

Chapter 4

Vector-Borne Diseases



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Abstract Vector-borne diseases (VBDs) are illnesses caused by parasites, viruses or bacteria that are transmitted by a vector such as mosquitoes, ticks, sandflies, triatomine bugs, tsetse flies, fleas, black flies, aquatic snails and lice. In this chapter, we aim to show how climate change impacts VBDs and what role biodiversity (and its loss) plays for VBDs. (1) We show how climatic changes shape the distribution and abundance of disease vectors. To point out current triple vulnerabilities regarding climate change, biodiversity and VBDs, we selected ticks and mosquitoes as examples. (2) We point out important knowledge gaps on VBDs and biodiversity, which make prognoses for VBDs under climate change challenging. (3) We review vector control tools as well as policy options and related infrastructural responses to manage VBDs under climate and biodiversity changes.

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Highlights

- Climatic change shapes the regional distribution and abundance of disease vectors.
- There are important knowledge gaps with relation to VBDs and biodiversity.
- A variety of new biological and genetic vector control tools are under development.
- VBD control needs a trans-sectoral One Health approach, not just the health sector.
- VBD control and elimination should be based on a wider understanding of planetary health.

4.1 Triple Vulnerability: Climate Change, Biodiversity and Vector-Borne Diseases

Both climate change and biodiversity loss are current challenges to humankind. Climate and biodiversity change have health impacts that range widely from direct effects such as progressive temperature increases from global warming, flooding or heat waves due to increased climate variability and extreme weather events, to indirect effects such as changes in ecosystem services, food productivity or species distributions (Montag et al. 2017). Indirect effects also include the redistribution of vector species or extended seasonal transmission periods and spatial extension, as well as the disappearance of vector-borne diseases (VBDs).

VBDs are illnesses caused by parasites, viruses or bacteria that are transmitted by a vector, such as mosquitoes, ticks, sandflies, triatomine bugs, tsetse flies, fleas, black flies, aquatic snails and lice (Table 4.1, WHO 2017a). The current spatial distributions of ten important vector-borne diseases are shown in Fig. 4.1.

Currently, on average, 77,000 people living in Europe fall sick from VBDs every year, but numbers are predicted to increase as vector species emerge (e.g. the Asian tiger mosquito, *Aedes albopictus*) or re-emerge (e.g. the yellow fever mosquito, *Aedes aegypti*) (<http://www.euro.who.int/en/media-centre/sections/press-releases/2014/77-000-europeans-fall-sick-every-year-with-vector-borne-diseases>). Globally, every year there are more than 700,000 deaths from zoonotic vector-borne diseases such as malaria, dengue, schistosomiasis, human African trypanosomiasis, leishmaniasis, Chagas disease, yellow fever, Japanese encephalitis and onchocerciasis (WHO 2017a). These zoonotic diseases account for around 17% of the estimated global burden of communicable diseases and disproportionately affect poorer populations that live in environmentally degraded environments and housing conditions that are favourable to VBDs (WHO 2017a). They impede economic

Table 4.1 Main vectors and diseases they transmit

Mosquitoes		Ticks	Sandflies	Triatomine bugs	Tsetse flies	Fleas	Black flies	Aquatic snails	Lice
<i>Aedes</i>	<i>Anopheles</i>	<i>Ixodes</i> , <i>Dermacentor</i> , <i>Hyalomma</i>	<i>Phlebotomia</i>	<i>Triatominae</i>	<i>Glossina</i>		<i>Simuliidae</i>	<i>Biomphalaria</i> , <i>Bulinus</i>	Lice
Chikungunya, Dengue fever, Lymphatic filariasis, Rift Valley fever, yellow fever, Zika	Malaria, Lymphatic filariasis	Crimean- Congo haemorrhagic fever, Lyme disease, relapsing fever (borreliosis), Rickettsial diseases (spotted fever and Q fever), Tick-borne encephalitis, Tularaemia	Leishmaniasis, sandfly fever (phlebotomus fever)	Chagas disease (American trypanosomiasis)	Sleeping sickness (African trypanosomiasis)	Plague (transmitted by fleas from rats to humans), Rickettsiosis	Onchocerciasis (river blindness)	Schistosomiasis (bilharziasis)	Typhus and louse- borne relapsing fever
	Japanese encephalitis, lymphatic filariasis, West Nile fever								

Adapted from the WHO fact sheet *Vector-borne diseases* (WHO 2017a)

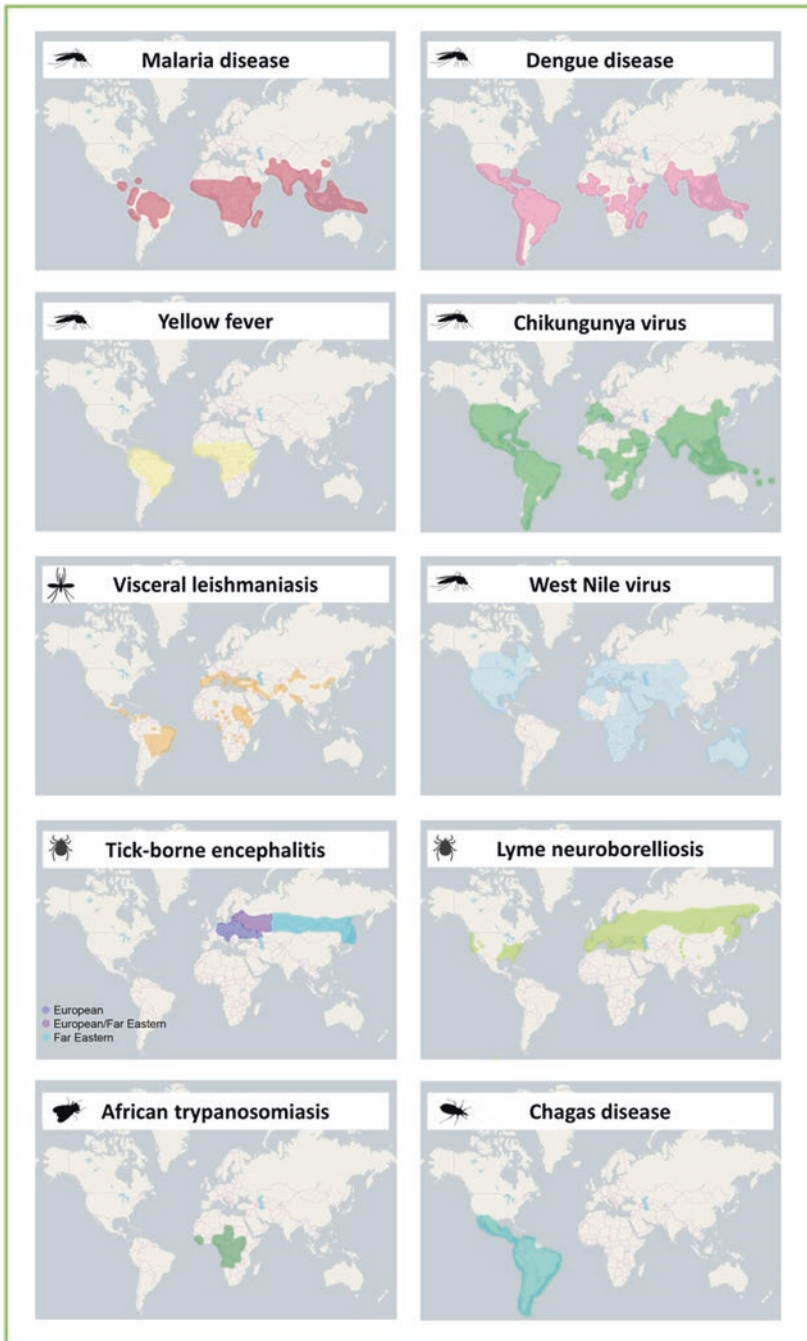


Fig. 4.1 Overview of countries/territories where ten important vector-borne diseases/related pathogens have been reported: malaria disease¹, dengue disease², yellow fever³, chikungunya virus⁴, visceral leishmaniasis⁵, West Nile virus⁶, tick-borne encephalitis⁷, Lyme neuroborreliosis⁸, African trypanosomiasis, and Chagas disease¹⁰. (Data sources: ¹Centers for Disease Control and Prevention (CDC), 2017; ²World Health Organization (WHO), 2013, ^{3,4}CDC, 2018, ⁵WHO, 2010, ⁶CDC, 2012, ⁷Holbrook (2017) *Viruses* 9(5):97, based on CDC and WHO data, ⁸Pachner & Steiner (2007) *Lancet Neurology* 6(6):544–52, ⁹WHO, 2016, ¹⁰WHO, 2004)

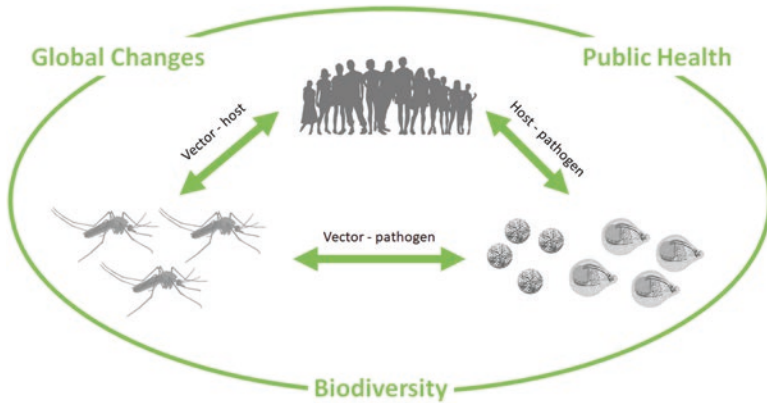


Fig. 4.2 Scheme of vector-host-pathogen interactions indicating the complex interplay of public health, biodiversity and global changes

development through direct medical costs and indirect costs such as loss of productivity and tourism (Narrod et al. 2012).

Epidemiological dynamics of VBDs are complex interactions of the vector, the pathogen and the host (Fig. 4.2). VBDs are clearly highly intertwined with climatic change and the degree of biodiversity (Engering et al. 2013). In addition to temperature alterations and rainfall changes, among other factors, heterogeneity of landscapes (Chaves et al. 2011), urbanisation (Wood et al. 2017) and local forest degradation (Brownstein et al. 2005) are extrinsic factors determining VBD risk or burden.

In this chapter, we show how climate change impacts VBDs and what role biodiversity (and its loss) plays for VBDs. (1) We show how climatic changes shape the distribution and abundance of disease vectors. To point out current triple vulnerabilities regarding climate change, biodiversity and VBDs, we selected ticks and mosquitoes as examples. (2) We point out important knowledge gaps on VBDs and biodiversity, which make prognoses for climate change challenging. (3) We review policy options to manage VBDs under climate and biodiversity changes and related infrastructural responses.

4.2 Disease-Transmitting Mosquitoes and Ticks

Due to global change, vector species may expand their distributions (Ogden et al. 2006; Gould and Higgs 2009) and shift their seasonal and spatial occurrences (Lafferty 2009), the latter particularly to higher latitudes and altitudes (Siraj et al. 2014; Dhimal et al. 2014a, b, 2015). This leads to increased species richness, e.g. a higher biodiversity of the vector species and pathogens at time of arrival in newly invaded regions. However, invasive species show a tendency to successfully establish in a new environment and outcompete native species sharing the same ecological niche. Thus, biodiversity can even decrease rather than increase under certain ecological conditions.

4.2.1 *Influence of Temperature on Vector Mosquitoes and Associated Pathogens*

In holometabolous vector mosquitoes, larval rearing temperature influences development times (Delatte et al. 2009; Reiskind and Janairo 2015; Couret et al. 2014; Müller et al. 2018), larval survival (Chang et al. 2007; Delatte et al. 2009; Couret et al. 2014; Müller et al. 2018), adult longevity (Aytekin et al. 2009; Delatte et al. 2009), length of female gonotrophic cycle (Delatte et al. 2009), and adult body size (Briegel and Timmermann 2001; Mohammed and Chadee 2011; Muturi et al. 2011). In arboviruses, temperature effects plaque growth (Jia et al. 2007) and replication speed (Kilpatrick et al. 2008). In addition, mosquito-arbovirus interactions such as virus susceptibility (Turell 1993; Kilpatrick et al. 2008; Westbrook et al. 2010), prevalence of dissemination (Turell 1993, Kilpatrick et al. 2008, Westbrook et al. 2010), transmission rate (Kilpatrick et al. 2008) and extrinsic incubation period (Chan and Johansson 2012) are influenced by temperature (reviewed in Samuel et al. 2016).

Altogether, temperature plays a key role in determining the viral transmission areas (Bayoh and Lindsay 2003; Lambrechts et al. 2010; Kilpatrick et al. 2008). Studies have shown that the ambient rearing temperature at immature stages influences the virus susceptibility and dissemination rate at adult stages for chikungunya virus in *Aedes albopictus* (Westbrook et al. 2010), Rift Valley fever virus and Venezuelan equine encephalitis virus in *Ae. taeniorhynchus* (Turell 1993) and Sindbis virus in *Ae. aegypti* (Muturi et al. 2011). Adult females of *Ae. albopictus* produced from larvae reared at 18 °C were more likely infected and disseminated with chikungunya virus than females from larvae reared at 32 °C (Westbrook et al. 2010) and *Ae. taeniorhynchus* females reared at 19 °C as larvae had a higher susceptibility and dissemination-prevalence for Rift Valley fever virus and Venezuelan equine encephalitis virus than larval cohorts reared at 26 °C (Turell 1993). *Ae. aegypti* females showed significantly higher infection and insemination rates with Sindbis virus when reared at their optimal larval temperature (25 °C) than when reared under temperature stress at 32 °C (Muturi et al. 2011). Therefore, knowledge on temperature effects triggering vector mosquitoes' mortality and development is important to explain disease outbreaks (Bangs et al. 2006).

4.2.2 *Distributional Changes of Mosquito Vector Species*

Climate change will not uniformly increase the burden of VBDs, but changes will differ between regions. In Ecuador, a modelling study examining the distributional changes of 14 vector species under climate change demonstrated that some arthropod vector species will become extinct in certain regions, while other regions, and in particular the Andean highlands, will experience a novel VBD burden (Escobar et al. 2016) (see Box 4.1). In accordance, the expansion of other VBDs such as

Box 4.1 VBD Risk Modelling for Climate Change Conditions and Suitable Policy Interventions in Ecuador

In their article, Escobar et al. (2016) analyse the current and potential future impact of climate change on vector diversity and geographical distribution in Ecuador through ecological niche modelling. The authors applied broader scale climate modelling concerning the current distribution of vectors, using remote sensing data. They defined suitable vector environments as potential high-risk areas, which were used to do future risk VBD modelling under climate change. Overall, they analysed current, medium-term and long-term predictions for vector distribution that can transmit dengue, malaria, Chagas and leishmaniasis. The model for the dengue transmitting vectors *Aedes aegypti* and *Ae. albopictus*, the latter not being officially reported in Ecuador but in neighboring countries, indicates a currently reduced, but future increased, risk for dengue transmission in highland regions, and long-term high risk in the coastal and Northeastern Amazonian areas. Importantly, climate change models predicted a change in vector-suitability environments, proposing an increased risk in western Andean valleys, which will pose additional public health and intervention challenges.

Escobar et al. (2016) present overall a higher risk for vector-borne diseases under future climate regimes, particularly in part of the Ecuadorian coast, valleys of the Northeastern Amazonian and western Andean region. Mitchell-Foster et al. (2015) have presented an integrated policy intervention that could propose a lasting option to vector-borne disease prevention and control, empowering communities and building future community health leaders. In their randomised controlled study in Machala, on the southwestern coast of Ecuador, they employed an integrated eco-bio-social approach among school children, aged 8–12 years, to significantly reduce the pupa per person index. Mitchell-Foster et al. (2015) used 20 clusters of 100 households, selected based on a two-stage-sampling design. Ten clusters were used for the integrated eco-bio-social approach and ten as control clusters. In addition, different forms of geographical mapping and pupa per person index (PPI) were used as an outcome measurement. The overall result showed a decreased PPI, and in those households where there were not any changes noted through monthly control visits, particular engagement activities were deployed (Mitchell-Foster et al. 2015, p.128). The integrative eco-bio-social approach among school children allowed for social empowerment, capacity building of future leaders and vector control. Given the projections for future dengue risk by Escobar et al. (2016), the findings of Mitchell-Foster's et al. (2015) randomised controlled study would present a suitable policy intervention, which could easily be scaled up on a national level.

Japanese encephalitis, dengue, chikungunya, lymphatic filariasis and visceral leishmaniasis towards a cooler mountainous region has been reported from Nepal (Dhimal et al. 2014a, 2015; Ostyn et al. 2015). Altitude is often used as a proxy for temperature changes, so one may speculate that this trend might also be true for more northern/temperate regions.

In Europe, four exotic *Aedes* types of mosquitoes are currently found (partly reviewed in Medlock et al. 2012): the Asian tiger mosquito (*Ae. albopictus*; Adhami and Reiter 1998), the yellow-fever mosquito (*Ae. aegypti*; Goncalves et al. 2008), the Asian bush mosquito (*Ae. japonicus japonicus*; Schaffner et al. 2009) and *Ae. koreicus* (Versteirt et al. 2012). Particularly, the Asian tiger mosquito *Ae. albopictus* with widespread European distribution is a competent vector for several VBDs and therefore poses human public health risks. It is suspected that the Asian tiger mosquito was the main vector for dengue viruses in France in 2015 (Succo et al. 2016) and for chikungunya virus in Italy in 2007 and 2017 (Rezza 2018) (autochthonous cases in Europe 2007–2012 reviewed in Tomasello and Schlagenhauf 2013). These cases show how human transport activities and temperature change facilitate the establishment of vector species and highlight the importance of actively preventing such establishments (Eritja et al. 2017; Ducheyne et al. 2018, Reuss et al. 2018, Dhimal et al. 2018).

Despite temperature, climate change will lead to hydrological changes. For *Ae. albopictus* in Europe, it is projected that Mediterranean locations will become more unsuitable habitats due to climatic variables and changed water regimes, while suitability is increased in middle and northern Europe up to 55°N (Fischer et al. 2014). Climate and photoperiod also alter the host-seeking and feeding activity in ticks as well as the seasonal occurrence of vector stages (Altizer et al. 2013; Kurtenbach et al. 2006).

4.2.3 *Distributional Changes of Ticks in Europe*

There are objective grounds that climate change influences the distribution and seasonal activity of disease-transmitting ticks (Ogden et al. 2014). The tick *Ixodes ricinus* is medically highly relevant as a vector for spirochaete bacteria *Borrelia burgdorferi*, with Lyme disease extending its distribution northwards in Europe, in a warmer climate (Lindgren et al. 2000). The taiga tick (*Ixodes persulcatus*), transmitting the ‘early summer’ meningo-encephalitis virus, is currently spread from Russia west-northwards to Scandinavia (Jaenson et al. 2016). Ticks of the genera *Dermacentor* with a previously Mediterranean distribution, for instance the *Coxiella burnetti*-transmitting sheep tick *Dermacentor marginatus* (Q fever,) are now established in cold-temperate Germany (Földvári et al. 2016). The Mediterranean tick *Hyalomma marginatum* is the main vector for the emerging pathogen Crimean-Congo Hemorrhagic Fever in Europe. International livestock trading guarantees the tick’s mobility, as ticks live on domestic animals, while the degradation of agricultural land favours the mass development of *Hyalomma marginatum* (Estrada-Pena

et al. 2012). This tick species has established populations in southern and eastern Europe but may extend its distribution to some areas of Italy, the Balkans and southern Russia when climatic conditions are improved, especially in autumn (Estrada-Pena et al. 2012).

4.3 Biodiversity and VBDs: The Large Unknowns

4.3.1 Pathogen Diversity

The diversity of potential human pathogens, the species diversity and phenotypic plasticity of vectors and the biodiversity of their reservoir hosts is largely unexplored. On our planet, an immense but largely unknown diversity of viral species is hosted by mammals and birds (estimate over 1.3 million, <http://www.globalviromeproject.org/overview/>). Approximately 38% of these viral species could result in VBDs in humans. The Global Virome Project will explore this biodiversity of viruses over the next 10 years, which may result in many surprises for the VBD research community.

4.3.2 Vector Diversity

The understanding of spatio-temporal phenotypic diversity and genetic architectures of vector populations under current and climate change conditions is crucial for vector control management. Local knowledge on phenotypic diversity to insecticide resistance can foster success in chemical vector control. The worldwide insecticide resistance network WIN is currently tracking insecticide resistance in mosquito disease vectors on a global scale and consults with the WHO and member states on how to improve insecticide resistance surveillance and implement alternative vector control tools (<https://win-network.ird.fr/>). Likewise, the understanding of vector ecology and in particular the understanding of age-structure of field populations, the adaptive behaviour of vectors, and context-dependence of vector capacities fundamentally affect the success rate of biotechnological interventions. The efficiency of biological and genetic vector control is in some cases defined by the available number of targeted life stages. In others, the ratio of released *Wolbachia* contaminated insects and genetically modified or radiation-sterilised males and the virgin wildtype counterparts in a field population determines the suppression rate of vector populations and hence the degree of disease control (Iturbe-Ormaetxe et al. 2011; Ross et al. 2017). Our lack of basic ecological knowledge even with a prominent vector such as *Anopheles gambiae* for malaria disease could blunt our new biotechnological weapons for vector control (Alphey and Alphey 2014; Ferguson et al. 2010).

4.3.3 Host Diversity

Mosquitoes and ticks feed on a wide range of hosts, and their pathogens circulate in diverse animal species. Lyme disease is caused by *Borrelia burgdorferi*, which is transmitted to humans through the bite of *Ixodes* ticks. For *Borrelia burgdorferi* sensu lato, a broad range of reservoir hosts have been identified, for instance nine small mammals, seven medium-sized mammals and 16 bird species in Europe (Gern et al. 1998), and eight small mammals in the USA (summarised in Salkeld et al. 2008). As another example, the Zika virus is known to circulate in monkey and wild mammal populations in Africa, and has been detected in domestic sheep, goats, horses, cows, ducks, rodents, bats, orangutans and carabaos in Indonesia and Pakistan (Vorou 2016). However, large knowledge gaps on the diversity of reservoir hosts for mosquito- and tick-borne pathogens in old and new areas of distribution still exist (Baráková et al. 2018; Hashiguchi et al. 2018). Certainly, these gaps will never be closed given the complex dynamics of adaptations between pathogens, vectors and hosts.

The conceptual model of the dilution effect in Lyme disease (Ostfeld and Keesing 2012) is the textbook example about how biodiversity on the level of the host species can directly influence the transmission of an arthropod-transmitted disease. Humans are aberrant hosts for the pathogen, because the pathogens cannot replicate in humans. In a natural cycle of *Borrelia burgdorferi*, the bacteria are maintained by small mammals and birds (reservoir hosts). The dilution effect model in the Lyme-disease system states that the relative abundance of host individuals should be evenly distributed across host species to decrease the potential for an encounter of the tick with the most competent reservoir host. This model also applies to other vector-host systems in which a generalist vector uses many host species of which only a few are competent reservoir hosts (Swaddle and Calos 2008; Civitello et al. 2015). The smaller the risk for a host to become infected and thereby maintain and release pathogens, the more species-diverse and abundant is the host community (Civitello et al. 2013; Levi et al. 2016). However, this dilution effect is still under academic debate (e.g. Civitello et al. 2015 and Salkeld et al. 2015), and there is an urgent need for further research.

4.4 How to Manage VBDs?

Different public health measures exist, ranging from epidemic control through vector control (of mosquitoes, bugs, flies, fleas) and eradication of diseases through vaccination, case treatment and breeding site elimination (WHO 2017b). Vector control tools target specific life stages of arthropod vectors and are of a chemical (e.g. pyrethroid insecticides), biological (e.g. *Wolbachia* bacteria) or transgenic nature (e.g. genetically modified mosquitoes). Chemical insecticides are additionally used for preventive measures such as insecticide-treated bed nets,

insecticide-treated livestock or indoor residual spraying in highly VBD endemic areas, which complements other preventive actions such as source reduction and information campaigns. All pest control measures can influence biodiversity in manifold ways, whereas prospective evaluations of positive and negative effects of pest control under global changes is rarely available in the VBD context.

4.4.1 Chemical Insecticides

Arthropod pest control in epidemic regions is based on chemical insecticides, which work efficiently against vectors, but are mostly associated with undesirable side effects for biodiversity. The past use of dichloro-diphenyl-trichloroethane (DDT), for example, successfully eliminated malaria in North America and Europe and significantly decreased the number of deaths in other regions of the world (WHO 2008; Keiser et al. 2005). However, DDT is highly persistent in the environment, accumulates in fatty tissues of organisms, and biomagnifies from low trophic levels to predators such as ice bears and eagles (e.g. reviewed in Van den Berg 2009). The high ecotoxicological risk of DDT for wildlife and ecosystem functioning was first discovered by Rachel Carlson in 1962 (Carson 2002). Consequently, the Stockholm Convention on Persistent Organic Pollutants (2001) banned DDT and a number of other chemicals that were used as insecticides in the past (NO 2005). The use of DDT is, however, allowed under the Stockholm Convention for disease vector control, within the recommendations and guidelines of the WHO until locally effective and affordable substitutes and methods are available. Concerted large-scale efforts are now underway to reduce both the burden of VBDs and the use of DDT (Van den Berg 2009).

The generations of insecticides following DDT were organophosphates (e.g. parathion), carbamates, pyrethroids (e.g. deltamethrin) and neonicotinoids (e.g. imidacloprid), all designed to increase the efficiency to kill pest insects, overcome problems with insecticide resistance in pest species, and lower the environmental burden by increasing specificity (and thereby decreasing applied amounts for the same efficiency). In every insecticide class, however, negative health effects on human and/or wildlife occurred. For example, pyrethroids are recommended for indoor spraying and bed net treatment by the WHO. However, pyrethroid resistance evolved in several insect species and hence vector control cannot rely exclusively on this insecticide class in the long term (Hemingway and Ranson 2000). As another example, neonicotinoids, the most recent insecticide class (developed in the 1990s) are discussed as a good candidate (clothianidin) for indoor residual spraying in areas with pyrethroid-resistant mosquito populations (Agossa et al. 2018). Neonicotinoids are currently under restricted use in the European market due to increasing evidence of toxic effects on honey bees (honey-bee colony-collapse disorder), wild pollinators and indirectly on insectivorous birds, which are already challenged by climate change (e.g., Le Conte and Navajas 2008; Hladik et al. 2018).

On 17 May 2018, the European Commission banned the neonicotinoids imidacloprid, clothianidin and thiamethoxam for field applications in EU member states.

With climatic changes, the efficiency of chemical insecticides can change (thermal-dependent toxicity of specific chemicals; Kreß et al. 2014) and the distribution of chemical insecticides in the environment will alter (Op de Beeck et al. 2017). Probably enhanced by a warmer climate, insecticide resistance of arthropod vectors to chemical insecticides will evolve further (Maino et al. 2018). In contrast, non-target organisms in aquatic environments are threatened by manifold stressors, while the combined effects of pesticides and warming may accelerate the ongoing biodiversity loss (Liess et al. 2016). Thus, even if the use of chemical insecticides currently appears to be an easy-to-use tool, in the long term, we need new, eco-friendly and sustainable vector control tools.

4.4.2 *Biological Insecticides*

There is a consensus between researchers, that biodiversity is a valuable resource for discovering novel insecticides (Silva-Filha 2017; Huang et al. 2017). The ongoing dramatic loss of biodiversity under climate and other global changes may empty this treasure chest faster than new biological insecticides can be discovered.

For a few decades, control measures have made use of natural insect toxins from *Bacillus israelensis thuringiensis* (B.t.i.) and the bacterial endoparasite *Wolbachia* spp. (mostly *W. pipientis*) (Baldacchino et al. 2015). The application of B.t.i. in wetlands against floodwater mosquitoes, which are primarily annoying insects but are also known as vectors for Usutu and West Nile viruses, is assumed to be environmentally safe, although discussions on this topic are highly controversially discussed (Niemi et al. 2015; Jakob and Poulin 2016). Unfortunately, first resistance against B.t.i. has been observed, for instance in the dengue vector *Aedes aegypti*, and is expected to be supported by a warming climate (Paris et al. 2011).

A great success story is the contamination of *Aedes* mosquitoes with natural *Wolbachia* bacteria (Iturbe-Ormaetxe et al. 2011). The presence of the bacteria inhibits the dengue and West Nile virus replication and hence reduces the pathogen load of mosquitoes (Ant et al. 2018). This biological technique can also be used to suppress mosquito populations since wild females become sterilised when mating with a *Wolbachia*-contaminated male mosquito. The World Mosquito Program developed a *Wolbachia* method that enables the transmission of *Wolbachia* to offspring and spreads through the whole population (<http://www.eliminatedengue.com/our-research/wolbachia>). This theoretically self-sustaining *Wolbachia* method is now in the large-scale trial phase (reviewed in Mishra et al. 2018).

Many other biological approaches have been discussed (Huang et al. 2017). As one example, copepods have been used for a long time to control *Aedes* species (e.g. Vu et al. 1998) and are now also proposed as biological agents against *Culex* mosquitoes. Copepods feed on mosquito larvae (and other prey) and hence suppress populations. Since the growth rates of both prey and predator strongly depend on

temperature, the *Relative Control Potential* metric has been developed to allow the right selection of a living biological control agent for specific temperature conditions (Cuthbert et al. 2018).

4.4.3 *New Genetic Tools in Vector Control*

Recent advances to modernise and develop new vector control and surveillance tools mean that there has never been a better time to reinvigorate vector control. The genetic control of vectors will add to the existing vector control toolbox. Certain genetic vector control strategies have a greater advantage as they will perform even better when climatic conditions favour vector population growth and development. Furthermore, genetic vector control targets only one species and thereby could avoid direct negative effects on non-target species.

The sterile insect technique (SIT) is based on the release of sterile mosquito males, produced by irradiation or sterilising chemicals, mating with wild females and thereby suppressing the mosquito population growth. However, the successful implementation of SIT requires a repeated release of a high number of mosquitoes with ideally no fitness costs if compared to wild counterparts. Therefore mass-rearing facilities have been set up and several sex-sorting techniques for pupae have been developed. SIT successfully eliminates or suppresses populations, as shown for *Cx. quinquefasciatus* on an island in Florida and *Anopheles albimanus* in El Salvador or *Ae. albopictus* in Italy (reviewed in Baldacchino et al. 2015). Alternatively, insects can be sterilised or immunised by genetic modifications (GMs), which is a more precise procedure and goes along with less fitness costs for male mosquitoes. The release of transgenic sterile male mosquitoes carrying a dominant lethal genetic system (RIDL technique) has been successfully applied for dengue-carrying mosquitoes in the Caribbean (Harris et al. 2011), Malaysia (Lacroix et al. 2012) and Brazil (Carvalho et al. 2015). However, as with SIT, repeated releases with large numbers of males are necessary to efficiently control insect vectors and agricultural pest insects.

The release of gene-drive insects for population suppression or vector immunisation might be an even more promising technique. Preliminary studies have confirmed the feasibility of using gene drive-based modifications for vector control (Hammond et al. 2016; Burt et al. 2018). Gene-drives rely on an endonuclease cassette (e.g. CRISPR-Cas9) targeting genes important for fitness of the vector or inhibit parasite development. This endonuclease cassette spreads through the target population by modifying/cutting the DNA of target genes in the germline of every offspring. When the DNA in wild-type insects is repaired, the DNA of genetically modified insects serves as the DNA template. As a result, the endonuclease cassette copies to the wild-type DNA. This way, the gene-drive construct passes via germline modification to almost every offspring and from generation to generation. This hypothetical self-sustaining behaviour of gene-drives might be a clear advantage, because the reduction of release efforts is necessary to save costs,

lower infrastructural needs and may also work in large and remote areas. However, the technique lacks post-release control and the required data for environmental risk assessment are not yet available. Further research is needed before allowing the release of gene-drive insects to the wild.

4.4.4 Sustainable Control Programs

The ecological risk assessment of chemical, biological and genetic vector control measures on non-target biodiversity will remain difficult because our basic knowledge on non-VBD biodiversity as well as on cryptic viral, microbiological, genetic, phenotypic and reservoir host biodiversity under global changes is so fragmentary. One may also hope for the future, that biodiverse nature endows us with new biological insecticides and medically active compounds to help us to treat VBDs. Such ecosystem services could deliver a very good reason to preserve existing biodiversity and respect traditional lifestyles and related knowledge of local communities.

Traditionally, single-intervention approaches such as insecticide treatment dominated the toolbox of vector control managers in the past. The Integrated Vector Control Management (IVM) makes use of vector surveillance, risk mapping and a variety of vector prevention and control tools, and adjusts the set of applied tools to local conditions in a time- and dose-dependent manner. However, it must be kept in mind that just a reduction of mosquito breeding sites (prevention), use of insecticides (control), IVM or SIT have brought only few benefits in the attempt to control the vector populations (Baldacchino et al. 2015). Building sustainable control programs that are resilient in the face of technical, operational and financial challenges will in addition require the engagement and collaboration of local communities.

Efforts to limit the breeding of disease vectors are often hampered by lack of community awareness of the interconnections between disease, vectors and viruses/parasites. On the other hand, community mobilisation and the implementation of an integrated community-based approach can probably render dengue fever control effective (Andersson et al. 2015; Mitchell-Foster et al. 2015). Lessons learned from previous studies should be used to inform previously VBD-unaffected populations. For example, a study from Nepal shows that only 12% of the sample population had good knowledge of dengue fever and those living in the lowlands with regular outbreaks of mosquito-borne diseases were five times more likely to possess good knowledge than highlanders experiencing rare or zero outbreaks of mosquito-borne diseases (Dhimal et al. 2014b). Thus, VBD-naïve populations such as in remote mountainous regions may be at special risk under the impact of climate change fostering the spread of disease vectors to cooler ecoregions (Dhimal et al. 2014a, b, c, 2015; Escobar et al. 2016). The same might be true for northern/temperate regions if considering altitude as a proxy for temperature conditions.

4.5 Responses to VBDs Along with Biodiversity Loss and Climate Change

4.5.1 *Target the Complexity*

Though the world is complex, our understanding of VBDs comes mainly from individual research disciplines. Who is at a high risk of VBDs is determined by biological, ecological, climatic, social, cultural, historical, political and economic factors (Lacey 2012; Marmot and Wilkinson 2005). Ecological factors refer, for example, to micro-climate, the natural landscape and anthropogenic settings. Biological factors relate to population dynamics of vectors and the transmission dynamics of pathogens. Socio-cultural, political and economic factors comprise a number of variables relating to conservation of biodiversity, mitigation and adaptation strategies of climate change impacts and health systems, including vector control, health services, the political context, public and private services (such as water supply), ‘macro-social’ events (such as urbanisation), and community and household-based practices, and how these are shaped by large-scale forces (such as gender, ethnicity, education, social and economic status) (Chu-Agor et al. 2012; Huffaker 2015). All those factors need to be understood in a systemic context, rather than as individual factors, if we want to understand altered geographical and temporal distributions of VBDs. To give an example, dengue and chikungunya viruses are transmitted by the mosquitoes *Aedes albopictus* and *Aedes aegypti*. Their local transmission of dengue and chikungunya viruses is coupled with meteorological and climatological conditions, and ecological, socio-economic, demographic and cultural factors (Morrison 2014; Teurlai et al. 2015; Harapan et al. 2017, 2018).

4.5.2 *Interconnecting People and Knowledge*

There are several promising developments to interconnect people and knowledge in Europe and beyond.

At the G7 summit on 7 and 8 June 2015, G7 member states committed themselves to research and development in the field *Neglected Tropical Diseases*, which includes many VBDs such as Zika, dengue, chikungunya and leishmaniasis. As a result, for example, the four German ministries Federal Ministry of Education and Research, Federal Ministry of Food and Agriculture, Federal Ministry of Health and Federal Ministry of Defence signed a research agreement on One Health that supports interdisciplinary research on zoonotic diseases for the health of animals and humans. In accordance, the national network on zoonoses (<https://www.gesundheitsforschung-bmbf.de/de/nationales-forschungsnetz-zoonotische-infektionskrankheiten-6820.php>) was founded in 2017, which interacts strongly with the German Research platform for zoonoses (<http://www.zoonosen.net/EnglishSite/Home.aspx>). Both German initiatives aim to improve our understanding of zoonotic

diseases and to improve the knowledge transfer from science to practice and *vice versa*.

At the European level, the European Food Safety Authority (EFSA) and the European Centre for Disease Prevention and Control (ECDC) support the European VectorNet initiative. The VectorNet network assembles data on vector distributions and cases of animal and human VBDs. The information on biogeography of vectors and latest VBD outbreaks can be freely accessed at <https://ecdc.europa.eu/en/about-us/partnerships-and-networks/disease-and-laboratory-networks/vector-net>. Moreover, the European Union funds the InfraVec2 project, which offers free access to European infrastructures for research on insect vectors and their pathogens and thereby interconnects the VBD research community (<https://infravec2.eu/>). The InfraVec2 project aims to set up common quality standards and operating frameworks in the field of arthropod VBDs (standardise test procedures, develop accepted, traceable reference standards for biological material, etc.) and thus improve inter-laboratory reproducibility and finally the quality of research outcomes.

4.5.3 Policy Options

The recent unprecedented global spread of dengue and chikungunya viruses and the outbreaks of Zika virus and yellow fever in 2015–2016 have highlighted the challenges faced by countries. The need has never been greater for a comprehensive approach to vector control. Most VBDs can be prevented through vector control, but only if it is implemented effectively. This is, however, hampered by numerous challenges that include: lack of capacity and capability (human, infrastructural and institutional) in country programmes; lack of a comprehensive national strategy for vector control and the necessary legal framework; a limited toolbox of interventions; lack of community involvement; and ongoing environmental and social changes that result in the proliferation and geographic expansion of vectors. The global vector control response 2017–2030 (GVCR) approved by the World Health Assembly provides strategic guidance to countries and development partners for urgent strengthening of vector control, preventing disease and responding to outbreaks (WHO 2017a, b). In addition, WHO provides fact sheets on *VBDs* and *Climate change and Health* in different languages for lay people and public health workers. To achieve the re-alignment of vector control programs and increased technical capacity, improved infrastructures, strengthened monitoring and surveillance systems, and greater community mobilisation are required. One of the priority activities outlined in the GVCR is for countries to conduct or update their vector control needs assessment. This information can then be utilised to develop or update countries' vector control strategies and to plan necessary activities. This Framework for a National Vector Control Needs Assessment sets the standards for baseline assessment and progress tracking in line with the goals, targets, milestones and priorities of the GVCR. Ultimately, all these activities will support implementation of a comprehensive approach to vector control, disease surveillance and VBD

research that will enable the achievement of disease-specific national and global goals and contribute to achievement of the Sustainable Development Goals and Universal Health Coverage (WHO 2017a, b).

One important policy area is with climate change mitigation policies under the Paris Agreement. Keeping global warming under 2 °C in relation to global temperatures before the Industrial Revolution will have an impact on VBD's spread to zones that have previously been uninhabitable for vectors. However, with current global warming we are already seeing an impact (Dhimal et al. 2014a, 2015; Ostyn et al. 2015); therefore, climate change adaptation policies are also directly linked to VBD control and elimination, particularly in those areas that have previously not shown any risk to VBD's or evidence of prevalence.

VBD control and elimination need to be addressed from an interdisciplinary and trans-sectoral approach, not just in the health sector. It is highly important to situate VBD control and elimination within a wider understanding of planetary health (Whitmee et al. 2015). Global policy approaches need to address a One Health approach, which interlinks human and animal health within planetary ecosystem processes that are determined by human action and therefore global change (Steffen et al. 2015; Whitmee et al. 2015).

Another policy area is influenced by Sustainable Development Goals that guide regional, national and local policies and practices and are directly interlinked with VBD control (Table 4.2).

We argue that Sustainable Development Goals will only be lasting if ensuring good health and well-being, which will rely on effective vector control as well as on initiatives for clean water and sanitation (Goal 6), sustainable cities and communities (Goal 11), climate action (Goal 13), life on land and biodiversity (Goal 15), among others. Multiple approaches that are implemented by different sectors will be required for control and elimination of VBDs, such as those promoting healthy environments (Pruss-Ustun et al. 2016).

Recognition that climate change mitigation and adaptation strategies can have substantial benefits for both health and biodiversity conservation presents policy options that are potentially both more cost-effective and socially attractive than are those that address these priorities independently. Any policy, for example the move and expansion of vectors, through transportation and livestock trade and movement on a local, national and sub-national level, needs to be coordinated in a regional context addressing global change challenges.

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Table 4.2 Relationship between Sustainable Development Goals and control of VBDs

SDG	Relationship to VBDs	Example
Goal 3. <i>Ensure healthy lives and promote well-being for all at all ages</i>	VBDs are a major contributor to global morbidity and mortality	VBDs account for > 17% of the global burden of infectious diseases; > 80% of the global population is at risk from one VBD, with > 50% at risk of two or more VBDs.
Goal 6. <i>Ensure access to water and sanitation for all</i>	Investment in clean water and sanitation can reduce the risk from VBDs	Open stored water containers are a major habitat for immature dengue, chikungunya and Zika virus vectors worldwide; provision of piped water and/or mosquito-proof water storage containers can reduce the transmission of these diseases.
Goal 11. <i>Make cities inclusive, safe, resilient and sustainable</i>	Ending VBDs makes cities (and slums) safer	Resilience against VBDs needs to be included in strategic planning for urban development.
Goal 13. <i>Take urgent action to combat climate change and its impacts</i>	Mitigating the impacts of climate change has the potential to reduce VBDs	VBDs are highly sensitive to climatic conditions, especially temperature, rainfall and relative humidity; patterns of epidemiology change more rapidly than health policy can respond; climate change can impact all VBDs.
Goal 15. <i>Sustainably manage forests, combat desertification, halt and reverse land degradation, halt biodiversity loss</i>	Maintaining terrestrial ecosystems and halting biodiversity loss will help reduce VBDs in some places, but increase it in others	Bio-reserves can harbour vector populations in protected areas. Biodiversity loss (such as that associated with deforestation) may enhance the risk of some diseases such as malaria, while biodiversity gains (such as that associated with reforestation) could sometimes increase the risk for other diseases
	Significantly reduce the impact of invasive alien species on land and water ecosystems	Invasive vector species (e.g. <i>Aedes albopictus</i>)
	Promote fair and equitable sharing of the benefits arising from the utilisation of genetic resources and promote appropriate access to such resources	Biological vector control

Adapted from: WHO (2017a, b). The Global vector control response (GVCR) 2017–2030

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