate	[98]
	Maxent	NA/A2a/2050s	t, p	Brazil	- the vector's range in Brazil will decrease in the future, but will spread further south	[99]
	Maxent	GCM: NA/NA (CMIP5)/2020s, 2050s	t, p	Tanzania	- risk for dengue is currently concentrated in the coastal areas - large-scale spread is projected for 2050s	[100]
Aedes aegypti, Aedes africanus, Aedes albopictus	Biomod2 ensemble model	GCM: HadGEM2-ES/RCP8.5/ 2050s	t, p, NDVI[g]	Global	- Zika's distribution may be far more constrained than dengue - Zika is unlikely to become cosmopolitan in temperate regions	[80]
Aedes aegypti, Aedes albopictus	Maxent	6 GCM/B1, A1B, A2/2050s	t, p	Global	- complex global rearrangements of potential distributional areas under climate change - digitization and sharing of existing distributional data for vectors needs to be a priority	[101]
Aedes albopictus	GARP	GCM: MPI-ESM-LR/RCP 4.5/ 2050s, 2070s	t, p	Mexico, US, Italy, Brazil, Asia	- ENM fit on occurrence data from different regions transfer to Mexico well	[102]
	Maxent	RCM: COSMO-CLM/A1B/ 2020s, 2050s, 2080s	t, p, cargo movement	Europe	- combining ENM with measures of cargo movement can help to identify hot spots for potential areas of introduction - availability of transport data in Europe needs to be improved	[103]
	Maxent	GCM: CSIRO-Mk3.6.0/RCP 2.6, 4.5, 6.0, 8.5/ 2030s, 2050s, 2070s	t, p	Germany	- establishment in Germany is possible - northward range expansion under climate change	[104]
Anopheles arabiensis	LOBAG-OC	GCM: Hadley CM 3/A1B, A2A, B2A/2050s	t, p	Africa	- the suitable range for the vector in Africa will be strongly reduced under climate change	[105]
Anopheles darlingi, Anopheles nuneztovari	Maxent	GCM: GISS-E2-R, HadGEM2-AO/RCP 2.6/2050s, 2070s	t, p, topo[h], soil moisture, pop[i], lcov[j]	South America	- vectors are projected to experience range expansion under climate change	[43]
Anopheles spp.	Maxent, BRT	GCM: GISS-E2-R, HadGEM2-ES/RCP 8.5/2070s	t, p, topo, terrestrial biomes	South America	- current main vector will experience reduced habitat suitability under climate change - other species of the genus show significant potential for expansion	[44]

Table 1. (continued)

Vector/pathogen modelled	ENM	Climate model[a]/scenario[b]/ future time period[c]	Environmental variables	Country, region	Main findings	Refs
Anopheles, An. dirus, An. minimus, An. lesteri, An. sinensis	Maxent	GCM: BCC-CSM1-1, CCCma_CanESM2, CSIRO-Mk3.6.0/RCP 2.6, 4.5, 8.5/ 2030s, 2050s	t, p, lcov	China	- the different vector species' ranges will react differently to climate change - an overall net increase in the population exposed to the vectors is expected	[46]
Culicoides imicola, C. insignis, C. variipennis, C. sonorensis, C. occidentalis, C. brevitarsis	Maxent	62 GCM/RCP 2.6, 4.5, 6.0, 8.5/2050s	t, p	Global	- potential distribution is projected to broaden under climate change, especially in central Africa, United States and western Russia	[106]
Culicoides imicola	CLIMEX	GCM: CSIRO-MK3.0, Miroc-h/A1B, A2/1975, 2030s, 2070s	t, p, rh[k], irrigation	Global	- vector's potential distribution under climate change is projected to expand northward in the northern hemisphere - potential distribution may contract in Africa	[41]
Culicoides sonorensis	Maxent	GCM: CanESM2/RCP 2.6, 4.5, 8.5/ 2030s, 2050s	t, p, topo, lcov, VPD[l]	North America	- the current northern range limit of the vector is expected to shift northward under climate change	[42]
Lutzomyia evansi, Lutzomyia longipalpis	Maxent	GCM: CSIRO/A2, B2/2020s, 2050s, 2080s	t, p, topo	Colombia	- the range of the vectors is projected to decrease in size under climate change	[45]
Lutzomyia intermedia, Lutzomyia neivai	GLM, MaxEnt, RF, SVM, GARP	GCM: HadGEM2-ES/RCP 4.5, 8.5/2050s	t, p	South America	- the different vector species show a different response to climate change - 'Ecological niche models should be species specific, carefully selected and combined in an ensemble approach.'	[81]
Lutzomyia flaviscutellata	6 SDM	17 GCM/RCP 4.5, 8.5/2050s	t, p	[N/n]orthern South America	- the suitable area for the vector is projected to expand towards higher latitudes and altitudes under climate change	[82]
Lutzomyia major, Lutzomyia tropica	biomod2 ensemble model	GCM: MPI-ESM-LR/RCP 4.5/ 2050s	t, p	Libya	- coastal regions of Libya show higher risk because of more suitable climate - risk of cutaneous leishmaniasis is projected to increase under climate change	[107]
Chikungunya	Maxent	5 GCM/RCP 4.5, 8.5/2030s, 2050s, 2070s	t, p, pop	Global	- transmission potential is projected to increase across the globe under climate change - some parts of India may see a relative decrease in transmission	[20]

[a] Names of the climate models being used (RCM or GCM, see Glossary and Box 1), unless their number exceeds 5.
[b] Climate change scenario: typically RCPs and/or scenarios following SREP, see Glossary.
[c] 2030s etc. = marks the center of the 30-year time period covered, stands for 2021–2040 or 2020–2039 depending on data source.
[d] NA = information not available.
[e] t = temperature.
[f] p = precipitation.
[g] NDVI = normalized difference vegetation index.
[h] topo = topography (elevation, altitude, slope, aspect ratio).
[i] pop = human population density.
[j] lcov = land cover, land use.
[k] rh = relative humidity.
[l] VPD = vapour pressure deficit.

pathogens [1]. This makes them a practical tool for understudied, that is, 'neglected' VBDs. However, this comes at the price of accuracy, and consequently ENMs are most useful on medium to large spatial scales. If at least some of the environment-dependent mechanisms are known, those can be used to refine the results [47]. And finally, estimates of distributions or abundances of host and vector species derived from ENMs can also serve as input data for mechanistic models [9].

Mechanistic Models

Mechanistic models are built on biophysical relationships between environmental factors vectors, pathogens, and hosts (Figure 2). These relationships are generally derived from laboratory- or field-based studies (see also section 'Adaption and Evolution'). Different mechanistic approaches can be applied. The most common methodology is derived from the standard Ross–MacDonald model [3] or its generalization. A set of differential equations define the different compartmental stages of vectors and hosts (susceptible, exposed, infectious, and recovered for **SEIR** models, or susceptible, infectious, and recovered for **SIR** models).This set of equations can be directly utilized to model the population size in each compartment, based on their relationship to climatic factors [48]. The steady-state solution of this system of differential equations also yields the basic reproduction number, $R_{0.}$ R_0 is commonly employed in epidemiology to estimate the propensity of an outbreak to expand ($R_0 > 1$) or to shrink ($R_0 < 1$) in a fully susceptible population. Mathematical formulations of R_0 are available for several VBDs. They depend on the number of vectors and hosts considered in the model; see, for example, [49] for a one-host–one-vector formulation of R_0 for malaria, [50] for a two-host–one-vector formulation of R_0 for African trypanosomiases, or [51] for a one-host–two-vector formulation of R_0 for Zika. Other empirical mechanistic models are based on environmental risk factors, such as fuzzy logic models to simulate the risk of malaria [52], or empirical-rule-based models, to assess the risk of helminth infections in ruminants based on soil moisture availability and temperature conditions [53].

Mechanistic models can be utilized to model the risk of VBDs backwards (using past environmental data) or forwards (using demographic, economic, and climate-change scenarios) in time. They are generally driven by daily or monthly climate data to simulate the burden of a particular VBD. Their complexity varies; some models include additional effects of population density, surface hydrology [54], and herd immunity factors [55].

In terms of methodology, the first necessary step (which is common to all modelling approaches) is model validation. For this purpose, mechanistic models are run for the past, and the output is compared to observed VBD burden indicators in space and time. This can be a daunting task as this step depends on the quality and spatiotemporal coverage of observed disease burden information (prevalence, incidence, number of confirmed cases etc.). Different skill scores (like AUC, correlations, or reliability diagrams) are employed to estimate the model capability in reproducing past observed outbreaks and mean seasonality of a VBD. The mechanistic model is then projected forward in space and time, using calibrated climate model data outputs and population scenarios, to estimate future human populations at risk (see [56,57] for malaria).

Another significant progress lies in the study of historical VBD outbreaks and their relationship with climate variability. An R_0 model showed optimal climatic conditions when an outbreak of bluetongue occurred in northern Europe in 2006 [58]. A similar modelling framework highlighted optimal environmental conditions for mosquito-borne transmission risk of Zika virus over South America in 2015, when the largest outbreak occurred [51]. These findings are consistent with

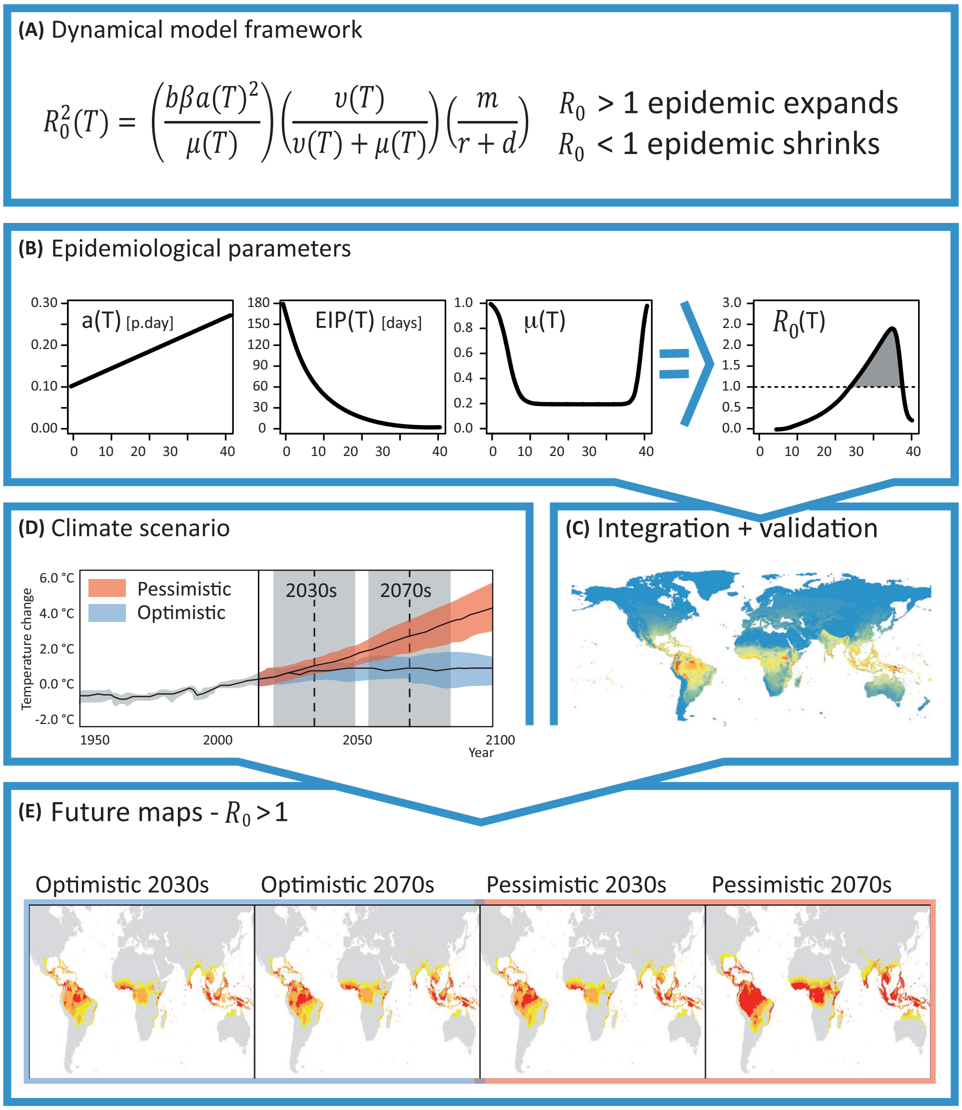

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Figure 2. Typical Workflow of a Mechanistic Disease Model Derived from the Ross–MacDonald Framework [*R0*(T) Model]. (A) Dynamical model framework. T = temperature (°C); b = vector–host transmission probability; β = host–vector transmission probability; m = vector-to-host ratio; r = recovery rate; d = infectious recovery rate; a(T) = vector biting rate per day; EIP(T) = 1/υ(T) = extrinsic incubation period in days; μ(T) = vector mortality rate. (B) Epidemiological parameters derived from laboratory experiments or field data are fed into the model to gain an estimate of R_0(T). (C) A risk map is derived from the model. (D) A set of future climate-change scenarios and relevant time frames is chosen. Shown here is the observed and expected future average temperature increase over time for an optimistic (blue) and a pessimistic (red) climate-change scenario. Color shadings around the black lines show an estimate of the uncertainties. (E) Using data from global or regional climate models, further projections for the selected scenarios and time frames (grey vertical bars in panel E) are made. Ideally, different climate models are used to drive the model.

former results by Patz *et al*. [59], who showed the capability of a mechanistic model to reproduce past dengue outbreaks over Nicaragua, Honduras, and Thailand. Another advantage of mechanistic models lies in their integration with operational seasonal climate forecasting systems to anticipate the risk posed by a particular VBD for the upcoming season [60–62].

Most mechanistic models tend to project an increase in VBD transmission risk to higher latitudes and elevation in the future (Table 2). However, marked differences are shown in the literature, depending on the considered VBD, the studied region, the selected GCM and emission scenario, and the employed disease and vector model. Future risk of malaria transmission is generally expected to increase in the tropical highlands, particularly in eastern Africa where the local population will be highly susceptible to infection [57,63–65]. Conversely, malaria transmission risk is likely to decrease over the warmer plains of western Africa [57] and at the fringes of its current distribution across the Sahel. Rift Valley fever might also be on the rise in eastern Africa in future [66]. The West Nile virus transmission season in the USA might lengthen, leading to increased disease burden [67]. Important mosquito vectors such as *Aedes albopictus* and *Aedes aegypti*, which are competent to transmit dengue, Zika, and chikungunya, are expected to spread further north in Europe [39,68,69] and North America [70], while their future range might contract over the tropics due to extreme temperature conditions [39,68–70]. The diseases they transmit, like chikungunya and dengue, are likely to follow similar trends [71–75].

Mechanistic models can be useful; however, there is still room for improvement. Because they require dynamic drivers available in both space and time, they often lack important parameters, such as socioeconomic and vulnerability indicators, land-use change factors, host immunity parameters, population movement, and indicators of disease-control measures in place. This caveat is a critical point, in particular when considering the progress made in malaria control over the African continent during the past decades, in a warmer climatic background [76].

Challenges in Modelling Vector-Borne Diseases under Climate Change

Using Climate Data in VBD Modelling

The usage of both ENM and mechanistic models has proven to be useful in anticipating the spread of invasive vector species. One of the best examples is the Asian tiger mosquito, *Ae. albopictus*, one of the most invasive species worldwide. Several modelling studies, based solely on environmental factors, anticipated the spread of *Ae. albopictus* in many European countries, years before that species was introduced[iii] [77,78].

Future projections of disease models need to be carried out for an ensemble of calibrated global (GCM) or regional (RCM) climate models (Box 1), because of the different sensitivities of these climate models to global warming. GCMs are often favoured over RCMs, even for national-scale models. This might be related to the output from GCMs being readily available in preprocessed formats from data portals such as worldclim.com or ccafs-climate.org. Output from RCMs is usually free to use for scientific purposes as well, but often requires additional processing before it can be easily utilized by the impact modelling community. Simulating the impact of extreme weather events on the VBD burden remains difficult, in particular when using climate-change scenarios. However, sensitivity experiments could be designed to test the sensitivity of VBD models to idealized temperature and rainfall distributions.

The climate model outputs used to drive the model, such as rainfall and temperature, have to be statistically calibrated (‘bias correction’) with respect to observed climate [79]. This is an important necessary step because VBDs are sensitive to critical climatic thresholds – for example, *Plasmodium falciparum* transmission by *Anopheles* mosquitoes starts when the temperature exceeds 18°C [61]. Impact simulations have to be driven by an up-to-date ensemble of emission scenarios **(representative concentration pathways**, **RCPs)**, consistent with the guidelines of the **Intergovernmental Panel on Climate Change (IPCC)**, in order to provide decision makers with a range of best- and worst-case scenarios. The impact of

Table 2. Recent Studies Using Mechanistic Models to Assess Vector-Borne Disease Risk under Climate Change

Vector/pathogen modelled	Model type	Climate model[a]/scenario[b]/ future time period[c]	Environmental variables	Country, region	Main findings	Refs
Aedes albopictus	Mapping indicators of climatic constraints	10 RCM/RCP 4.5, 8.5/2020s, 2050s	t[d] p[e]	North America	- northward range expansion predicted under climate change - additional field studies and surveillance needed to better identify relevant environmental factors	[70]
	Multi-model approach: climatic suitability, seasonal activity	RCM: EBU-POM/A2/2010s, 2080s	t, p, photoperiod	Serbia	- most of Serbia is projected to become significantly more suitable for the vector under climate change	[68]
	Fuzzy logic	GCM: EMAC, CMIP5 multi-model ensemble/A2, RCP 8.5/ 2050s	t, p, rh[f]	Global	- environmental conditions in the tropics are projected to become less suitable under climate change, while suitability increases in other regions	[69]
Aedes aegypti	CLIMEX	GCM: CSIRO-Mk3, MIROC-H/ A1B, A2/2030s, 2070s	t, p, rh	Global	- environmental conditions in the tropics are projected to become less suitable under climate change, while suitability increases in other regions	[39]
Anopheles gambiae, Anopheles arabiensis	CLIMEX	0.1 and 2.0°C increase by 2100; increased precipitation seasonality	t, p, rh	Africa	- climate change effects on vector distribution are projected to be strongest in eastern and southern Africa	[40]
Avian malaria	Epidemiological model	RCM: HRCM/A1b, RCP 4.5, 8.5/2010–2100 (continuous)	t, p	Hawaii	- abundance and diversity of Hawaiian bird populations are projected to decrease under climate change due to higher potential for avian malaria - current conservation strategies are insufficient	[108,109]
Chikungunya	R_0	RCM: CRCM5/RCP 4.5, 8.5/ 2020s, 2050s	t, p	Canada	- the current risk for chikungunya in Canada is low - small parts of southern coastal British Colombia are projected to become progressively suitable under climate change	[71]
Dengue	Ross–MacDonald (relative vectorial capacity)	5 GCM/RCP 8.5/2080s	t, DTR[g]	Global	- there is a strong connection between epidemic potential and diurnal temperature range - large increases in epidemic potential are projected under climate change	[72]
	CIMSiM, DENSiM	+1°C	t, virus importation rate	Malaysia	- moderate increases in temperature do not necessarily lead to greater incidence	[110]
	GAM and uncertainty	RCM: COSMO-CLM/A1b/ 2020s, 2050s, 2080s	t, p, rh, pop[h], urbanisation,	Europe	- climate change is likely to contribute to increased dengue risk	[73]

Table 2. (continued)

Vector/pathogen modelled	Model type	Climate model[a]/scenario[b]/ future time period[c]	Environmental variables	Country, region	Main findings	Refs
			GDP per capita and population size			
	CIMSiM, DENSiM	GCM: ECHAM5/A2, B1/ 2050s	t	Australia	- depending on which climate scenario is used, dengue risk may be projected to increase or decrease	[74,75]
Dirofilariasis	GIS-based	NA[i] (Russian Committee of Hydrometeorology)/NA/2030	t	Former USSR	- an increase of potential transmission area and population exposure is projected under climate change	[111]
Malaria	Five malaria models: LMM_RO, MIASMA, MARA, VECTRI, UMEA	5 GCM/RCP 2.6, 4.5, 6.0, 8.5/ 2030s, 2050s, 2080s	t, p, socioeconomics	Global	- an overall global net increase in climate suitability and population at risk is projected under climate change. Future risk increases in tropical altitude regions	[57]
	R_0	GCM: HadCM3/A1B/2020s, 2050s, 2080s	t, NDVI[j], pop	Africa	- a modest increase in the overall area suitable for malaria transmission is projected under climate change, with a net decrease in the most suitable area	[63]
	Malaria Ecology Index	16 GCM/A1B/2080s	t, p	Global	- a strong increase in malaria R_0 is projected under climate change	[112]
	VECTRI	GCM: CanESM2, MPI-ESM-LR, IPSL-CM5A-LR, MIROC-ESM/RCP 2.6, 8.5/2030–2099	t, p, pop, lcov[k]	Africa	- land use change effects on climate are projected to be of minor importance for malaria	[64]
	VECTRI, LMM	5 GCM, 18 RCM/ RCP 2.6, 4.5, 6.0, 8.5/2020s, 2050s, 2080s	t, p, pop	Eastern Africa	- malaria transmission is projected to move to higher altitudes under climate change	[65]
	Epidemiological model: lifetime transmission potential	8 GCM/A2/2050s	t	Kenya	- downscaling of coarse-scale GCM output can improve epidemiological models	[113]
Rift Valley fever	LRVF	GCM: GFDL ESM 2M/RCP 4.5, 8.5/2011–2050, 2051–2099	t, p	Eastern Africa	- there is a high risk for further spread of RVF under climate change	[66]
West Nile fever	DyMSiM	GCM: NCCSM/A2, B1 /2050s, 2090s	t, p	US	- vector activity is projected to lengthen under climate change	[67]

[a] Names of the climate models being used (RCM or GCM, see Glossary and Box 1), unless their number exceeds 5.
[b] Climate change scenario: typically RCPs and/or scenarios following SREP, see Glossary.
[c] 2030s etc. = marks the center of the 30-year time period covered, stands for 2021–2040 or 2020–2039 depending on data source.
[d] t = temperature.
[e] p = precipitation.
[f] rh = relative humidity.
[g] DTR = diurnal temperature range.
[h] pop = human population density.
[i] NA = information not available.
[j] NDVI = normalized difference vegetation index.
[k] lcov = land cover, land use.

initial conditions used to perform the long-term climate change scenarios also needs to be investigated to provide additional uncertainty estimates. Ideally, uncertainties related to the disease models, the different climate models, and the various emission and population pathways have to be communicated to end users [77], and this is a difficult task. Overall, the usage of different climate models and emission scenarios in various future risk assessments of VBD has greatly improved over the past 10 years for Europe and the world (Tables 1 and 2), thanks to significant funding efforts from national and European research councils.

Model Approaches and Their Comparability

The parallel or joint use of multiple disease models within the same study in order to gain more reliable results is increasingly common (Tables 1 and 2; [44,57,65,80–82]). However, there still appears to be a gap between the mechanistic and correlative modelling communities, with studies utilizing both approaches being rare exceptions. This may reflect differences in the underlying paradigms leading to scepticism towards the unknown, but also with differences in model outputs (e.g., R_0 vs. ‘suitability’) that make direct comparisons difficult. The Coupled Model Intercomparison Project (CMIP) has done an excellent job in setting standards for climate models and thus granting comparability of models created by researchers across the globe. A similar project for VBD modelling could potentially work in a similar manner by defining standard output variables for all disease models. Such a large intercomparison of impact models was pioneered by the ISI-MIP project [83] but it should be further encouraged and funded in the near future to include a larger ensemble of disease and vector models.

Cross-Sectoral Comparison of Climate Change Impacts

Changing long-term trends, extreme weather events, and climate variability have various direct and indirect impacts which will increasingly interact. For instance, there are negative consequences of climate change on biodiversity [84], which, in turn, is closely related to ecosystem functioning and services [85]. A loss of biodiversity and ecological complexity is likely to have consequences for the stability and resilience of ecosystems. For example, a loss of native predators or reduced competition through native mosquitoes may facilitate establishment of invasive vector species such as *Ae. albopictus*. As human society depends on these traits in many sectors (e.g., health, food production, and economy), these negative feedback loops can hardly be ignored. Biodiversity and ecosystem functioning are also buffering the impacts of climate change and particularly of climatic extremes [86]. Additionally, climate change may have an influence on poverty [87] and can hamper food security [88], which can further increase the population’s vulnerability to VBDs.

Clearly, there is a need for multisectorial risk assessments, including the links between climate change impacts on agriculture and food production, water resources, biodiversity and ecosystem services, and health.

Health and Vector Data Availability

One of the greatest challenges in VBD modelling, regardless of the type of model being used, is undoubtedly the acquisition of the required input data. Much can be learned from the climate-modelling community, which is well organized and publicly shares their data on the centralized repository of the Earth System Grid Foundation (ESGF, https://esgf.llnl.gov). Such a repository, that is jointly used by all scientists across the globe for occurrence records of arthropod vector species, is currently still missing. A promising attempt in this direction is the VectorMap platform offered by the Walter Reed Biosystematics Unit of the Smithsonian Institution (http://vectormap.si.edu), where entomologists can share their field records with the scientific community. For Europe, the VectorNet project hosted by the

European Centre for Disease Prevention and Control and the European Food Safety Authority[iv] follows a similar approach, but only publishes maps at a 'regional' level without providing scalar coordinates. Another interesting approach is followed by the German 'Mückenatlas' citizen science project (https://www.mueckenatlas.de). Here, the general population is asked to catch and send in mosquitoes (along with information on time of capture and location) which will be identified by experts and entered into a database (not publically accessible yet). For important mosquito vectors, publicly available global occurrence data sets exist (e.g., *Ae. aegypti* and *Ae. albopictus* [89]), but they currently do not offer the possibility for real-time updates of newly found records. While these examples are a step in the right direction, what is ultimately needed is a unified, publicly accessible global database for vector-occurrence records. The Global Biodiversity Information Facility (http://www.gbif.org) already provides such necessary infrastructure; it is now up to the VBD community to realize and optimize its potential.

In theory, for human- or livestock-related cases of VBD it should be relatively easy to compile anonymized, georeferenced global databases. The data for this exist, at least for communicable diseases that are recorded by the national health agencies, but are difficult to access. Current global systems, such as ProMED-mail, HealthMap, or WHO's Global Outbreak Alert and Response Network (GOARN), mainly communicate current cases and outbreaks, rather than providing an accessible, structured archive of laboratory-confirmed cases. The Global Health Data Exchange (http://ghdx.healthdata.org) has the potential to fill this niche if spatiotemporal resolution of the data can be improved. The Malaria Atlas Project is an example of good practice: globally observed malaria prevalence data and ENM model outputs can easily be accessed and downloaded from the related web site (http://www.map.ox.ac.uk). At the European level, the Expert Groups of Health Information (EGHI) and Health System Performance Assessment (HSPA) are currently working on improving the health data information structure. However, this is a difficult task as there are many parties involved [90]. Of course, observed health data can suffer from a variety of problems related to the consistency of disease surveillance systems (over/under-reporting issues), the quality and modus operandi of public health systems in a given country and region, or the accuracy of diagnostic tests to confirm clinical cases. Still, it can be gathered in a much more systematic and comprehensive way than any kind of vector-occurrence data.

Adaptation and Evolution – A Stony Path

Another critical point is evolution and adaptation. Important model parameters, such as biting rate, EIP, or mortality rate, are very often derived from old published studies (see e.g., [91,92] for the EIP of dengue). Vectors and pathogens have changed over recent decades, and there is a significant need to improve and update what K. Lafferty calls 'thermal response curves of VBD' [93]. There is huge potential for vectors to mutate and adapt to new environmental conditions; and a vector's adaptation can greatly vary in space and time. New mosquito infection experiments that are conducted in the laboratory are needed and should be performed at various temperature and humidity conditions, using different strains of pathogen and fresh vectors collected from different populations [94]. Because vectors rarely experience laboratory conditions, these experiments should further be complemented by field studies [95] to also better estimate vector mortality, the relationship between local rainfall and carrying capacity, and vector-to-host ratios, and to track the evolution of vector behaviour in the field. Overall, interdisciplinary approaches, involving health specialists, field entomologists, biologists, mathematicians, and climate scientists, are and will be key to improving VBD models in the future.

Climate Services – The Connecting Bridge

Climate services translate climate data and information into customised tools, products, and information to support decision-makers to make informed decisions when addressing existing or emerging risks. Although various good examples for the implantation of climate data in VBD risk assessment already exist, the lack of transfer of knowledge outside the scientific realm often prevents practical applications of the gained insights. Bridging this gap between science and the public sector is essential for developing solutions to climate change [96]. One example is the 'Healthy Futures' project that aims to communicate several aspects of high-impact VBDs in eastern Africa through an interactive online atlas (http://www.healthyfutures.eu/).

Concluding Remarks and Future Perspectives

Great progress has been made in understanding the possible impacts of climate change on VBDs by means of correlative, mechanistic, and hybrid models. The increasingly common use of ensemble models is an important step towards better reliability and assessment of uncertainties. However, mechanistic and correlative models are still mostly used separately. It is now time for researchers from different backgrounds to join their forces to bring VBD research and modelling to the next level.

Although methodological approaches and climate change input data have improved, open questions remain (see Outstanding Questions). Cross-sectoral comparison of climate change impacts is in its infancy and needs to be assessed by multisectorial risk assessments at the agriculture, water resources, and health nexus. The development of climate service tools based on mechanistic and ecological niche models is needed to guide decision-making processes. There is a need for perturbed parameter experiments for mechanistic models and large multivariate statistics for ENMs to describe models' uncertainties. Model outputs have to be validated with respect to observed health data. The impact of climate modes of variability on VBD burden in Europe, for example, North Atlantic Oscillation and Atlantic Multi-Decadal Oscillation, has not been investigated and tested in detail yet. Mosquitoes and pathogens have also evolved: there is a need for new field- and laboratory-based studies in closer cooperation with modellers to improve model parameter setting. Further integration of remotely sensed data will also support the development of operational forecasting systems and early-warning systems.

In conclusion, after many decades, during which VBDs hardly played a role in Europe, awareness is rising. It is important in times of climate change and globalization to build up appropriate competences and bring together existing knowledge in research in close cooperation with policy, practitioners, public health, and the population concerned, to develop tools and measures that can identify, anticipate, assess, and mitigate risks at an early stage. Of great importance is knowledge already gained in more affected areas of the world to develop concepts and models which can be adapted for temperate regions under changing climatic conditions. That is what Jürg Utzinger, in a recent presentation at the 'Impact of Environmental Change on Infectious Diseases' conference in May 2017, in Trieste, called the 'need for reverse innovation'.

Outstanding Questions

How can the comparability between different modelling approaches be increased?

How can mechanistic and correlative (ENM-type) models be coupled with each other?

How can extreme events, precipitation regimes, and seasonality be depicted more accurately in models?

How can entomological data of vector distributions and anonymized human clinical data be shared more effectively across the globe?

What is the next step towards cross-sectoral studies of climate change impacts to further investigate the links between the biodiversity–food–water–health nexus?

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Resources

[i] https://cran.r-project.org/package=dismo
[ii] https://cran.r-project.org/package=biomod2
[iii] https://ecdc.europa.eu/en/publications-data/development-aedes-albopictus-risk-maps
[iv] https://ecdc.europa.eu/en/disease-vectors/surveillance-and-disease-data

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