

# **Mathematical and behavioural ecology of mosquitoes in response to environmental change**

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*This thesis is dedicated to the memory of the mosquitoes that gave their lives to  
facilitate this research.*



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## **Statement of originality**

I hereby certify that the work within this thesis is entirely my own apart from the exceptions listed below.

### **Chapter 1:**

Katherine Heath wrote the Introduction. Prof. Michael B. Bonsall reviewed the text and provided comment.

### **Chapter 2:**

Katherine Heath conceived of the research question, designed and executed the mathematical model and prepared the manuscript. Dr. Lincoln Muniz Alves provided guidance on the use of climate data and provided critical comment on the model design. Prof. Michael B. Bonsall provided technical assistance with coding. Both Dr. Lincoln Muniz Alves and Prof. Michael B. Bonsall reviewed the manuscript and provided comment.

### **Chapter 3:**

Katherine Heath and Robert Paton conceived of the study design. Katherine Heath conducted the experiments with input from Robert Paton. Dr. Anthony J. Wilson provided guidance on the empirical study design and facilitated insectary access. Katherine Heath analysed the data and prepared the manuscript. Robert Paton, Dr. Anthony J. Wilson and Prof. Michael B. Bonsall reviewed the manuscript and provided comment.

### **Chapter 4:**

Katherine Heath conceived of the study design. Dr. Hervé Bossin provided critical comment on the study design and facilitated field site access. Katherine Heath conducted the empirical work, analysed the data, designed the mathematical model and wrote the manuscript. Dr. Sean Hackett, Dr. James C. Terry, Prof. Michael R. Heath, Dr. Hervé Bossin and Prof. Michael B. Bonsall reviewed the manuscript and provided comment.

### **Chapter 5:**

Katherine Heath wrote the discussion. Tom Brewer, Prof. Michael R. Heath and Prof. Michael B. Bonsall reviewed the text and provided comment.



## **Format of chapters**

This thesis is presented as an integrated thesis, with each of three chapters presented in the format of journal articles. All three articles have been or intend to be submitted to academic journals in an edited form. The supplementary materials for each chapter are presented in Appendices A-C. The articles and their publication status are detailed below.

### **Chapter 2:**

Heath K, Alves LM, Bonsall MB. Climate change, urbanisation and *Aedes aegypti* mosquitoes in Brazil. *Nature Climate Change* (editor approved; resubmitted with responses to reviewer comments)

### **Chapter 3:**

Heath K, Paton RS, Wilson AJ, Bonsall MB. Nutritional availability and larval density dependence in *Aedes aegypti*. *Ecological Entomology* (under review)

### **Chapter 4:**

Heath K, Bossin HC, Bonsall MBB. Environmental heterogeneity influences *Aedes polynesiensis* mosquito density in French Polynesia. *In preparation*

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## **Additional manuscripts during the funding period**

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Heath K. Cost effectiveness analysis of treatment timing considering the future entry of lower cost generics for Hepatitis C. *Clinicoeconom Outcomes Res.* 2018; 10:539-550

Levi J, Pozniak A, Heath K, Hill A. The impact of HIV prevalence, conflict, corruption and cash on treatment cascades: data from 137 countries. *J Virus Erad.* 2018; 4: e30-e41

Hill A, Dauncey T, Levi J, Heath K, Perez C. Higher risks of mother-to-child HIV transmission (MTCT) in countries with lower HIV prevalence: UNAIDS 2013 results for 32 countries with generalised epidemics. *J Virus Erad.* 2015; 1(4): 257-263

Simmons B, Saleem J, Heath K, Cooke G, Hill A. Long-term treatment outcomes of patients infected with Hepatitis C virus: a systematic review and meta-analysis of the survival benefit of achieving a Sustained Virological Response. *Clin Infect Dis.* (2015) 61 (5):730-740



## **Thesis abstract**

Mosquito-borne disease presents an enormous global health challenge. Malaria remains the leading cause of stillbirth, dengue fever affects over 300 million people each year and chikungunya has caused numerous large outbreaks over the last two decades. Mosquito-borne diseases continue to affect some of the most socioeconomically disadvantaged and vulnerable sectors of society; higher levels of mosquito-borne disease occur in developing regions and disproportionately affect children. Rapid changes in climate, land use and human movement all have consequences for the ecology of mosquitoes and, consequently, the diseases they spread. Incidentally, it is thought that rapid global environmental and climate change are likely to most severely affect developing nations. Therefore, it is imperative that mosquito control initiatives acknowledge the effects of environmental change upon mosquito life history to have maximum impact.

In this thesis I endeavour to understand some of the mechanisms by which environmental heterogeneity and environmental change affect mosquito populations. In Chapter 1, I introduce important aspects of mosquito ecology and suggest primary mechanisms by which environmental change affects mosquito ecology.

Chapter 2 presents a model of *Aedes aegypti* population dynamics in response to climate change in Brazil. The model estimated mosquito populations to increase across most of Brazil as a consequence of changes in temperature and precipitation. Seasonal patterns in mosquito populations were also predicted to be disrupted.

Understanding the finer details of the effects of environmental change on specific mosquito life-history traits is also imperative. This is because (a) environmental

perturbation has unimodal effects at multiple life-cycle stages and (b) mathematical population models must be accurately parameterised to reflect biological traits. Chapter 3 considers one such trait – larval density dependence – and demonstrates that nutritional availability modifies density dependence in *Aedes aegypti*. Therefore, density dependence in *Aedes aegypti* larvae is a multi-dimensional process that requires mechanistic empirical study designs.

In Chapter 4 I present a methodological approach by which environmental heterogeneity can be accounted for in models of mosquito population dynamics, using *Aedes polynesiensis* in French Polynesia as a study system. I demonstrate that different patterns of environmental change can have spatially non-linear effects upon mosquito populations.

In Chapter 5, I synthesise the preceding findings and place them in a broader ecological context. For successful mosquito control, there must be extensive empirical research and theoretical modelling undertaken to catalogue the ways in which environmental change affects mosquito ecology. This thesis endeavours to provide some movement towards this. However, the extent to which future mosquito-borne disease outbreaks is mitigated depends more than ever upon what we do now to mitigate damaging changes in land use and climate.

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# Chapter 1

## Introduction

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## **Background and motivation**

### **The mosquito-borne disease burden**

Mosquito-borne diseases present one of the greatest challenges for modern global health. Vector-borne disease is thought to account for 17% of the global disease burden (World Health Organization, 2017a, 2017b, 2017c). Almost half of the global population live at risk of dengue and over 300 million people contract dengue each year (Bhatt et al., 2013). Over three million cases of the alphavirus chikungunya were reported in the Indian ocean region during a major outbreak from 2005-2006 with 38% of the population of La Réunion infected with the disease (Burt et al., 2012; Chhaabra et al., 2008; Pialoux et al., 2007). Zika virus has been reported in 84 countries and in 2016 was declared an international public health emergency by the World Health Organization (WHO) (World Health Organization, 2017d, 2016). There were an estimated 219 million cases of malaria in 2017, an increase of two million from 2016 (World Health Organization, 2018). Malaria continues to affect some of the most vulnerable sectors of society, including developing countries and children. Infants under five years old accounted for 61% of global malaria deaths in 2017 (World Health Organization, 2018). Region-specific mosquito-borne diseases also present substantial threats. In the South Pacific, the mosquito *Aedes polynesiensis* is the major vector of *Wuchereria bancrofti* and a secondary vector of dengue (Lardeux et al., 2002a). It is imperative that global health strategy is committed to alleviating the burden placed upon public health services by mosquito-borne disease over the coming decades.

Many mosquito-borne diseases are increasing in their geographic range (Bhatt et al., 2013; Messina et al., 2015; Nsoesie et al., 2016). Imported cases of chikungunya were reported in Europe, Asia and the USA following large outbreaks in the Indian Ocean in 2005-2006 (Depoortere et al., 2006; Parola et al., 2006; Weaver and Lecuit, 2015). Local transmission ensued in Italy, France and Southeast Asia (Weaver and Lecuit, 2015). Between the 1950s and 2010s the incidence of dengue increased 30-fold globally (World Health Organization, 2012a). At the end of the 20<sup>th</sup> century, regions in the Pacific and Americas which were previously dengue-free became hypo- and hyper-endemic with dengue (Gubler, 2002; Gubler and Clark, 1995; Murray et al., 2013). Not only is mosquito-borne disease an enormous global health problem, it is one which has been steadily increasing in many regions.

Mosquito-borne disease has remained a global public health problem over the last century due to, in part, slow vaccine development. Yellow fever has been a notable exception and the yellow fever vaccine has been considered one of the most successful vaccines ever developed (Barrett and Teuwen, 2009). The complex epidemiology of many mosquito-borne diseases, such as cross-reactivity between serotypes in dengue fever, has hindered progress towards other vaccines (Ghosh and Dar, 2015; McArthur et al., 2014). The extensive world-wide use of long-lasting insecticidal nets (LLINs) and indoor residual spraying (IRS) has been effective in limiting the growth of malaria incidence (Snow et al., 1988b, 1988a), but these approaches have recently been hampered by emerging insecticide resistance (Hemingway et al., 2016; Ranson and Lissenden, 2016; World Health Organization, 2012b).

## **An ecological focus**

Rapid increases in the geographic range of mosquito-borne diseases and slow vaccine development have shifted the public health focus from control of mosquito-borne diseases to the control of mosquito populations. Mosquito control strategies are numerous and diverse and include transgenic mosquitoes, insecticides and biocontrols. Mathematical models of mosquito populations have been of particular importance for mosquito control strategies in order to pre-empt unintended negative ecological consequences of control strategies. Such models require a comprehensive understanding of mosquito behaviour derived from rigorous empirical study (Alphey and Alphey, 2014) and mathematical models of mosquito populations have begun to focus on establishing robust mathematical frameworks of mosquito ecology (Cator et al., (in review).; Reiner et al., 2013). Indeed, the importance of mosquito ecology for population suppression was acknowledged as early as 1905 when Ross modelled the consequences of random mosquito dispersal for malaria elimination strategies (Ross, 1905).

Ultimately, mitigation of the global mosquito-borne disease burden cannot occur without comprehensive understanding of the ecology and behaviour of mosquitoes themselves. Herein, I review several important aspects of mosquito ecology. In particular, I highlight that environmental heterogeneity and change have modifying effects upon mosquito life history and behaviour. I then discuss existing control methods and highlight the importance of our understanding of mosquito ecology for the success of these strategies.

## **Mosquito-borne disease and mosquito ecology**

### **Mosquito life history**

The mosquito life cycle has four distinct stages which are common between most species (Nelson, 1986). Female mosquitoes blood-feed in order to acquire the necessary proteins for egg production. Female mosquitoes then oviposit eggs in pools of fresh water. Eggs of most species are resistant to desiccation, which allows them to persist in periods of drought, although the degree of resistance to desiccation varies between species (Farnesi et al., 2017). Hatched larvae filter feed on detritus and organic matter in the aquatic habitat before moulting into pupae. Within a few days, pupae emerge into adult mosquitoes to complete the life cycle.

Although most mosquito species have comparable life cycles, the mosquito life-history can differ between species in terms of development time (Araújo et al., 2012; Wormington and Juliano, 2014), responses to temperature (Mordecai et al., 2019, 2017; Shapiro et al., 2017), habitat preference (Dowling et al., 2013; Kroeger et al., 2014; Reiskind et al., 2016), dispersal behaviour (Alcalay et al., 2018b) and host preference (Takken and Verhulst, 2013). For example, Mordecai et al. (2017) collated data on the responses of life-history traits to temperature and found adult lifespans to reach ~30 days in *Aedes aegypti* under optimal thermal conditions whilst adult lifespans reached ~150 days in *Aedes albopictus* (Mordecai et al., 2017). Adult mosquito longevity is epidemiologically important because the mosquito lifespan must exceed the extrinsic incubation period (EIP) for a given disease in order for the mosquito to become infectious (Alto and Bettinardi, 2013; Beck-Johnson et al., 2013;

Liu et al., 2017; Marinho et al., 2016). Therefore, the age structure of mosquito populations is a crucial component of disease transmission.

Differences in life history between species are important because individual mosquito species are vectors of different sets of mosquito-borne diseases. *Ae. aegypti* is the major vector of arbovirus such as chikungunya, dengue, yellow fever and Zika. *Ae. albopictus* is a competent secondary vector of these viruses, which has displaced *Ae. aegypti* in much of the USA (Kraemer et al., 2019; Lounibos et al., 2011; Moore, 1999). Mosquitoes of the *Anopheles* genus are vectors of malaria whilst *Culex* mosquitoes spread Japanese encephalitis and West Nile Fever.

Consideration of the entire mosquito life cycle is important because adult mosquito phenotypes can be determined indirectly by the environmental conditions experienced in previous life stages. Many environmental features at the larval stage have been shown to have carry-over effects on life history traits that are important for disease transmission, such as temperature (Lyimo et al., 1992; Muturi et al., 2012; Westbrook et al., 2010), diet (Buckner et al., 2016; Joy et al., 2014; Takken et al., 2013; Telang et al., 2012), soil quality (Okech et al., 2007; Pfaehler et al., 2006) and predation pressure (Roux et al., 2015). Evans et al. (2018) found carry-over effects of larval rearing in different land use classes and seasons for adult *Ae. albopictus* body size (Evans et al., 2018). Dickson et al. (2017) showed that bacterial communities of larval aquatic habitats had carry-over effects on adult *Ae. aegypti* wing length (Dickson et al., 2017). Alto and Bettinardi (2013) have demonstrated that larval rearing temperatures affect the within-vector progression of dengue-1 virus infection in adult *Ae. albopictus* (Alto and Bettinardi, 2013). The above examples demonstrate the importance of considering the entire mosquito life cycle for successful mosquito control strategies in the context environmental heterogeneity and change.

## Mosquito spread

The increasing geographic range of many mosquito-borne diseases is inextricably linked to the expansion of mosquito populations (Kraemer et al., 2019; Miller and Loaiza, 2015). The geographic distribution of *Ae. aegypti*, in particular, has been increasing and this species now breeds consistently in regions it did not previously inhabit, as reported in Madeira, California and Washington, DC (Almeida et al., 2007; Gloria-Soria et al., 2014; Lima et al., 2016). Recent trends in the spread of *Aedes* mosquitoes have demonstrated that the process of mosquito population expansion is more complex than previously supposed (Powell, 2016). *Ae. aegypti* has expanded its native range from rural, African forests by altering its host preference from zoophilic to anthropophilic and adopting new oviposition behaviour (Gloria-Soria et al., 2016; Mangudo et al., 2015; Powell, 2013). *Ae. albopictus* has similarly adapted to breeding in artificial containers in urbanised environments. Adaptation to the same ecological niche has initiated competition between these two species and *Ae. albopictus* has since displaced *Ae. aegypti* in large areas of the USA (Kraemer et al., 2019; Lounibos et al., 2011; Moore, 1999). The behavioural plasticity displayed by *Ae. aegypti* and *Ae. albopictus* is thought to be a response to urban expansion disrupting native mosquito habitats in forested areas (Powell, 2016).

Increased urbanisation, global trade routes and comprehensive travel networks have facilitated the global spread of mosquitoes. *Ae. aegypti* expanded from West Africa by taking advantage of the slave trade, thus invading countries across Europe before reaching the Americas (Lounibos, 2002). *Anopheles gambiae* was introduced into Brazil by steamship or aircraft in the 1930s and subsequently caused catastrophic malaria epidemics that killed over 16,000 people (Killeen et al., 2002; Soper and



Bruxe, 1943). Mosquito-borne diseases have also spread as a result of public transport networks; the spread of chikungunya to Europe in 2006 was largely attributed to tourists returning from La Réunion (Parola et al., 2006).

The world is currently undergoing a period of accelerating global change with the effects of increased urbanisation, human movement and climate change all manifesting in various aspects of mosquito ecology (Kweka et al., 2016; Messina et al., 2015; Mordecai et al., 2017; Norris, 2004; Paul et al., 2018; Zahouli et al., 2017). The expansion of mosquito populations is largely attributable to rapid environmental change worldwide, which has facilitated mosquito spread into previously inhospitable or inaccessible areas (Kraemer et al., 2019; Powell, 2016). The next decade will bring unprecedented environmental and climatic transitions across the world (IPCC, 2018). It is therefore paramount to understand what these environmental changes will mean for mosquito ecology and the devastating diseases that they transmit. Below I discuss two major types of environmental change and the consequences for mosquito ecology.

## **Mosquitoes and climate change**

It is well established that the life cycle traits of epidemiologically relevant mosquito species are affected by temperature. Traits such as survival probability, development rate, adult longevity and fecundity are temperature sensitive for numerous mosquito species (Eisen et al., 2014; Schmidt et al., 2018). These life cycle traits respond to temperature unimodally and have thermal limits (Eisen et al., 2014). Mordecai et al. (2019) synthesised existing empirical data on unimodal thermal responses to temperature for different mosquito life history traits and demonstrated that the thermal

optima and limits differ between species (Mordecai et al., 2019); their thermal niches do not always overlap (Cunze et al., 2016). As a consequence, climate change has the potential to increase or decrease mosquito fitness depending on the current temperature and the species in question.

Rainfall also has a non-linear relationship with aspects of the mosquito life cycle. High levels of precipitation maintain freshwater pools that mosquitoes require as larval habitats. However, excessive precipitation can dilute nutritional resources required by mosquito larvae and wash out habitats, killing inhabiting larvae (Duchet et al., 2017). The effects of climate change on mosquito ecology via precipitation are therefore non-linear and depend upon on future projections of rainfall or aridity.

Historically, seasonal trends in climate have been associated with both mosquito abundance (Roiz et al., 2011) and mosquito-borne disease occurrence (Servadio et al., 2018). Given the suitability of temperatures in the range of 25-30 °C for many tropical mosquito species (Eisen et al., 2014; Mordecai et al., 2019), it is unsurprising that future climate change has generally been predicted to expand the thermal niche of mosquitoes in many populous regions in Europe and the Americas (Campbell et al., 2015; Eisen et al., 2014; Khormi and Kumar, 2014). The majority of existing studies have adopted a ‘climate envelope’ approach and have focussed on predicting mosquito-borne disease risk directly from climate change projections (Faria et al., 2017; Thai and Anders, 2011; Tjaden et al., 2017). It must be noted that, due to the unimodal responses of life history traits to both temperature and precipitation, mosquito abundance should be expected to respond non-linearly to future climate change. A prevailing focus in the literature upon estimating disease distributions directly from climate projections without considering mosquito ecology may therefore fail to acknowledge the complex effects of climate upon mosquito ecology.

Mechanistic ecological models of mosquito populations are required for accurate estimations of mosquito distributions under a changing climate.

## **Mosquitoes and land use change**

Mosquito community composition varies considerably between habitat types (Steiger et al., 2016). For example, *Anopheles* mosquitoes in central America use the herbaceous plant *Typha domingensis* as a primary habitat (Grieco et al., 2006). Nutrient runoff from agricultural expansion promotes *T. domingensis*, thereby benefiting *Anopheles* populations (Pope et al., 2005). In the case of *Aedes* mosquitoes, it is urban expansion that has largely benefitted the species. As previously noted, *Aedes* mosquitoes – particularly *Ae. aegypti* – have become heavily domesticised over the last century. *Ae. aegypti* have evolved anthropophily and oviposition preferences for artificial containers due to encroachment upon forested habitats by urban expansion (Powell, 2013). Ecotones of mosquito species from adjacent habitats are known to occur when habitat types meet, further demonstrating that mosquito species inhabit distinct ecological niches (Steiger et al., 2016). Ecotones of humans and mosquitoes have also been known to occur along forest fringes (Claflin and Webb, 2017), which has had epidemiological consequences, particularly for zoonoses such as yellow fever. The virus is endemic in forest primates and thus highly transmissible to humans settled in forest-edge ecotones (Despommier et al., 2006).

Anthropogenic land use change has substantially affected mosquito distributions. Urbanisation provides mosquito oviposition sites in the form of artificial containers and drainage systems. This is of epidemiological importance because breeding site availability is known to promote disease transmission (Day, 2016; Fillinger et al.,

2009). An excellent example of the importance of artificial oviposition sites for mosquito spread is the introduction of *Ae. albopictus* to the Americas in the 1940s via the used tyre trade (Hawley et al., 1987; Reiter and Sprenger, 1987). It was discovered that used tyres arriving to the USA by ship from Asian ports were heavily infested with as many as seven species of mosquito, including *Ae. albopictus* (Pratt et al., 1946), which subsequently colonised and has remained an invasive species in the Americas ever since. Tyres have continued to be an important source of larval habitats for *Ae. aegypti*, *Ae. albopictus* and *Culex pipiens* in the Americas (Rubio et al., 2011). In addition, artificial containers promoting mosquito breeding in urban environments may reduce mosquito reliance upon seasonal precipitation cycles; the occurrence of artificial, water-filled containers is predominantly determined by human behaviour and is not necessarily seasonally dependent.

Land use change also affects mosquito populations via changes in local temperature and humidity. Deforested areas are warmer and brighter than primary and secondary forest (Camargo and Kapos, 1995), which can have beneficial effects for tropical mosquito species. In Uganda, temperatures were higher in communities near cultivated swamps compared to natural swamps; all malaria indices were also higher in these areas (Lindblade et al., 2000). Urban and pasture development in New Zealand has been shown to increase aquatic temperatures, resulting in larger *Culex pervigilans* populations (Leisnham et al., 2005).

Despite the general empirical consensus that land use change can affect mosquito populations in diverse ways, there are very few mathematical models of mosquito populations that consider environmental heterogeneity (Acevedo et al., 2015; Grenfell and Dobson, 1995; Lutambi et al., 2013; Smith et al., 2004; Torres-Sorando and Rodríguez, 1997). This may be partly due to the plethora of ways that land use change

can affect mosquito populations, some of which have been discussed above. It may also be due to the challenge of specifying which life history parameters are most affected by changes in land use within a mathematical framework. With land cover heterogeneity affecting various aspects of the mosquito life history, such as development rate and longevity, models could quickly become intractably complex.

## **Mosquito control strategies**

In some locations, mosquito-borne disease epidemics have been more affected by variation in vector control and vector-borne disease control efforts than any other environmental factor (Mouchet et al., 1998). Strategies combatting mosquito-borne disease have been numerous and diverse. The development and distribution of drugs has been crucial in reducing the morbidity and mortality of mosquito-borne diseases (Bannister et al., 2004; Beesetti et al., 2014; The malERA Consultative Group on Drugs, 2011). However, due to slow vaccine development and the high cost of drug investment (Sadanand, 2010; Schwameis et al., 2016), a focus on mosquito control strategies has begun to emerge. It is now frequently considered more practical and effective to use multiple, integrated mosquito control strategies to maximise efforts (World Health Organization, 2012c). Newer strategies to address mosquito-borne disease have been heavily informed by mosquito ecology (World Health Organization, 2012c). Two main approaches are discussed below.

## Environmental control

Larval source management (LSM) is the elimination of aquatic larval habitats and mosquito breeding sites. The success of LSM relies upon a comprehensive understanding of the interaction between mosquito behaviour and the environment in order to effectively target the most productive larval habitats. Reduction in the number of habitats arising due to human activities has been particularly effective in controlling mosquito populations (Imbahale et al., 2012; World Health Organization, 2013) and was integral to the elimination of *An. gambiae* in Egypt and Brazil (Fillinger and Lindsay, 2011). However, the situation becomes more challenging when natural habitats such as swamps, floodwater or agricultural irrigation are major sites for mosquito breeding (Imbahale et al., 2012; Kweka et al., 2012; Majambere et al., 2010; Tusting et al., 2013). Large scale LSM strategies employed in such cases have included ditching or impoundment; the latter was particularly widely used in Florida in the 1990s (Carlson et al., 1991). However, these large-scale LSM strategies are not possible in resource-limited settings.

Other environmental control strategies have included biocontrols, such as the release of larvivorous fish, predatory copepods, or entomopathogenic fungi (Awasthi et al., 2015; Benelli et al., 2016; Chandra et al., 2008; Lardeux et al., 1992; Schaper, 1999; Udayanga et al., 2019). Biocontrol strategies have been shown to have context-dependent strengths and weaknesses. For example, despite the widespread efficacy of larvivorous fish in many parts of the world, fish can present a threat to other native aquatic fauna (Kats and Ferrer, 2003; Kumar and Hwang, 2006; Rupp, 1996). The *Mesocyclops* copepod was very effectively applied in Vietnam to target *Ae. aegypti*, however, the larval habitats of many mosquito species cannot support copepod

populations (Hales and van Panhuis, 2005; Vu et al., 2005). Therefore, biocontrol strategies must carefully evaluate the ecology of the target mosquito species and their native habitat.

## **Biological and genetic control**

Biological and genetic control methods for mosquito populations have taken several approaches, most notably the Sterile Insect Technique (SIT) (Alphey, 2014; Knippling, 1959). The SIT strategy requires sterilisation of mass-reared insects using  $\gamma$ -radiation. SIT has several limitations, most importantly that sterilisation using  $\gamma$ -radiation incurs substantial fitness costs; males released during SIT have shorter lifespans and are less competitive against wild-type mosquitoes. In addition, SIT can produce counter-intuitive, non-linear effects upon population sizes; the unviability of offspring due to sterilisation reduces the number of larvae in aquatic habitats, which has implications for the outcomes of density-dependent larval competition (Gilles et al., 2011). SIT is self-limiting, as it requires continuous releases to maintain population suppression.

Recent transgenic technologies have facilitated novel genetic approaches to mosquito control that address many of the deficiencies of traditional SIT (Alphey et al., 2002). In a similar way to SIT, self-limiting genetic control methods release sterile transgenic males. Transgenic mosquitoes can compete successfully with wild-type males because their longevity is not compromised (Black et al., 2011; Harris et al., 2012, 2011; Howell and Benedict, 2009; Lacroix et al., 2012; Lee et al., 2013; Qsim et al., 2017; Thomas et al., 2000). In addition, the juvenile mortality induced by transgenic technologies can be late-acting, thereby maintaining competitive pressures within mosquito populations at the larval stage (Phuc et al., 2007). Like SIT, self-

limiting transgenic mosquitoes are not intended to persist in the field without continuous releases, which are resource, labour and cost intensive.

Self-sustaining transgenic release strategies endeavour to modify the capacity of mosquitoes to vector disease (Alphey, 2014). This could be achieved by either (a) propagation of detrimental life-history traits such as decreased longevity or (b) inheritance of a modification which reduces susceptibility to pathogens (Gantz et al., 2015; James, 2002). Self-sustaining transgenic technologies do not require continuous releases as self-limiting strategies do. However, once released, mosquitoes from self-sustaining control strategies continue to propagate within the ecosystem and cannot be retrieved if unintended ecological consequences arise.

Another notable biological control method is the maternally-inherited *Wolbachia pipientis* bacterium. Mosquitoes infected with *Wolbachia* are subject to life history modifications that vary between species. For example, in *Ae. aegypti*, *Wolbachia* infection inhibits dengue and chikungunya infection within the mosquito (Bian et al., 2010; Moreira et al., 2009; Walker et al., 2011). *Wolbachia* infection also decreases vector competence by shortening the mosquito lifespan (McMeniman et al., 2009).

Successful field trials have been conducted for self-limiting transgenic technologies and *Wolbachia* control methods in mosquitoes (Bargielowski et al., 2011; Bellini et al., 2013; Chambers et al., 2011; Facchinelli et al., 2013; Klein et al., 2012; Lacroix et al., 2012; Lee et al., 2013; Nordin et al., 2013; Walker et al., 2011; Wise de Valdez et al., 2011). Each trial has been successful and none have highlighted serious negative consequences to either human health or the environment. Empirical studies of mosquito ecology remain imperative to understanding the effects of biological and genetic mosquito control, as do mathematical models, which have been indispensable



both for predicting the outcomes of transgenic mosquito release and for estimating the cost-effectiveness of such programs (Alphey et al., 2011; Atkinson et al., 2007).

## **Outline of thesis**

This thesis explores how environmental change can affect mosquito population dynamics and life history traits. Mosquito populations are challenging to empirically study in the field. Mathematical models are therefore an invaluable tool for estimating mosquito distributions and predict the effects environmental change upon mosquito populations. This work integrates mathematical modelling, laboratory studies and fieldwork in order to construct ecologically relevant mosquito population models and consider how they can be appropriately parameterised using empirical data.

Chapter 2 aims predict the effects of climate change upon *Ae. aegypti* populations in Brazil. To this end, a mechanistic, ecological model of *Ae. aegypti* is presented and applied to two climate change projections. This work provides a unique improvement on existing studies by quantifying mosquito population sizes – a measure that is imperative for many mosquito-borne disease models – and providing a focus upon the ecological mechanisms by which climate affects mosquito life history. The results are placed in an epidemiological context and the consequences for mosquito-borne disease transmission are discussed.

Chapter 3 examines specific life-history parameters from Chapter 2 that have historically been difficult to parameterise in both mosquito ecology and entomology more generally. This chapter aims to unravel the multi-dimensional nature of larval density dependence and the consequences for models of mosquito populations using an empirical approach.

Chapter 4 aims to develop a methodological approach for estimating mosquito distributions in spatially heterogeneous environments. First, field data are integrated with remote sensing data to estimate spatially heterogeneous environmental suitability for mosquitoes. Second, a population dynamics model for *Ae. polynesiensis* is applied to a heterogeneous landscape and the effects of environmental change through vector control techniques are examined.

Subsequently, the findings of the preceding chapters are integrated and suggestions are made for areas for future work.

# Chapter 2

## Climate change and *Aedes aegypti* mosquitoes in Brazil

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## **Abstract**

Temperature affects *Aedes aegypti* non-linearly at different life cycle stages with substantial implications for disease transmission. Despite this, few ecological or epidemiological models have embodied mosquito life history. Of those that have, none have been applied to future climate projections on a spatial scale. Spatiotemporal mosquito abundance data are necessary to inform vector and disease management strategies. To this end, we have developed a climate-driven population dynamics model to investigate the effects of climate change on *Ae. aegypti* density in Brazil. We further used entomological surveillance data to incorporate the effects of urbanisation into model estimates. Model predictions were successfully validated against existing historical *Ae. aegypti* surveillance data, demonstrating the predictive accuracy of the model. Mean annual *Ae. aegypti* densities were predicted to increase by up to 9.5% by 2030 and 41.1% by 2050. Seasonal *Ae. aegypti* density will be particularly disrupted in North cities including Manaus. The transmission potential for dengue fever was estimated to increase in up to 78% of Brazilian municipalities by 2030 and 99% of municipalities by 2050. Crucially, we demonstrate that climate change in Brazil will result in substantial increases in *Ae. aegypti* density in many areas, facilitating mosquito-borne disease transmission.



## **Introduction**

The mosquito *Aedes aegypti* is a major vector of arboviruses such as dengue, Zika and chikungunya. Climatic suitability for *Ae. aegypti* is associated with arbovirus case occurrence (Faria et al., 2017) because temperature influences the *Ae. aegypti* life cycle and the capacity of *Ae. aegypti* to transmit arboviruses (Liu-Helmersson et al., 2014; Massad et al., 2011). Mosquito-borne disease is of particular focus in Brazil, which has sustained the largest Zika burden worldwide (Faria et al., 2017). Environmental and climate change are also focal topics in Brazil. Rapid urban growth has exacerbated environmental degradation and social inequality (Nobre, 2011). Temperature increases of 0.5 °C have significantly altered precipitation patterns in some Brazilian regions, contributing to extreme weather events affecting disease management, water availability and agricultural production (de Barros Soares et al., 2016; de los Milagros Skansi et al., 2013). The effects of climate and environment on *Ae. aegypti* population dynamics are therefore of crucial importance for targeted disease management in Brazil.

*Ae. aegypti* larval development time, larval survival, adult fecundity and adult longevity have all been observed to respond to temperature variation (de Almeida Costa et al., 2010; Eisen et al., 2014; Schmidt et al., 2018). Life history traits in *Ae. aegypti* respond unimodally to temperature with mosquito development promoted at optimal temperatures and suppressed beyond upper and lower thermal limits (Craig et al., 1999; Lafferty, 2009; Mordecai et al., 2019, 2017). Mechanistic, biological models of *Ae. aegypti* population dynamics are therefore imperative to capture the non-linear effects of temperature on multiple life-cycle stages (Eisen et al., 2014; Mordecai et al., 2019; Schmidt et al., 2018).

Despite the complex effects of climate on mosquito life history traits, few models have embodied mosquito life history. Several epidemiologically focussed studies have predicted arboviral disease occurrence directly from climatic variables (Faria et al., 2017; Lowe et al., 2018; Thai and Anders, 2011; Tjaden et al., 2017). Other models have estimated spatial climatic suitability for *Ae. aegypti* occurrence (Tjaden et al., 2017). These models are powerful because they are able to process substantial datasets on a large geographical scale without the complexity and computational costs of mechanistic models of the mosquito life history. However, although understanding of the geographical extent of epidemiological mosquito species is imperative, models of climatic suitability or occurrence probability do not assess relative mosquito population sizes between locations. Estimates of mosquito density are indispensable to provide targeted mosquito-borne disease control interventions because mosquito population size heavily influences disease transmission (Massad et al., 2011; Petrić et al., 2014).

A small number of studies have modelled the stage-dependent effects of temperature upon *Aedes* population dynamics. However, to the best of our knowledge, none has extended to a spatiotemporal scale or considered climate change. Erickson et al. (2010) developed a stage-structured model of *Aedes albopictus*, allowing temperature-dependent life history traits to be dynamic through time (Erickson et al., 2010). Wang et al. (2016) developed a similar stage-structured model applied to entomological surveillance data in Guangzhou, China (X. Wang et al., 2016). However, in both of these models, individuals begin to mature from a life history stage immediately upon entering it at a maturation rate determined by the present temperature. For many mosquito species, this may not be realistic because mosquito larvae require a minimum gestation period, even under optimal conditions (Nelson,



1986). Beck-Johnson et al. (2013) and Ewing et al. (2016) addressed this problem by facilitating variable, temperature-dependent stage durations using delay-differential equation (DDE) models (Beck-Johnson et al., 2013; Ewing et al., 2016), an approach first detailed by Nisbet and Gurney (1983) to model instar durations in insect populations (Nisbet and Gurney, 1983). We offer a unique improvement on existing studies by applying our model to future climate projections to consider the effects of climate change on *Ae. aegypti* populations on a spatial scale.

Most models of mosquito population dynamics in response to climate have not considered additional environmental variables, despite the crucial importance of anthropogenic variables such as urbanisation, transport networks and socioeconomics (Dhar-Chowdhury et al., 2016; Ferraguti et al., 2016; Messina et al., 2015). An important distinction must be made between climatic suitability of a region for *Ae. aegypti* and the occurrence of *Ae. aegypti* in that region. Dickens et al. (2018) found almost all of Brazil to be climatically suitable for *Ae. aegypti*, however, inclusion of anthropogenic variables in their model notably contracted *Ae. aegypti*'s habitable geographic range (Dickens et al., 2018). Khormi and Kumar (2014) predicted North Brazil to be highly climatically suitable for *Ae. aegypti* but observed from collated occurrence data that *Ae. aegypti* were generally limited to highly urbanised coastal and South regions (Khormi and Kumar, 2014). Crucially, hospitable temperature is a necessary but insufficient condition for *Ae. aegypti* occurrence. *Ae. aegypti* is a highly anthropophilic species (McBride et al., 2014) and careful consideration of anthropogenic variables is paramount in predictive models. We address this consideration by detailing the effects of spatial heterogeneity in anthropogenic variables on mosquito populations within our model.

We present a biological model of *Ae. aegypti* density in Brazil driven by temperature and precipitation. Analyses were carried out under two Representative Concentration Pathways (RCPs), RCP 4.5 and RCP 8.5, using data from the UK Hadley Centre's Earth System Model, HadGEM2-ES (Bellouin et al., 2007; Collins et al., 2011; Martin et al., 2011). The use of more than one RCP facilitates estimation of *Ae. aegypti* density under more or less conservative assumptions about future climate change mitigation. Model results were validated against existing entomological surveillance data for *Ae. aegypti*. We explored changes in *Ae. aegypti* habitat range, seasonality and density in key regions in Brazil over the next 60-80 years. We subsequently used dengue fever as an example of the application of our model results and consider changes in dengue fever transmission potential as a consequence of climate change.

## **Methods**

### **Main model**

A stage-structured DDE model with stage-dependent delays was used to model adult and juvenile *Ae. aegypti* populations. This modelling structure is analogous to those presented by Gurney and Nisbet (Gurney and Nisbet, 1998; Nisbet and Gurney, 1983) where a full derivation is available. Similar DDE structures have previously been used to model mosquito populations (Beck-Johnson et al., 2013; Ewing et al., 2016). However, such models have not yet been applied to generate spatial predictions of *Ae. aegypti* populations under a changing climate. The model in this study was limited to adult and juvenile (encompassing eggs, larvae and pupae) stages for model simplicity. Each stage was defined by recruitment in and maturation out in addition to stage-specific mortality as follows:

$$\frac{dJ(t)}{dt} = R(t) - M(t) - (\mu_J(t) + \delta(t)J(t))J(t) \quad (2.1)$$

$$\frac{dA(t)}{dt} = M(t) - \mu_A(t)A(t) \quad (2.2)$$

$R(t)$  and  $M(t)$  are time-dependent rates of recruitment (egg-laying) and maturation (pupation) between adult,  $A(t)$ , and juvenile,  $J(t)$ , stages at time,  $t$ . Parameters  $\mu_J(t)$  and  $\mu_A(t)$  are the mortality rates for juveniles and adults, respectively.  $\delta(t)$  captures density-dependent mortality at the juvenile stage. Recruitment,  $R(t)$ , and maturation,  $M(t)$ , were defined as follows:

$$R(t) = \frac{A(t)b(t)}{2} \quad (2.3)$$

$$M(t) = R(t - \tau_J(t))S_J(t) \frac{g_J(t)}{g_J(t - \tau_J(t))} \quad (2.4)$$

where  $b(t)$  is the number of eggs laid per female at time,  $t$ .  $R(t)$  is scaled by a factor of  $\frac{1}{2}$  to account for the gender distribution of the population, thereby implicitly assuming that the female:male emergence ratio is 1:1.  $S_J(t)$  is the juvenile survival rate. The juvenile development time from hatch to emergence,  $\tau_J(t)$ , was defined as follows:

$$\frac{d\tau_J(t)}{dt} = 1 - \frac{g_J(t)}{g_J(t-\tau_J(t))} \quad (2.5)$$

where  $g_J(t)$  is the juvenile development rate and  $g_J(t) = 1/\tau_J(t)$ . The instantaneous juvenile survival rate was defined as follows.

$$S_J(t) = e^{-\int_{t-\tau_J(t)}^t (\delta(t)J(t) + \mu_J(t)) dt} \quad (2.6)$$

and the rate of change in juvenile survival was defined as follows:

$$\frac{dS_J(t)}{dt} = S_J(t) \left[ \left( \delta(t - \tau_J(t))J(t - \tau_J(t)) + \mu_J(t - \tau_J(t)) \right) \frac{g_J(t)}{g_J(t - \tau_J(t))} - \delta(t)J(t) - \mu_J(t) \right] \quad (2.7)$$

A full derivation of the rate of change in survival is available in Appendix A.1. Each model iteration corresponded to 24 hours. All analyses were conducted using R version 3.6.1 and DDEs were solved using the `dede()` function in the `deSolve` package (R Core Team, 2018; Soetaert et al., 2010).

## Temperature variation

Four parameters were temperature dependent: adult fecundity,  $b(t)$ , adult mortality,  $\mu_A(t)$ , juvenile development rate,  $g_J(t)$ , and juvenile mortality,  $\mu_J(t)$ . All parameters and confidence intervals (CIs) for the following relationships between temperature and key life history traits are presented in Appendix A.2.

Mordecai et al. (2017) fitted quadratic and Brière thermal response models to available empirical data of the responses of life history traits to temperature in *Ae. aegypti* and *Ae. albopictus* (Mordecai et al., 2017) and defined adult *Ae. aegypti* fecundity (eggs/female/day) using a Brière fit. From Mordecai et al. (2017), we therefore defined adult fecundity as follows:

$$b(t) = c_b T(t)(T(t) - T_{0b})(T_{Mb} - T(t)) \quad (2.8)$$

where  $T_{0b}$  and  $T_{Mb}$  are the thermal minimum and maximum respectively,  $c_b$  is a numeric constant and  $T(t)$  is the current temperature in °C.

Mordecai et al. (2017) presented fitted functions for adult longevity and juvenile development rate,  $g_J(t)$ . However, due to the Brière and quadratic fits respectively, these functional forms return values  $<0$  at temperatures within the desired range for the current study. Truncation at 0 would result in biologically implausible parameter values. For example, adult mortality was defined as  $\mu_A(t) = 1/\tau_A(t)$  since there were no other transition states out of state variable  $A(t)$ . At  $\tau_A(t) = 0$ ,  $\mu_A(t) \rightarrow \infty$ , which is biologically implausible. Therefore, we fitted alternative functions for  $\mu_A(t)$  and  $g_J(t)$ .

A comprehensive literature search extracted data for adult *Ae. aegypti* longevity (Beeuwkes et al., 1933; Beilhe et al., 2012; Beserra, 2009; Chadee et al., 2017; Goindin et al., 2015; Marinho et al., 2016; McMeniman et al., 2009; Muttis et al., 2018; Yang et al., 2009) and juvenile egg-to-adult development time (Bar-Zeev, 1958; Beilhe et al., 2012; Beserra, 2009; Couret et al., 2014; Kaimura et al., 2002; Marinho et al., 2016; Reuda et al., 1990; Richardson et al., 2011; Shannon and Putnam, 1934; Tun-Lin et al., 2000; Westbrook, 2010; Yang et al., 2009) across a spectrum of temperatures. A Gaussian function was fitted to adult longevity data

using non-linear least squares regression. The p-value was  $<0.001$  for all parameters.

Adult mortality was subsequently defined as:

$$\mu_A(t) = \frac{1}{ke^{-1/2(T(t)-\gamma/\sigma)^2}} \quad (2.9)$$

A 2<sup>nd</sup>-degree polynomial was fitted to juvenile development time, which was a significantly better fit than a linear function ( $p < 0.001$ , likelihood ratio test (LRT)).

Since  $g_J(t) = 1/\tau_J(t)$ , the instantaneous juvenile development rate was defined as:

$$g_J(t) = \frac{1}{\beta_{0g} + \beta_{1g}T(t) + \beta_{2g}T(t)^2} \quad (2.10)$$

Temperature-dependent juvenile mortality,  $\mu_J(t)$ , was estimated by rearranging Equation (2.6) and assuming both  $\delta_J(t)J(t)$  and variation in  $\tau_J(t)$  to be negligible for the purposes of parameter estimation:

$$\mu_J(t) = \frac{\ln(S_J(t))}{\tau_J(t)} \quad (2.11)$$

where  $\tau_J(t) = \tau_J(t - 1)$  and  $\delta_J(t)J(t) \approx 0$ . Parameter  $\tau_J(t)$  is already defined by the denominator in Equation (2.10). From Mordecai et al. (2017),  $S_J(t)$  – for the purposes of fulfilling Equation (2.11) – was estimated using the following quadratic function:

$$S_J(t) = -c_S(T(t) - T_{0S})(T(t) - T_{MS}) \quad (2.12)$$

where  $T_{0S}$  and  $T_{MS}$  are the thermal minimum and maximum respectively and  $c_S$  is a numeric constant.  $S_J(t)$  and  $\tau_J(t)$  were estimated for  $T = 1, 2, \dots, 50$  using Equation (2.12) and the denominator of Equation (2.10). Values of  $S_J(t)$  from Equation (2.12) were truncated at zero. Juvenile mortality,  $\mu_J(t)$ , was subsequently calculated for  $T = 1, 2, \dots, 50$  using Equation (2.11). When  $S_J(t) = 0$ , then  $\mu_J(t) \rightarrow \infty$ . Therefore, a 4<sup>th</sup>-degree polynomial was fitted to the resulting estimates of  $\mu_J(t)$  using non-linear least-

squares regression. This 4<sup>th</sup>-degree polynomial was a significantly better fit than 2<sup>nd</sup>- and 3<sup>rd</sup>-degree polynomials ( $p < 0.001$  for both, LRT). The 4<sup>th</sup>-degree polynomial describing  $\mu_J(t)$  was:

$$\mu_J(t) = \beta_{0\mu} + \beta_{1\mu}T(t) + \beta_{2\mu}T(t)^2 + \beta_{3\mu}T(t)^3 + \beta_{4\mu}T(t)^4 \quad (2.13)$$

## Precipitation variation

Rainfall was assumed to increase the carrying capacity of the environment by producing more oviposition sites and sustaining existing sites. The carrying capacity,  $K$ , was proportional to exponentially weighted past daily rainfall ( $\text{mm day}^{-1}$ ),  $p(t)$ . Exponential weighting of past rainfall has previously been found to be the best fit to entomological field data compared to linear weighting (White et al., 2011). The carrying capacity was

$$K(t) = \lambda \frac{1}{\omega(1-e^{-t/\omega})} \int_{t-30}^t e^{-(t-t')/\omega} p(t') dt' \quad (2.14)$$

where  $\omega$  is the number of previous days of past rainfall contributing to the current carrying capacity and  $\lambda$  is a numeric constant. Density-dependent mortality was therefore  $\delta(t) = 1/K(t)$ . The value of  $\lambda$  controls the upper bound on mosquito population sizes but does not affect seasonal trends. Further details are available in Appendix A.3. Parameter values for Equation (2.14) are shown in Appendix A.2.

## Climate data

Monthly average temperature ( $^{\circ}\text{C}$ ) and precipitation ( $\text{mm day}^{-1}$ ) data were obtained

from HadGEM2-ES for 1961-2100 in Brazil (Bellouin et al., 2007; Collins et al., 2011; Martin et al., 2011) for two RCPs: RCP 4.5 and RCP 8.5. RCPs represent greenhouse gas concentration trajectories, which differ depending on the projected quantity and concentration of emissions (van Vuuren, 2011). RCP 4.5 has more optimistic predictions of future reductions in greenhouse gas emissions than RCP 8.5. Climate data were at a coarse resolution of  $\sim 29,000 \text{ km}^2$ . 30 daily temperature and precipitation estimates were derived from each monthly data point by cubic spline interpolation using the `splint()` function from the `fields` package in R version 3.6.1 (Nychka et al., 2017; R Core Team, 2018). Cubic spline interpolation is an exact interpolator; therefore, all original HadGEM2-ES data points were retained. We applied our mosquito population dynamics model to each projected temperature and precipitation time-series from the HadGEM2-ES data. Therefore, our model provides spatial estimates of mosquito populations but does not have an explicit spatial component. The model was run for each location using data for years 2010-2100.

## **Anthropogenic variables**

Favourable temperatures may be a necessary but insufficient condition for *Ae. aegypti* occurrence as *Ae. aegypti* are highly anthropophilic. Boosted Regression Trees (BRTs) were used to estimate *Ae. aegypti* occurrence probability and isolate the effects of anthropogenic variables. BRTs have been effectively used to map mosquito and mosquito-borne disease occurrence due to their capacity to fit complex functions of non-linear predictors (Bhatt et al., 2013; Kraemer et al., 2019; Messina et al., 2019). BRTs iteratively improve regression trees using gradient boosting; the variation in the response variable unexplained by the model is minimised iteratively



in each new tree. We fitted BRTs using the `gbm.step()` function from the `dismo` package for R (Elith et al., 2008; R Core Team, 2018). We used the default hyperparameters for the `gbm.step()` function (tree complexity = 4, learning rate = 0.005, bag fraction = 0.75, step size = 10, cross-validation folds = 10). Each BRT underwent ten-fold cross-validation whereby ten data subsets were used to train the BRT model and the predictive accuracy on the remaining data in terms of the predictive deviance was assessed. 100 cross-validated BRT models were fitted to the data and the mean across all BRT models was evaluated in order to account for variability between models.

The median municipal building index (the proportion of sampled buildings infested with *Ae. aegypti*) for the sampling period 2014-2018 in each Brazilian municipality (shown in Appendix A.4, Figure A.2(a)) was used as the response variable. These data were provided and collected by the Brazilian Ministry for Health using the LIRAA protocol (Coelho, 2012; Coelho et al., 2014; Secretaria de Vigilância Sanitária em Saúde, 2005). The LIRAA protocol determines the sampling methodology in each municipality according to municipal population density and the number of buildings. In this way, the sampling protocol takes appropriate steps to hold the sampling effort constant between locations. An expanded description of the LIRAA protocol is available in Appendix A.4 and from the Brazilian Ministry for Health (Secretaria de Vigilância Sanitária em Saúde, 2005).

As covariates to train BRT models, mean, minimum and maximum annual temperature in each Brazilian municipality were extracted from HadGEM2-ES data for 2018 as previously described. Mean municipal urban accessibility (minutes of travel time to the nearest city with >50,000 inhabitants) was extracted from Weiss et al.'s (2018) urban accessibility map (Weiss et al., 2018). Municipal population size

was extracted from the global population projections described by Jones & O'Neil (2016) for Socioeconomic Pathway 2 (SSP2) in 2020 (Jones and O'Neil, 2017, 2016). Projections of urban land cover were taken from Zhou et al. (2019) (Zhou et al., 2019) and the mean taken for each municipality in 2020.

The BRT model was then used to project *Ae. aegypti* occurrence probability every 10 years at a resolution of 5 km<sup>2</sup>. All covariates were extracted at 5 km<sup>2</sup> resolution and future estimates were used for population projections and urban extent. No data were used for climatic variables to project future *Ae. aegypti* occurrence probability; temperature was fixed in the prediction data at 26 °C in order to isolate the effects of anthropogenic variables. Estimated *Ae. aegypti* building index, assuming national climatic heterogeneity, is shown by municipality for the current dataset and at a resolution of 5 km<sup>2</sup> for current and future projections in Appendix A.4, Figures A.2(a) and A.3.

Model-predicted *Ae. aegypti* abundance was converted to mosquito density (mosquitoes per km<sup>2</sup>) to avoid pseudo-replication. *Ae. aegypti* density was spatially smoothed at each time point for improved visualisation using fixed rank kriging in the FRK package for R version 3.6.1 (R Core Team, 2018; Zammit-Mangion, 2018), retaining the original estimates. The estimated building index in each grid cell was multiplied by kriged estimates of mosquito density to incorporate anthropogenic variables into model estimates.

## **Model validation against existing time series**

A comprehensive literature search identified *Ae. aegypti* entomological surveillance

data to which model estimates could be compared. Where data were available as supplementary information or appendices, these were used. In other cases, where plotted data were presented and resolution was sufficiently high, data were digitised using WebPlotDigitizer (Rohatgi, 2015). Our search excluded studies assessing vector control methodologies and studies using only ovitraps. In cases of multiple studies utilising the same dataset, the study with the longest time horizon was used. Where multiple trap types were reported, the trap with the longest time horizon was used. Where data for traps in multiple sub-locations within an area were reported, the mean of these data was taken at each time point.

The similarity of temporal trends between model-predicted *Ae. aegypti* density and trap data was assessed using a modified Chelton method (Chelton, 1984; Pyper and Peterman, 1998) which assesses the correlation between two time series, adjusting the threshold for significance via the degrees of freedom to deal with cases of strong autocorrelation. See Appendix A.5 for further details.

## Calculation of $R_0$ for dengue fever

We consider a simple form of the Ross-Macdonald model as an example of how our predictions of *Ae. aegypti* density can be applied. The Ross-Macdonald model was as follows:

$$\frac{dH(t)}{dt} = aBV(t)\frac{A(t)}{2N(t)}(1 - H(t)) - rH(t) \quad (2.15)$$

$$\frac{dV(t)}{dt} = aCH(t)(1 - V(t)) - \mu_A(t)V(t) \quad (2.16)$$

where  $H(t)$  and  $V(t)$  describe the infected proportion of human and vector

populations respectively.  $a$  is the mosquito biting rate,  $B$  is the probability of a bite from an infectious mosquito infecting a human,  $C$  is the probability of an infectious blood meal infecting a mosquito and  $r$  is the human recovery rate.  $A(t)$  is the number of adult mosquitoes,  $N(t)$  is the human population size and  $\mu_A(t)$  is the adult mosquito mortality rate which is a function of temperature (see Equation (2.9)). The model was parameterised in accordance with Alphey et al. (2011); all values are shown in Appendix A.6 (Alphey et al., 2011).

By deriving the Jacobian matrix of the two-compartment Ross-Macdonald model the stability of the disease-free state is described by

$$R_0 = \text{Det} \begin{bmatrix} -r & \frac{aBA^*}{2N^*} \\ aC & -\mu_A^* \end{bmatrix} \quad (2.17)$$

where  $A^*$ ,  $N^*$  and  $\mu_A^*$  are the mosquito abundance, population size and adult mosquito mortality rate and a time,  $t$ , and  $R_0$  is the basic reproductive number. Full derivation is shown in Appendix A.6. If  $R_0 > 0$ , the disease-free state is unstable. If  $R_0 < 0$ , the disease-free state is stable.

Equation (2.17) was applied in each Brazilian municipality and compared to reported dengue cases. Dengue case data were acquired from DATASUS for the period 2015-2017 (Secretaria Executiva do Ministério da Saúde, n.d.) and the mean number of monthly cases was calculated. Estimates of the future human population size,  $N^*$ , were extracted from the global population projections described by Jones & O'Neil (2016) for Socioeconomic Pathway 2 (SSP2) for 2020, 2030 and 2050 (Jones and O'Neil, 2017, 2016).  $N^*$  for each Brazilian municipality was extracted by taking the sum of the projected population counts within each municipality. Temperature data came from HadGEM-2 ES as previously described and were used to calculate  $\mu_A^*$

under future climate scenarios using Equation (2.9). Municipal temperature was extracted from HadGEM2-ES data by taking the mean temperature within each municipality at each time point. The number of adult mosquitoes,  $A^*$ , was extracted from the rasterised model output by taking the mean predicted *Ae. aegypti* density (mosquitoes/km<sup>2</sup>) in each municipality and multiplying by the area of each municipality in km<sup>2</sup>. All extractions of municipal estimates from rasterised data were done using QGIS version 3.4 (QGIS Development Team, 2019).

## **Results**

### ***Ae. aegypti* density will increase across Brazil**

The predicted mean annual *Ae. aegypti* distribution for 2018, 2030 and 2050 is shown in Figure 2. 1. Seasonal patterns in *Ae. aegypti* density are shown in Appendix A.7. Mean annual *Ae. aegypti* density for the whole of Brazil was predicted to increase by 8.2% and 9.5% between 2018 and 2030 for RCP 4.5 and RCP 8.5, respectively. By 2050, the predicted increase was 27.2% and 41.1% for RCP 4.5 and RCP 8.5, respectively. By 2080, the increase was 50.1% and 57.5% for RCP 4.5 and RCP 8.5, respectively.

The highest *Ae. aegypti* densities were predicted in central and Northwest regions of Brazil due to stable, warm climates with heavy wet seasons; annual mean *Ae. aegypti* density in Manaus remained between 3.3-4.5 fold higher than both São Paulo and Rio de Janeiro between 2018 and 2050. However, the greatest increases in *Ae. aegypti* density were observed in South and Southeast Brazil. The region with the largest increase in mean annual *Ae. aegypti* density by 2030 was predicted to be the Southeast with an increase of 25.0% for RCP 4.5 and 29.5% for RCP 8.5. In 2050, the worst affected region will be Northeast for RCP 4.5 with an increase of 47.9% and Southeast for RCP 8.5 with 71.6%. In 2080, the Southeast for RCP 4.5 will see an increase of 90.6% and the South for RCP 8.5 will increase by 195.3%. Fold-changes in *Ae. aegypti* density are shown by region in Figure 2. 2 and by state and city in Appendices A.8-A.10. Maps of Brazilian regions and municipalities are shown in Appendix A.11 for reference.

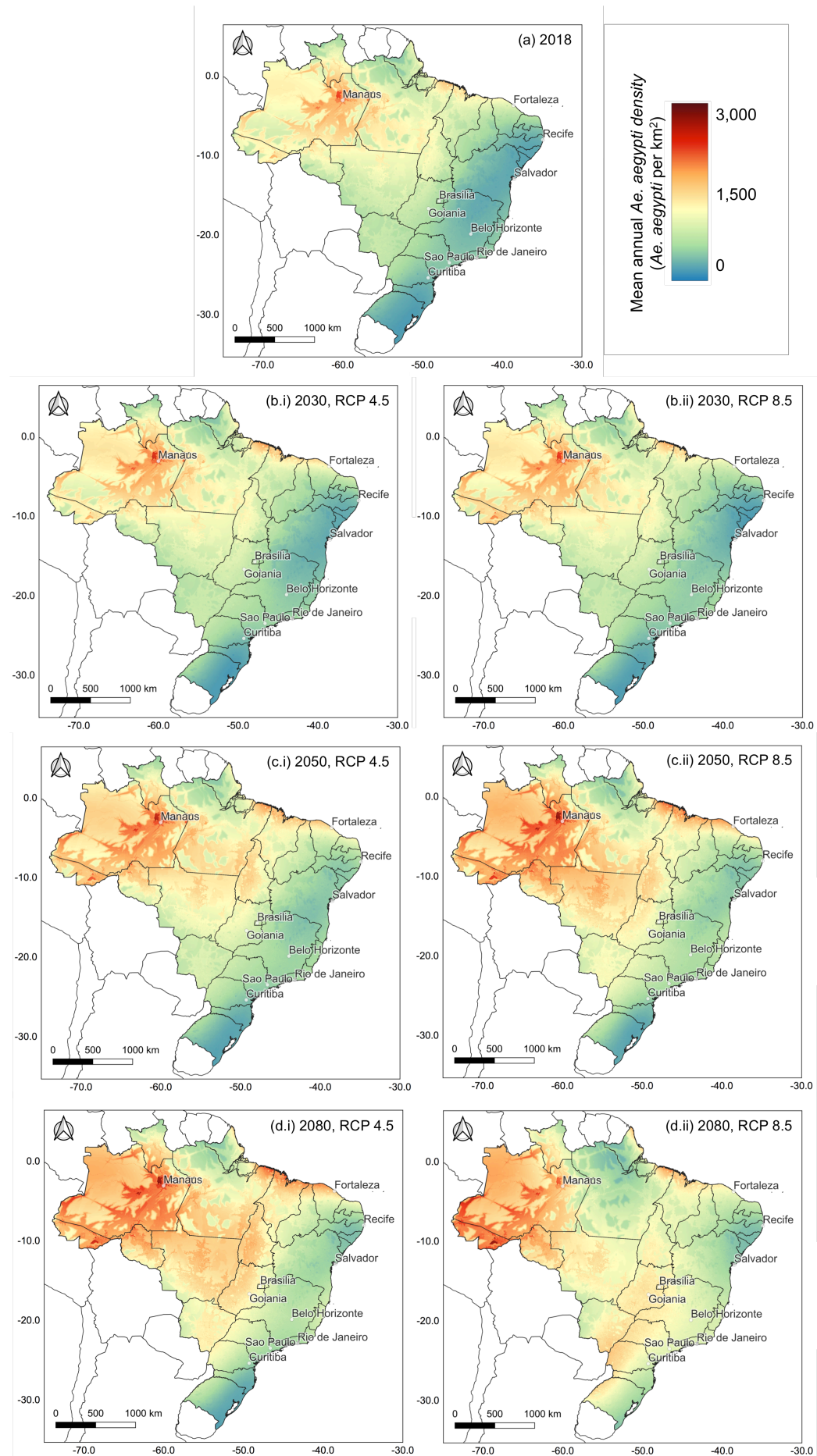


Figure 2. 1. Mean annual estimated *Ae. aegypti* density in Brazil for (a) 2018; 2030 for (b.i) RCP 4.5 and (b.ii) RCP 8.5; 2050 for (c.i) RCP 4.5 and (c.ii) RCP 8.5; 2080 for (c.i) RCP 4.5 and (c.ii) RCP 8.5. State boundaries and the ten most populous cities are indicated.

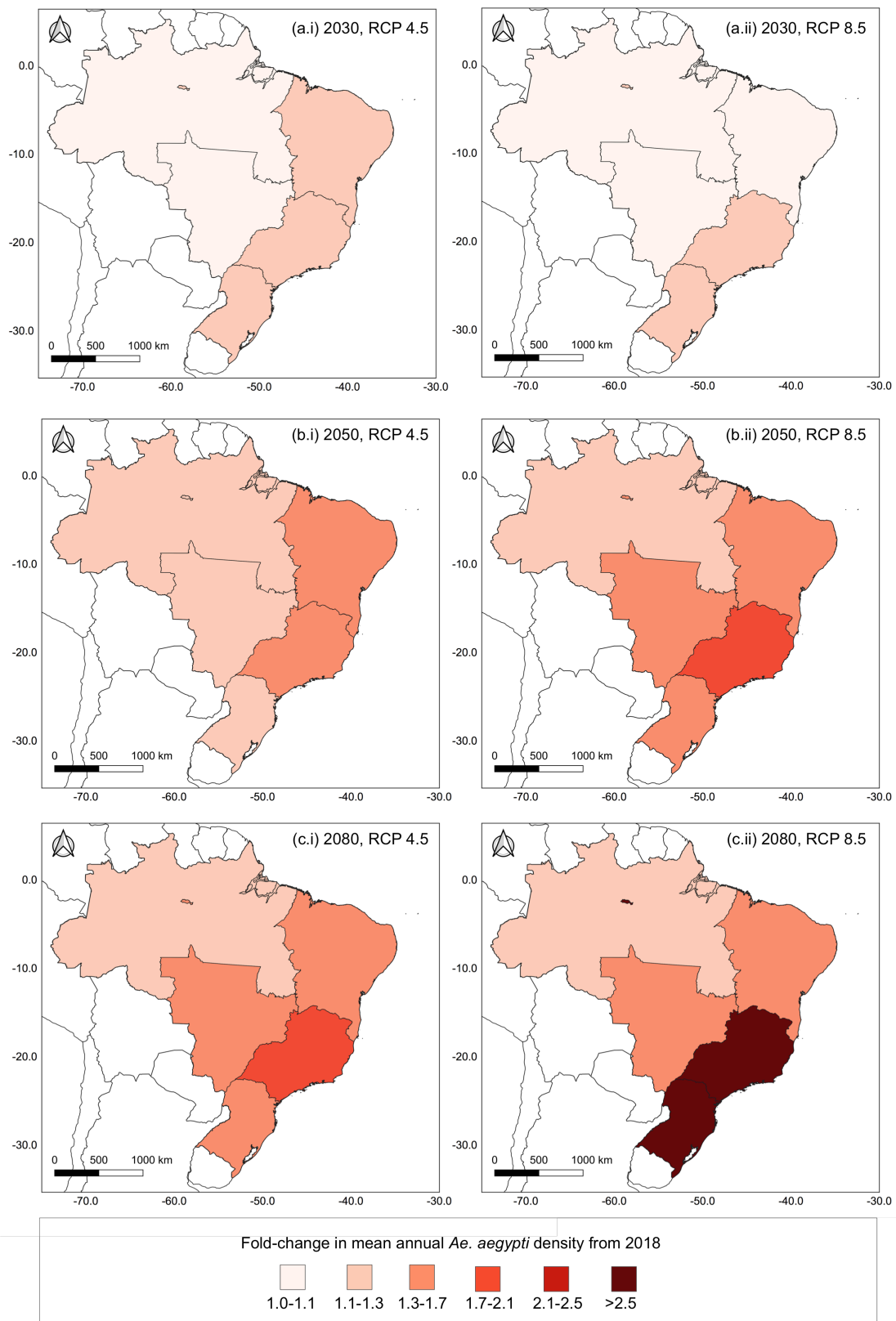


Figure 2. 2. Estimated fold-change in mean annual *Ae. aegypti* density from 2018 in each Brazilian region. The official Brazilian regions are North, Northeast, Central-West, Southeast and South. Fold-changes are shown for: 2030 for (a.i) RCP 4.5 and (a.ii) RCP 8.5; 2050 for (b.i) RCP 4.5 and (b.ii) RCP 8.5; 2080 for (c.i) RCP 4.5 and (c.ii) RCP 8.5 climate projections.



## Seasonal patterns of *Ae. aegypti* will be disrupted

Diverse seasonal *Ae. aegypti* dynamics were estimated in different climatic regions of Brazil as a result of climate change. Two contrasting examples – the cities of São Paulo and Manaus – are shown in Figure 2. 3; other large cities are shown in Appendix A.12. São Paulo has a humid, subtropical climate and was estimated to have highly seasonal *Ae. aegypti* populations with near extinction in cold, dry months of April-September. Hot, wet weather for the rest of the year facilitated large mosquito outbreaks, as shown in Figure 2. 3(a).

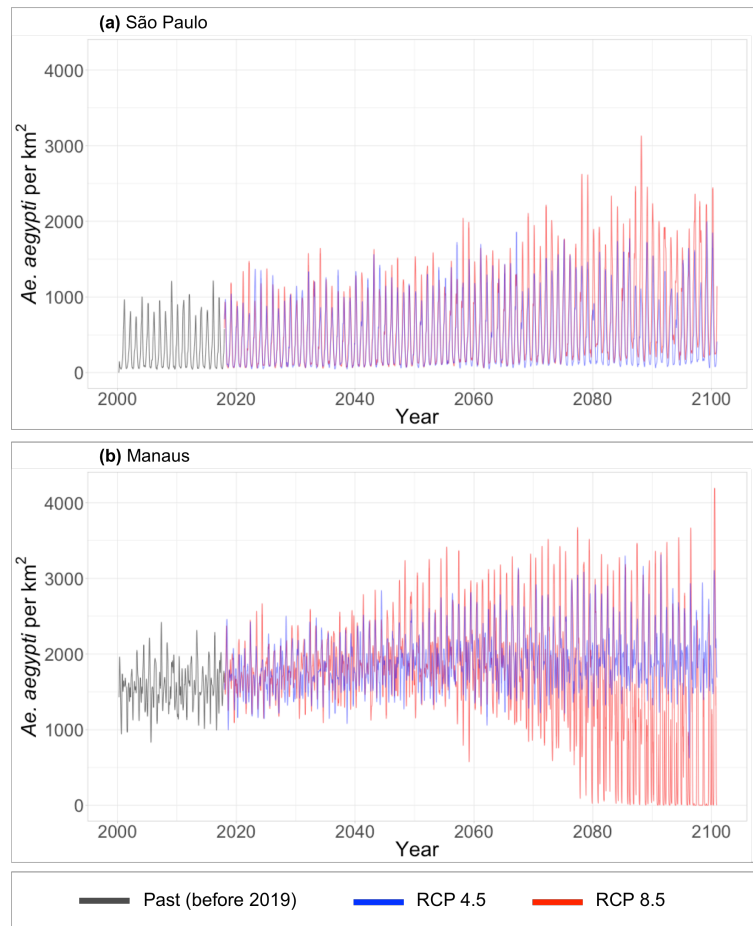


Figure 2. 3. Estimated *Ae. aegypti* density (mosquitoes per km<sup>2</sup>) in (a) São Paulo and (b) Manaus between 2000 and 2100. Estimates of historical mosquito densities are shown in grey and estimates of future densities are shown in blue and red for RCP 4.5 and RCP 8.5, respectively.

In contrast, Manaus has a humid, tropical monsoon climate with substantial precipitation and favourable temperatures for *Ae. aegypti*. We estimated Manaus to have a historically endemic *Ae. aegypti* population; the mosquito density remained above zero throughout the year, as shown in Figure 2. 3(b). Increasing aridity and extreme temperatures in Manaus under RCP 8.5 were predicted to alter *Ae. aegypti* seasonal trends from ~2060 onwards as larval development time and survival are both detrimentally affected by high temperatures in the range of 30-40° C and above (Eisen et al., 2014). These climatic changes resulted in large crashes in the mosquito population in hot, dry months; however, very large peaks in the population size were observed in the cooler, wetter months. Seasonal patterns in *Ae. aegypti* density were predicted to arise in other Northern cities which were predicted to have had stable, endemic *Ae. aegypti* populations for previous years. These included but were not limited to Coari in the Amazonas, Boa Vista in Roraima and Cruzeiro do Sul in Acre.

In addition to changes in seasonality, annual peaks in *Ae. aegypti* were predicted to shift to different times of the year beyond 2080, particularly for RCP 8.5 climate projections. This shift is demonstrated in Figure 2. 4, which shows the difference in mosquito density from the annual mean and contrasts winter and summer months. Current and historical *Ae. aegypti* populations were predicted to peak in North Brazil in the cold season (Figure 2. 4(a.i)) and in the rest of Brazil in the hot season (Figure 2. 4(a.ii)). However, in 2080, extremely high temperatures and aridity in the hot season were predicted to render North Brazil less habitable for *Ae. aegypti* and restrict peak populations to South Brazil (Figure 2. 4(b.ii)). *Ae. aegypti* was also predicted to inhabit a wider geographical range in cooler months in 2080 (Figure 2. 4(b.i)). This shift is due to inhospitably cold seasons becoming favourable for *Ae. aegypti*, and favourable seasons becoming inhospitably hot.

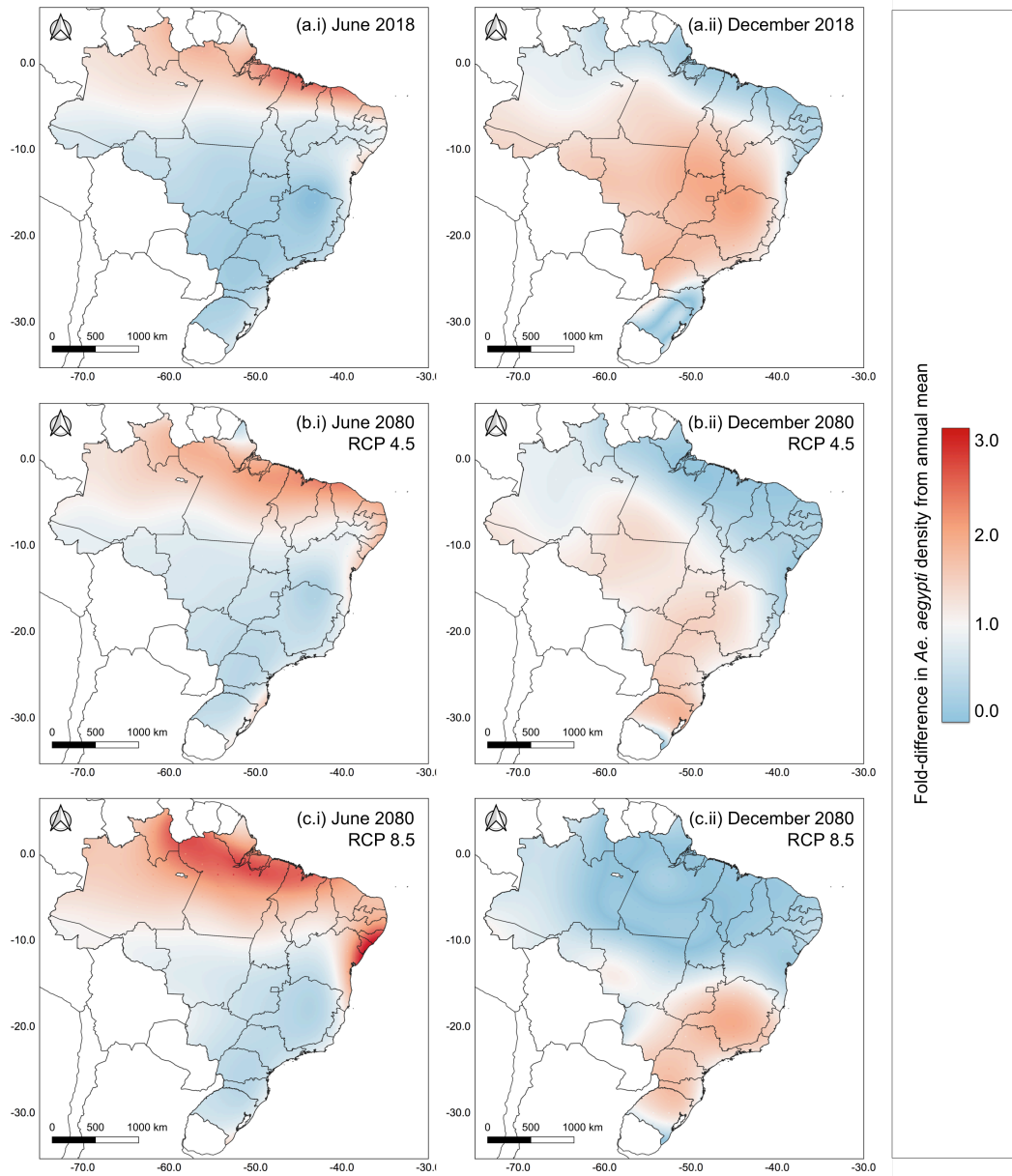


Figure 2. 4. Fold-difference in estimated *Ae. aegypti* density (mosquitoes per km<sup>2</sup>) from the estimated annual mean mosquito density for: 2018 in (a.i) June and (a.ii) December; 2080 for RCP 4.5 climate projections in (b.i) June and (b.ii) December; 2080 for RCP 8.5 climate projections in (c.i) June and (c.ii) December. Estimations are shown in June and December to represent the cold and hot seasons, respectively.

## **Model predictions are validated against existing time-series data**

Model-predicted *Ae. aegypti* densities were compared with time series of *Ae. aegypti* extracted from four studies (Codeço et al., 2015; da Cruz Ferreira et al., 2017; Degener et al., 2014; Pepin et al., 2015) and covering nine locations (Campo Grande, Duque de Caxias, Governador Valadares, Manaus, Novo Iguaçu, Paranamirim, Porto Alegre, Sete Lagoas and Vitória). Data were from either BG-Sentinal traps (BGS) (Biogents AG, Germany) or MosquiTraps (MQT) (Ecovec Ltda., Brazil). Time series data at seven of the nine locations were significantly correlated with model predictions ( $p < 0.05$ ). Comparison of model-predicted *Ae. aegypti* density and *Ae. aegypti* time series for four examples are shown in Figure 2. 5; the remaining five time series and details of comparison with model predictions are shown in Appendix A.13.

As is clear from Figure 2. 5, the model has a high degree of predictive accuracy at a number of locations across Brazil. Time series data from the three of the four example cases shown – Porto Alegre (da Cruz Ferreira et al., 2017), Vitória (Pepin et al., 2015) and Sete Lagoas (Pepin et al., 2015) – were significantly correlated with model-predicted *Ae. aegypti* densities ( $p = 0.02$ ,  $p < 0.001$  and  $p < 0.001$  respectively, modified Chelton method). Data from Parnamirim (Codeço et al., 2015), Figure 2. 5(d), were not significantly correlated with model predictions ( $p = 0.57$ ). It must be noted that the lack of correlation between data and model predictions at a small number of locations may be a feature of the data collection protocol or trapping methodology as much as it may be a feature of the model. Only 24 traps were used at non-significant locations Parnamirim and Novo Iguaçu ( $p = 0.57$  and  $p = 0.09$  respectively) compared to 1392,

373 and 411 traps at significant locations Vitória, Governador Valadares and Sete Lagoas ( $p < 0.001$  for all). Fewer traps and less frequent sampling could result in greater data variability and may affect the degree of correlation between data and model predictions. Data not significantly correlated with model predictions still displayed notable visual similarities as shown for Parnamirim in Figure 2. 5(d).

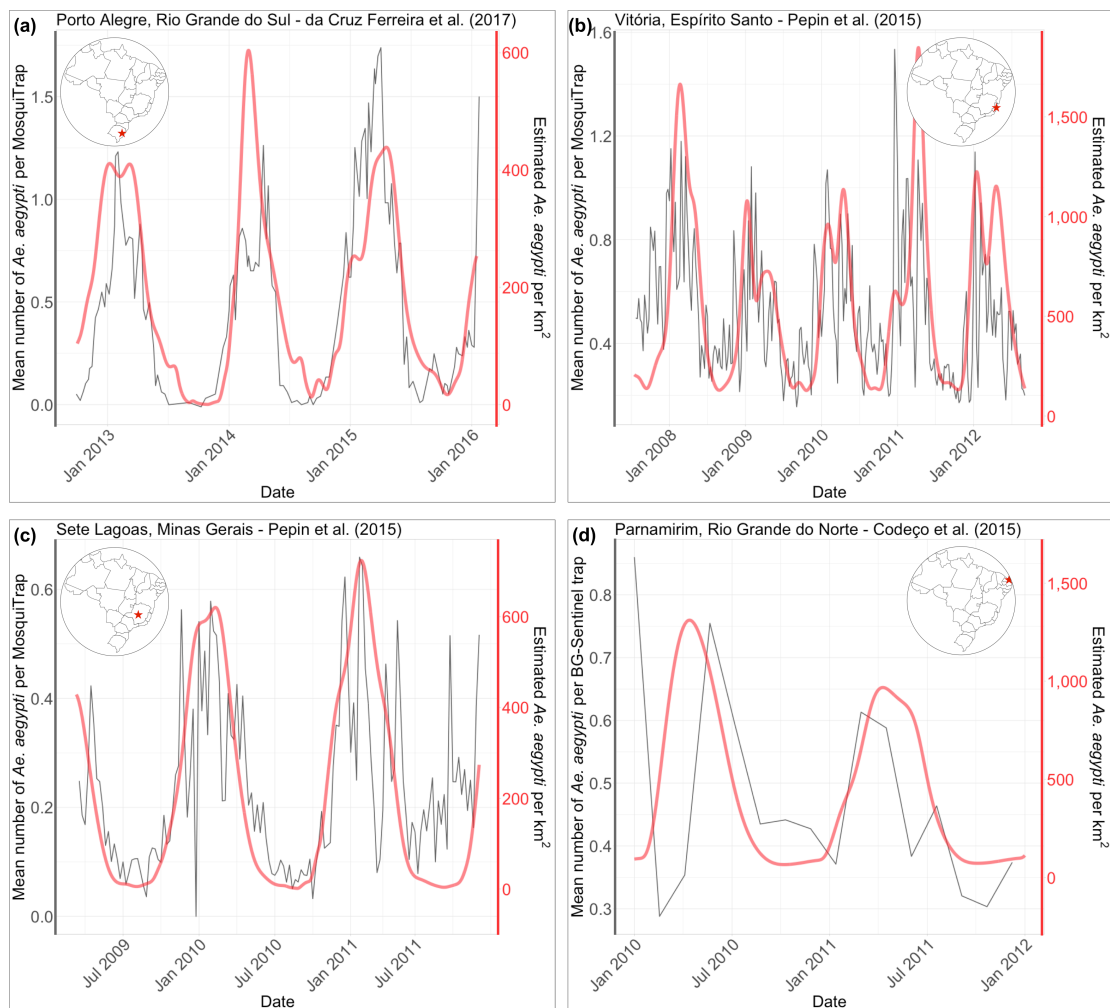


Figure 2. 5. Comparison of published *Ae. aegypti* trap data (grey lines) with model-estimated *Ae. aegypti* density (red lines) at four locations across Brazil. The four locations were selected for demonstration of model accuracy because they are geographically well spread therefore representing diverse climates and landscapes. Further examples are presented in Appendix A.13. Comparisons are shown for (a) Porto Alegre, (b) Vitória, (c) Sete Lagoas and (d) Parnamirim. Model estimates and published data were significantly correlated for locations (a)-(c) ( $p < 0.05$ , modified Chelton method) but not for (d) Parnamirim ( $p = 0.57$ ). Data have been adapted for presentation in this figure from (a) da Cruz Ferreira et al., 2017; (b)-(c) Pepin et al., 2015; (d) Codeço et al., 2015.

## **Rural areas are more vulnerable to mosquito-borne disease outbreaks**

The mean annual basic reproductive number,  $R_0$ , for a vector-borne disease such as dengue fever as calculated from model-predicted *Ae. aegypti* abundance is shown in Figure 2. 6(a). Higher  $R_0$  values indicate greater susceptibility of the population to disease outbreaks. The rural North and Northwest of Brazil were predicted to be particularly vulnerable to rapid dengue outbreaks. These are the same regions where *Ae. aegypti* density is predicted to be highest (Figure 2. 1). Our findings are consistent with previous studies finding elevated transmission in rural areas (Chareonsook et al., 1999; Chew et al., 2016; Schmidt et al., 2011).

Predicted future changes in  $R_0$  are shown in in Figure 2. 6(c)-(f). By 2030,  $R_0$  was predicted to increase in 78% and 69% of municipalities for RCP 4.5 and RCP 8.5, respectively. By 2050, the mean annual  $R_0$  was predicted to increase in 99% of municipalities for both RCP 4.5 and RCP 8.5. By 2080, the mean annual  $R_0$  was predicted to increase in 100% and 97% of municipalities for RCP 4.5 and RCP 8.5, respectively. The largest increases in  $R_0$  were predicted to occur in populous Southeast Brazil, due to projected increases in human population density in populous areas being unmatched in magnitude by increases in *Ae. aegypti* density; a low vector-to-human ratio results in a low  $R_0$  value.

Mean annual  $R_0$  was not significantly associated with mean annual dengue case rates ( $p>0.05$ , linear regression) for the period 2015-2017 as shown by comparing Figure 2. 6(a) and Figure 2. 6(b). There are multiple possible reasons for this such as a lack of reporting, a lack of dengue introduction into rural areas or a stronger effect of urban

accessibility than we are able to include in our model with available data. These reasons are further expanded in the discussion.

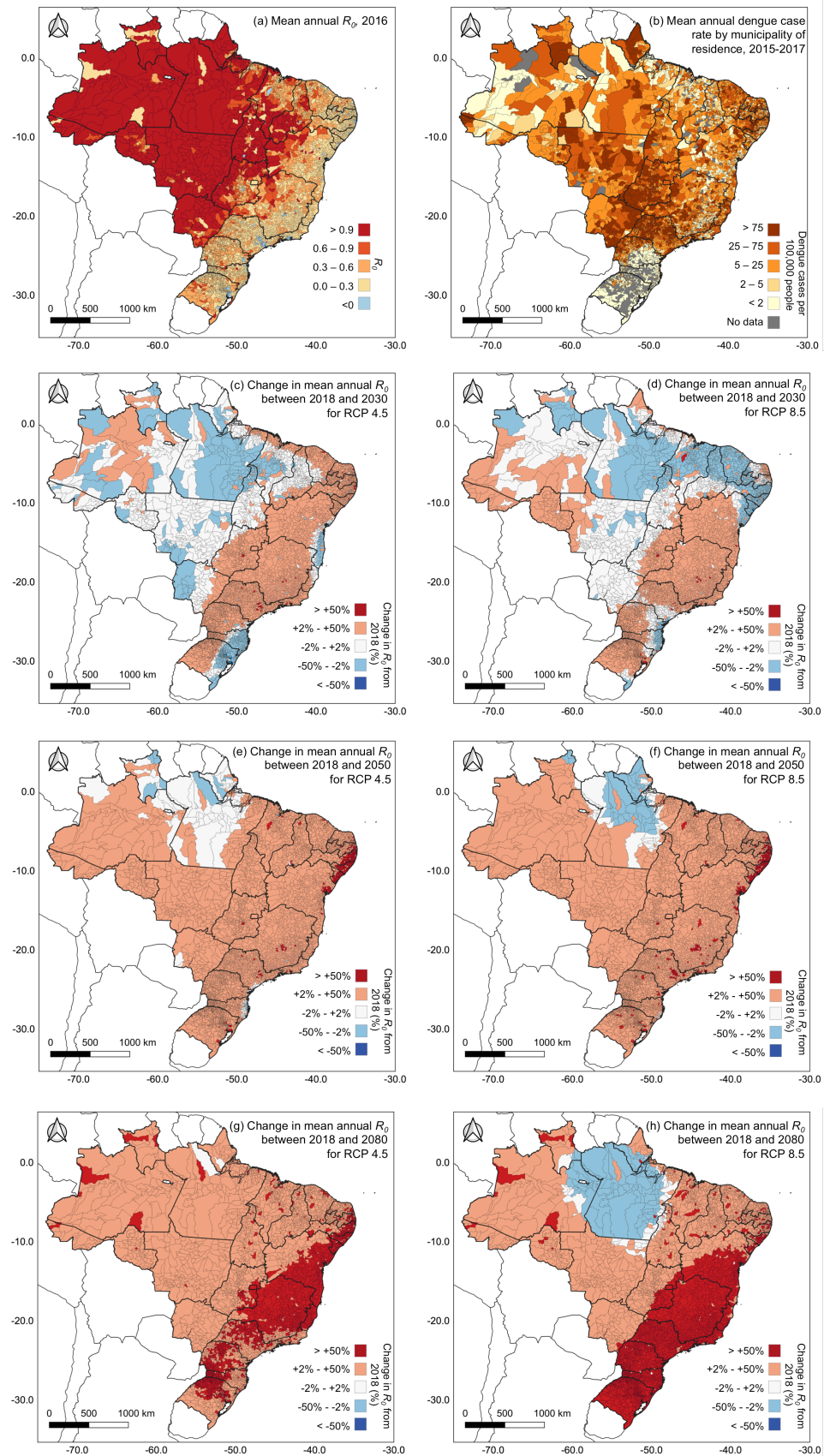


Figure 2. 6. Panels (a) and (b) show the mean annual predicted  $R_0$  of dengue fever and the annual reported dengue case rate (cases per 100,000) by municipality of residence respectively for the period 2015-2017. Monthly municipal dengue case numbers are available from DATASUS, Brazilian Ministry for Health. Panels (c) and (d) show the estimated change in mean annual  $R_0$  between 2018 and 2030. Panels (e) and (f) show the estimated change in mean annual  $R_0$  between 2018 and 2050. Panels (g) and (h) show the estimated change in mean annual  $R_0$  between 2018 and 2080.



## **Discussion**

We have predicted that the *Ae. aegypti* distribution in Brazil will be substantially disrupted as a consequence of climate change. We predicted increases in *Ae. aegypti* density across Brazil. Our results are in agreement with the existing literature that temperature increases will generally facilitate *Ae. aegypti* persistence. Several studies have predicted the climatic suitability for *Ae. aegypti* to increase as a result of climate change (Campbell et al., 2015; Eisen et al., 2014; Khormi and Kumar, 2014). Others have used climate and anthropogenic data to predict increases in the distribution of mosquito-borne disease (Faria et al., 2017; Thai and Anders, 2011; Tjaden et al., 2017) and increased *Ae. aegypti* occurrence probability (Kraemer et al., 2015) as a consequence of climate change.

Our study has offered two unique and novel improvements to existing approaches and models. First, few studies have incorporated a dynamic model of the mosquito life-cycle; those that have do not consider changes in mosquito density on a spatiotemporal scale or consider anthropogenic variables (Beck-Johnson et al., 2013; Erickson et al., 2010; Ewing et al., 2016; Khormi and Kumar, 2014; X. Wang et al., 2016). Both of these features are paramount as *Ae. aegypti* respond non-linearly to climatic variability across geographical regions at multiple life cycle stages (de Almeida Costa et al., 2010; Eisen et al., 2014; McBride et al., 2014; Schmidt et al., 2018). A reduction in climatic suitability for *Ae. aegypti* under extreme temperatures in North Brazil, as shown for Manaus in Figure 2. 3(b), demonstrates the importance of *Ae. aegypti* biology for population dynamics and climatic suitability; *Ae. aegypti* development is detrimentally affected by temperatures in the range 30-40°C and above (Eisen et al., 2014) and periods of aridity compromise the carrying capacity of

the environment for mosquito populations. The disruption of seasonal trends in *Ae. aegypti* due to climate change demonstrates the importance of mechanistic models based on biological theory to capture unprecedented changes in mosquito population dynamics.

Second, there has been a prevailing literature focus upon projected climatic suitability or occurrence probability for mosquitoes and mosquito-borne disease (Monaghan et al., 2018; Ryan et al., 2019). Whilst powerful, such models are not necessarily informative of the degree to which *Ae. aegypti* population sizes will increase; for example, two climatically suitable regions could have very different mosquito densities, depending on how ‘climatic suitability’ is defined or categorised. Mosquito population size heavily influences disease transmission (Massad et al., 2011; Petrić et al., 2014); therefore, it is important to estimate future *Ae. aegypti* population sizes in addition to occurrence probabilities. Further, epidemiological models of mosquito-borne diseases – such as the simple Ross-Macdonald model – are often structured around quantifiable mosquito populations (Andraud et al., 2012). Our approach has addressed the above considerations by estimating mosquito density. We predict increases in *Ae. aegypti* density in every major city in Brazil. In addition we predict widespread increases in the transmission potential of dengue fever. These results show that *Ae. aegypti* and its associated diseases will present substantial public health problems as a consequence of climate change.

Seasonal patterns of model-predicted *Ae. aegypti* density were significantly correlated with existing historical time series of *Ae. aegypti* at seven out of nine locations in Brazil for which data were available. This demonstrates a high degree of model accuracy in predicting temporal trends in *Ae. aegypti* density in heterogeneous locations across Brazil. The calculation of  $R_0$  for dengue fever by municipality

demonstrated the utility and application of model results and facilitated comparison of  $R_0$  estimates with reported dengue cases in order to evaluate the models spatial predictive accuracy. Elevated dengue transmission potential was predicted in rural areas of Brazil, a result consistent with previous observations from Vietnam (Schmidt et al., 2011) and Malaysia (Chew et al., 2016), where the risk of dengue and the annual increase in dengue prevalence were greatest in rural areas due to the high vector-to-host ratio.

Despite consistency of our results with previous empirical studies, mean annual  $R_0$  values for the period 2015-2017 were not significantly associated with the number of cases by municipality for the same time period. Monthly  $R_0$  values were also not associated with mean monthly case numbers. There are several possible reasons for this, three of which are discussed. First, dengue is underreported globally. The World Health Organization documented 2.2 million dengue cases in 2010 but models predicted that the number of cases may have reached 96 million (Bhatt et al., 2013; World Health Organization, 2012). Brazil has the highest global rate of underreporting for dengue (World Health Organization, 2012); as many as 17 dengue cases per reported case have been estimated in low transmission seasons (Silva et al., 2016). It is not known whether underreporting of dengue in Brazil varies by region. More rural areas of central and Northwest Brazil, where transmission potential is predicted to be highest, may have highly dispersed populations and reduced healthcare access leading higher rates of underreporting. Second, our calculation of  $R_0$  estimates the transmission potential in a fully susceptible population under the assumption that dengue is introduced into that population. It may be the case that dengue is simply not introduced into some rural areas due to a lack of human migration from more urbanised areas. If this is the case then our estimates still

indicate which regions are the most vulnerable; increased urban expansion may facilitate future disease introduction and spread in areas that are currently unaffected.

Whilst we have predicted that the greatest increases in *Ae. aegypti* density will occur in populous Southeast states, we have also demonstrated that rural North regions of Brazil are particularly susceptible to large *Ae. aegypti* populations due to the highly suitable predicted climate (see Figure 2. 1). This is particular concerning since rural-urban development in Brazil is currently predominantly affecting smaller cities in the North and central regions which include some of the poorest regions in the country (de Espindola et al., 2017), which, as noted above, promotes mosquito persistence and mosquito-borne disease in addition to the effects of climate (Dowling et al., 2013; Mondini and Chiaravalloti-Neto, 2008). Less populous areas also have a higher mosquito-to-human ratio, which results in higher  $R_0$  values. Not only is Brazil at risk of experiencing substantial increases in *Ae. aegypti* density, the negative health effects of these increases are likely to affect the poorest and most isolated sectors of the population.

Our results highlight further the devastating effects of climate change falling upon sectors of society least equipped to deal with the problem. Whilst our results predict climate change to exacerbate the challenges presented by mosquito-borne disease, the degree to which the problem is worsened will depend upon the action we take now to mitigate climate change and its socioeconomic effects. Further studies should investigate other climate models and the relevant contribution of land-use and climate variables to inform efficient mitigation strategies.

## **Data availability**

The HadGEM2-ES climate data that support the findings of this study are available for download via the ESGF portal (<https://esgf-index1.ceda.ac.uk/projects/esgf-ceda/>) and were accessed between 10-Jun-2018 and 30-Aug-2018. Urban accessibility data that support the findings of this study are available for download from the Malaria Atlas Project ([https://map.ox.ac.uk/research-project/accessibility\\_to\\_cities/](https://map.ox.ac.uk/research-project/accessibility_to_cities/)) as a .zip file of the raster data and were accessed on 29-Jan-2019. Further information is available in the associated manuscript from Weiss et al. (2018) with <https://doi.org/10.1038/nature25181>. Urban extent data that support the findings of this study are available for download from <https://doi.org/10.26188/5c2c5d0ed52d7> and were accessed on 16-September-2019. Further information is available in the associated manuscript from Zhou et al. (2019) with <https://doi.org/10.1038/s41597-019-0048-z>. Dengue case data that support the study findings came from DATASUS, Brazilian Ministry of Health, and are available from <http://www2.datasus.gov.br/DATASUS>. Global human population projections that support the findings of this study are available from SEDAC with identifier <https://doi.org/10.7927/H4RF5S0P>. Further details on the projection methodology is available from Jones & O'Neil (2016) with identifier <https://doi.org/10.1088/1748-9326/11/8/084003>. LIRAA sampling data that supported the findings of this study were provided by the Brazilian Ministry for Health upon request and will be made available on the Open Science Framework (OSF) at <https://osf.io/bvpsa> upon acceptance of this chapter for publication in an edited form.

## **Code availability**

Custom computer code, algorithms and pre-processed data will be made available on the Open Science Framework (OSF) at <https://osf.io/bypsa> upon acceptance of this chapter for publication in an edited form.

# Chapter 3

## Nutritional availability and larval density dependence in *Aedes aegypti*

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## **Abstract**

**Background:** Density dependence underpins the regulation and persistence of animal populations. In many species, density dependence has been shown to be an aggregate term for suites of complex interactions between animals and their environment. However, mechanistic studies of density dependence in mosquito ecology are sparse and the role of environmental factors is poorly understood.

**Methods:** Two empirical study designs were compared to test the role of nutritional availability in *Aedes aegypti*. The first design fed larvae on a per capita basis. The second design fed a fixed amount of food unadjusted for the number of individuals; therefore, at higher larval densities each individual received less food per capita.

**Results:** We observed decreased survivorship, adult wing length and larval development rate at high densities when larvae were fed a fixed amount of food irrespective of the number of individuals; we observed the opposite when food was adjusted per capita, suggesting that high densities can promote larval development when per capita nutrition is held constant. These results demonstrate that observed associations between *Ae. aegypti* larval density and larval development are a manifestation of decreased per capita nutrient uptake at high densities.

**Conclusions:** Our results demonstrate that population regulation is a proportional response to environmental variability in *Ae. aegypti*. Increased survivorship at high densities when larvae were fed per capita demonstrate that, whilst important, nutritional availability is unlikely to be the only mechanism of density dependence operating in mosquitoes. Further studies should seek to characterise density dependence in mosquitoes by employing mechanistic study designs across diverse environmental conditions.



## **Introduction**

Density dependence is defined as the effect of population density upon population growth. Density dependence is an aggregate term encapsulating numerous environmentally-dependent mechanisms, as has been demonstrated in a variety of species (Houston, 1982; King et al., 2003; McKinney et al., 2001; Nevoux et al., 2011). In other words, “density dependence” is the cumulative effect of multiple interactions between population density and environmental variables upon population growth. Characterisation of density dependence in entomology has been historically contentious due to a lack of consistent empirical support (Andrewartha and Birch, 1954; Dempster, 1983; den Boer and Reddingius, 1989; Dye, 1984; Gaston and Lawton, 1987; Stiling, 1988, 1987). Mosquito fitness is influenced by the environment encountered during development (Hawley, 1985; Westby and Juliano, 2017). Despite this, the role of environmental variables for density dependence in mosquitoes and other insects has not been comprehensively explored.

In Chapter 2, density dependence in *Aedes aegypti* was captured by variation in the carrying capacity,  $K(t)$ , at a time,  $t$ , as follows:

$$K(t) = \lambda \frac{1}{\omega(1-e^{-t/\omega})} \int_{t-30}^t e^{-(t-t')/\omega} p(t') dt' \quad (3.1)$$

where  $\omega$  was the number of previous days of past rainfall contributing to the current carrying capacity and  $\lambda$  was a numeric constant. The carrying capacity subsequently determined density-dependent juvenile mortality, which was defined as  $1/K(t)$ . Parameter  $\lambda$  controlled the strength of density-dependent population regulation.  $\lambda$  is difficult to assign value to because it is an aggregate term capturing a multitude of interactions between individuals and their environment. This chapter presents a

mechanistic study of one biological mechanism – nutritional availability – that may influence the value of  $\lambda$  for *Ae. aegypti*.

Since the work of Nicholson and Smith in the 1930s, the concepts of density dependence and population regulation have been prevailing views in animal ecology (Nicholson, 1933; Smith, 1935). Associations between population density and growth have been particularly well supported for some large mammal species (Gaillard et al., 1998; Huff and Varley, 1999; Krebs, 1995) such as the northern Yellowstone elk (Houston, 1982). However, uncertainty has prevailed elsewhere and particularly in insect species where little evidence for density dependence has been observed in field populations (Andrewartha and Birch, 1954; Dempster, 1983; Stiling, 1988, 1987). The lack of empirical support for density dependence in insect species culminated in long-standing debates between entomologists in the late 1980s and mid 1990s (Andrewartha and Birch, 1954; Dempster, 1983; den Boer and Reddingius, 1989; Gaston and Lawton, 1987; Stiling, 1988, 1987), appearing to end with “agreement to disagree” (Haak, 2002; Wolda et al., 1994). Some authors have deduced that density dependence is not present in insect populations (Dempster, 1983; Stiling, 1988). Andrewartha and Birch (1954), for example, proposed that density-dependent processes are “in general, of minor or secondary importance, and (...) play no part in determining the abundance of some species” (Andrewartha and Birch, 1954). Others have concluded that failure to detect density dependence in long term field studies has been due to weaknesses in the data and a lack of appropriate statistical tests (Hassell, 1986, 1985). We propose that the lack of consistent empirical support for density dependence in entomology is a product of the sensitivity of some insect populations to environmental variability; the effects of density alone may be challenging to isolate because they are inextricably linked to environmental factors.

Empirical studies in other taxa have not been so limited in scope. In many species there is substantial evidence that density dependence is an aggregate term for a suite of complex interactions between animals and their environment (Moss and Watson, 2001; Newsome et al., 2001; Zann et al., 1995). Annual and seasonal rainfall patterns have been found to significantly affect the distribution, recruitment and survival of desert bighorn sheep, likely via effects on forage quantity or quality (McKinney et al., 2001). The reproductive success of female stoats in New Zealand has been shown to vary with the abundance of mice (King et al., 2003). In Soay sheep, the effect of density was found to be modified by weather events (Coulson et al., 2001). In response to the prevailing evidence, White (2004) proposed that “the evidence from nature is that populations are not regulated; they are limited by the capacity of the environment to support them” (White, 2004). A small number of studies in mosquitoes have also observed environmental conditions to interact with density in complex mechanisms. For example, In *Aedes triseriatus*, the effect of delayed density dependence on mosquito development was substantial under most experimental conditions, but the effect became negligible when resources were abundant (Westby and Juliano, 2017). Density dependence in mosquito larvae is also modified through inter-specific larval competition with other mosquito species (Hardstone and Andreadis, 2012; Hoshi et al., 2017).

The above examples demonstrate that density dependence in mosquitoes is a dynamic and mechanistic process incorporating various environmental conditions. One mechanism of density dependence that has been particularly well documented for other species is nutritional availability. In zebrafish *Danio rerio*, Hazlerigg et al. (2012) have demonstrated that the associations between density and life history traits are not causal, but arise through a resource limitation mechanism (Hazlerigg et al.,

2012). Fish were fed under two feeding regimes: (i) a constant feeding regime resulting in per capita resource limitation at high densities and (ii) a per capita regime where the amount of food per individual was held constant irrespective of density. Under the second, per capita regime, the association between density and body growth rate was nullified. Borlestean et al. (2015) examined algae *Chlamydomonas reinhardtii* (Chlamydomonadaceae) over 12 nutrient conditions and observed that population regulation was a proportional response to nutrient variation (Borlestean et al., 2015). Both studies demonstrate clearly that the population growth rate is not always a function of population density and that environmental conditions are crucially important. Empirical studies in mosquito ecology should therefore assume a more mechanistic approach and consider the role of environmental variability.

Despite the above considerations, the mechanistic empirical study designs adopted to examine density dependence in other species have not been readily adopted in mosquito ecology. The majority of studies in mosquito ecology have sought to parameterise a statistically significant relationship between population size and population growth under controlled laboratory conditions. In general, high larval densities are believed to inhibit development and survival in multiple mosquito species including the major disease vectors *Ae. aegypti* and *Anopheles gambiae* (Dye, 1984; Gimnig et al., 2002; Legros et al., 2009; Muriu et al., 2013; Schneider et al., 2000; Southwood et al., 1972; Walsh et al., 2013, 2011; Yakob et al., 2008). A small number of studies have identified that density dependence in mosquitoes is complex and can incorporate numerous environmental factors such as temperature and nutritional availability (Couret et al., 2014; Jannat and Roitberg, 2013; Kearney et al., 2009; Lyimo et al., 1992; Schneider et al., 2000; Westby and Juliano, 2017). Crucially, the amount of nutritional resources available to mosquito larvae has been

observed to influence the outcome of density dependence (Juliano, 1998; Washburn et al., 1991). However, larval rearing conditions – particularly larval feeding regimes – are rarely held constant between studies. Empirical studies of density dependence in mosquitoes have fed larvae food *ad libitum* (Banerjee et al., 2017), not adjusted food quantities for the number of individuals (Maciá, 2009; Reiskind and Lounibos, 2009) or not reported their feeding conditions. This leads to two problems. First, it is impossible to ascertain whether associations between larval density and mosquito life history traits are due to (a) the effect of density via routes such as chemical inhibition or (b) reduced per capita availability of nutrients due to increased numbers of individuals. Second, if we assume (b) then empirical studies are simply measuring the carrying capacity of their laboratory system. A small number of studies have fed larvae per capita and observed decreased survival at high densities, although the effect was smaller than in previous studies (Alcalay et al., 2018a; Jannat and Roitberg, 2013; Koenraadt et al., 2004). This suggests that there may be other mechanisms of density dependence taking place, although they have not been identified.

We used the mosquito *Ae. aegypti* as a study species to address some of the confusion about density dependence that has arisen in entomology (Andrewartha and Birch, 1954; Dempster, 1983; Gaston and Lawton, 1987; Reddingius and den Boer, 1989; Stiling, 1988, 1987). We hypothesised that variations in certain life history traits (survival, development time and adult wing length) are a response to per capita nutritional availability. Therefore, we hypothesised that there is no single relationship between density and population growth, but that any observed relationship is a single cross section of a multidimensional parameter space of environmental factors. Density-dependent effects on life history parameters occur because increased density reduces per capita nutritional availability, promoting increased competition for

resources. *Ae. aegypti* is an excellent study species both because of its importance as a vector of human disease (Higa, 2011; Powell et al., 2018) and its pervasiveness in mathematical models of mosquitoes and mosquito-borne disease (Dye, 1984; Legros et al., 2016).

We tested the hypothesis that *Ae. aegypti* populations are regulated in a bottom-up manner from their food supply by comparing two empirical study designs over a spectrum of larval densities. In the first experimental design, larvae were fed a fixed amount of food unadjusted for the number of larvae. Therefore, increasing density resulted in declining per capita food availability. In the second experimental design, larvae were fed on a per capita basis. We hypothesised that controlling the per capita nutritional availability would eliminate the effect of larval density on survival, development time and adult wing length.



## **Methods**

### ***Ae. aegypti* rearing and colony maintenance**

Liverpool strain *Ae. aegypti* were used for all experiments in this study (Macdonald, 1962). This strain was originally established from eggs collected in West Africa and has been maintained at the Liverpool School of Tropical Medicine since 1936. All *Ae. aegypti* eggs used in this study were hatched in room temperature deionised water (~25°C) in a vacuum hatcher at 600 kPa for two hours to ensure age control. Colony larvae were kept in plastic trays (EFE GB Nets Educational Scientific Equipment, small heavy duty tray (SKU: ACCTHD2.5), 435×285×80 mm) and fed *ad libitum* on liver powder (NOW foods, Bloomingdale, IL, USA). Once pupated, pupae were transferred by Pasteur pipette to ~100 mL water in plastic containers in 40 cm<sup>3</sup> mesh insectary cages to emerge (MegaView Science Co. Ltd, Taichung, Taiwan). Emerged adults were fed *ad libitum* on sucrose solution and kept at 28±1°C with a 16h:8h light:dark cycle and 80% relative humidity. Female mosquitoes were blood-fed by a Hemotek<sup>®</sup> membrane feeding system (Hemotek Ltd, Great Harwood, Lancashire, UK) using defibrinated horse blood (TCS Biosciences, Buckingham, UK). Damp filter papers were placed in insectary cages to facilitate egg laying by blood-fed females. Egg papers were collected, dried and sealed in airtight plastic containers for later use, either in experiments or colony maintenance.

### **Experimental design**

Larval rearing conditions were manipulated along two axes: larval density and larval nutritional availability. Two experimental designs were compared. In the first, larvae

were fed on a population level basis; the quantity of food administered was not adjusted to the number of larvae. In the second experimental design, larvae were fed on a per capita basis; the amount of food administered was adjusted to match the number of individuals.

Table 3. 1. Overview of experimental design for per capita and per pot feeding experiments. The table displays the larval densities used and the corresponding number of larvae followed in each density condition.

|                                     | Densities |     |     |     |      |
|-------------------------------------|-----------|-----|-----|-----|------|
|                                     | D1        | D2  | D3  | D4  | D5   |
| Overview of experimental design     |           |     |     |     |      |
| Larval density (larvae/litre)       | 100       | 330 | 550 | 780 | 1000 |
| Pot volume (mL)                     | 100       | 100 | 100 | 100 | 100  |
| Larvae per pot                      | 10        | 33  | 55  | 78  | 100  |
| Number of pots per food treatment   | 30        | 9   | 6   | 6   | 3    |
| Number of larvae per food treatment | 300       | 297 | 339 | 468 | 300  |

Table 3. 2. Overview of feeding regimes for per capita and per pot feeding experiments. The quantity of food given per pot and per capita is given for each experimental design, converted onto the alternative scale. This is in order to demonstrate the fact that both experiments share a central axis at 550 larvae/litre. In the per pot experiment, food was given to each pot unadjusted for the number of larvae every two days for six days after hatching (three total feeds). For the per capita feeding experiment the food given per pot holds the per capita food quantity constant and is adjusted for the number of larvae.

| Larval density condition (larvae/litre) |      |      |      |      |                   |       |       |       |       |       |
|-----------------------------------------|------|------|------|------|-------------------|-------|-------|-------|-------|-------|
| 100                                     | 330  | 550  | 780  | 1000 | 100               | 330   | 550   | 780   | 1000  |       |
| Per capita food (mg)                    |      |      |      |      | Per pot food (mg) |       |       |       |       |       |
| Per capita feeding experiment           |      |      |      |      |                   |       |       |       |       |       |
| 0.05 mg larva                           | 0.05 | 0.05 | 0.05 | 0.05 | 0.05              | 0.50  | 1.65  | 2.75  | 3.90  | 5.00  |
| 0.30 mg/larva                           | 0.30 | 0.30 | 0.30 | 0.30 | 0.30              | 3.00  | 9.90  | 16.50 | 23.40 | 30.00 |
| 0.55 mg/larva                           | 0.55 | 0.55 | 0.55 | 0.55 | 0.55              | 5.50  | 18.15 | 30.25 | 42.90 | 55.00 |
| 0.80 mg/larva                           | 0.80 | 0.80 | 0.80 | 0.80 | 0.80              | 8.00  | 26.40 | 44.00 | 62.40 | 80.00 |
| Per pot feeding experiment              |      |      |      |      |                   |       |       |       |       |       |
| 2.75 mg/pot                             | 0.28 | 0.08 | 0.05 | 0.04 | 0.03              | 2.75  | 2.75  | 2.75  | 2.75  | 2.75  |
| 16.50 mg/pot                            | 1.65 | 0.50 | 0.3  | 0.21 | 0.17              | 16.50 | 16.50 | 16.50 | 16.50 | 16.50 |
| 30.25 mg/pot                            | 3.03 | 0.92 | 0.55 | 0.39 | 0.30              | 30.25 | 30.25 | 30.25 | 30.25 | 30.25 |
| 44.00 mg/pot                            | 4.40 | 1.33 | 0.8  | 0.56 | 0.44              | 44.00 | 44.00 | 44.00 | 44.00 | 44.00 |

A full outline of the experimental design and feeding regimes is given in Table 3. 1 and Table 3. 2. Each design considered four food conditions at five larval densities: 100, 325, 550, 775 and 1000 larvae per litre in order to span a range of densities which increased by tenfold. Experimental larvae were reared in 100 mL of room temperature, deionised water in clear plastic half-pint pots. First instar larvae were counted and transferred to pots immediately after hatching at numbers of 10, 33, 55, 78 and 100 to correspond to the appropriate densities. The unit of replication was the individual larva. The number of pots monitored for each larval density was controlled so that ~300 larvae were monitored for each density. This totalled 1,704 monitored larvae for each experimental design. The number of pots monitored for each density condition to achieve this is detailed in Table 3. 1. The number of pots was different between density conditions because it is not logically possible hold both the number of larvae and the number of pots constant. Once transferred to pots, counted larvae were fed with 1 mL of food suspension made with liver powder and deionised water. Food was administered as a suspension to avoid error associated with weighing small quantities of food. Suspensions were made in 50 mL falcon tubes with 50 times the food needed to feed one pot. Food weights were correct to 0.001 g (Product PA413, OHAUS Corp., Greifensee, Switzerland). Two feeding designs were assessed, each with four food quantities as outlined below. The most appropriate range of food treatments to capture the effects of food limitation was determined by a pilot experiment, which is presented in Appendix B.1.

### **Per capita feeding**

In the per capita feeding experiment, food given was adjusted for the number of individuals per pot to hold per capita nutritional quantity constant. Four per capita food treatments were considered: 0.05, 0.30, 0.55 and 0.80 mg per larva every two days for six days (three total feeds) after hatching as detailed in Table 3. 2. The amount of food given per capita was adjusted when dead larvae were identified. However, there was minimal observable larval mortality before day six; therefore, there was not frequent need to adjust the feeding quantity.

### **Per pot feeding**

In the per pot feeding experiment larvae were fed on a fixed basis irrespective of the larval density. The quantity of food administered per pot was determined by the feeding regime in the per capita feeding experiment. At the medial density (550 larvae/litre) in the per capita feeding experiment, the amount of food given per pot was 2.75 mg (0.05 mg/larva), 16.50 mg (0.30 mg/larva), 30.25 mg (0.55 mg/larva) and 44.00 mg (0.80 mg/larva) as shown in Table 3. 2. These quantities were adopted as the four per pot feeding conditions and were administered every two days for six days after hatching (three total feeds) and held constant across all larval density conditions. In this way, both the per capita and per pot feeding experiments shared a central axis at 550 larvae/litre.

## Data collection

Pots were monitored daily for pupating larvae. Once pupated, the date of pupation was recorded and pupae were removed and placed in insectary cages to emerge. This facilitated the calculation of the development time (days from hatch to pupation) for each surviving larva. The number of surviving larvae was recorded for each pot. Two days after first emergence, adult mosquitoes were removed from cages via aspiration, snap frozen and sorted by gender. Male mosquitoes were discarded. A random subsample of adult females was taken from each cohort. The maximum sample size was 25; however, the sample size was limited by (a) the gender distribution of surviving adults and (b) the number of surviving adults, since low food treatments often had few survivors. The right wing of each female was removed using a scalpel and placed on a microscope slide. Wing length measurements were taken from the end of the axillary incision to the tip of the wing, excluding the fringe (Carron, 2007; Nasci, 1986) using a dissecting microscope and eye piece graticule calibrated using a 1 mm stage micrometer ruler. Wing length was used as a surrogate measure for adult body size, which is expected to modify adult vectorial capacity (Takken et al., 1998).

## Data analysis

All analyses were conducted in R version 3.6.1 (R Core Team, 2018). Bayesian GLMs were used to analyse the data using JAGS for R (Plummer, 2003; R Core Team, 2018).

Larval survival was analysed using a Bayesian hierarchical beta-binomial model with an inverse-logit link function. A beta-binomial model offers an advantage over a non-

hierarchical binomial model as the beta distribution facilitates modelling of the variance of the survival probability. The beta-binomial model is also flexible for modelling proportions such as the survival proportions seen in this study. The beta distribution was re-parameterised by its mean,  $\mu$ , and its standard deviation,  $\theta$ , as follows:

$$S_j \sim \text{Bin}(p_j, N_j) \quad (3.2)$$

$$p_j \sim \beta(\mu_j \theta_j, (1 - \mu_j) \theta_j) \quad (3.3)$$

$$\mu_j = \frac{e^{(\alpha_0 + Y_i)}}{1 + e^{(\alpha_0 + Y_i)}} \quad (3.4)$$

$$\theta_j = e^{(\gamma_0 + Z_i)} \quad (3.5)$$

where  $S_j$  is the proportion of larvae surviving to pupation in a pot,  $j$ ,  $N_j$  is the number of larvae in a pot,  $j$ , at the start of the experiment and  $p_j$  is the survival probability.  $Y_i$  and  $Z_i$  hold the relevant covariates and associated parameters. Three formulations of  $Y_i$  and  $Z_i$  were compared as detailed below leading to nine individual models.

$$Y_i = \begin{cases} \alpha_1 D_i \\ \alpha_1 D_i + \alpha_2 F_i \\ \alpha_1 D_i + \alpha_2 F_i + \alpha_3 D_i F_i \end{cases} \quad (3.6)$$

$$Z_i = \begin{cases} \gamma_1 D_i \\ \gamma_1 D_i + \gamma_2 F_i \\ \gamma_1 D_i + \gamma_2 F_i + \gamma_3 D_i F_i \end{cases} \quad (3.7)$$

where  $D$  is larval density (larvae/litre) and  $F$  is food administered. Survival models were applied to data from the per capita and the per pot feeding experiments separately. Therefore  $F$  can refer to either per capita or per pot food quantities depending on the experiment under analysis. Uninformative priors were assigned such that  $\{\alpha_0, \dots, \alpha_3\} \sim N(0, 10^{-4})$  and  $\{\gamma_0, \dots, \gamma_3\} \sim N(0, 10^{-4})$  where the normal distribution is parameterised by its mean and precision in accordance with the specifications used by JAGS for R (Plummer, 2003; R Core Team, 2018). The beta distribution controls for between-pot variability via parameter  $\theta_j$ , which models the

variance for a pot,  $j$ . Pot was not controlled for explicitly because the number of pots monitored was correlated with the density conditions (i.e. the lowest density condition had ten pots whilst the highest density condition had one). Top-down model selection was performed using the Deviance Information Criterion (DIC) as a measure of model parsimony (Spiegelhalter et al., 2002).

For analysis of larval development time, the unit of replication was the individual larva. Larval development time was analysed using Bayesian Gamma-distributed GLMs with a log link function as follows:

$$T_i \sim \Gamma\left(\kappa_i, \frac{\kappa_i}{m_i}\right) \quad (3.8)$$

where  $T_i$  is the development time in days,  $\kappa_i$  is the shape parameter and  $m_i$  is the mean of the Gamma distribution such that

$$m_i = e^{(\eta_0 + X_i)} \quad (3.9)$$

where  $X_i$  can take the form

$$X_i = \begin{cases} \eta_1 D_i \\ \eta_1 D_i + \eta_2 F_i \\ \eta_1 D_i + \eta_2 F_i + \eta_3 D_i F_i \end{cases} \quad (3.10)$$

where  $\{\eta_0, \dots, \eta_3\} \sim N(0, 10^{-4})$ ,  $\kappa_i \sim U(0, 100)$  and top-down model selection was performed using the DIC.

Wing lengths were also analysed using Bayesian Gamma-distributed GLMs with a log link function as follows:

$$W_i \sim \Gamma\left(v_i, \frac{v_i}{n_i}\right) \quad (3.11)$$

where  $W_i$  is the wing length in mm,  $v_i$  is the shape parameter and  $n_i$  is the mean of the Gamma distribution such that

$$n_i = e^{(\delta_0 + Q_i)} \quad (3.12)$$

where  $\mathbf{Q}_i$  can take the form

$$\mathbf{Q}_i = \begin{cases} \delta_1 D_i \\ \delta_1 D_i + \delta_2 F_i \\ \delta_1 D_i + \delta_2 F_i + \delta_3 D_i F_i \end{cases} \quad (3.13)$$

where  $\{\delta_1, \dots, \delta_3\} \sim N(0, 10^{-4})$ ,  $v_i \sim U(0, 100)$  and top-down model selection was performed using the DIC. The Gamma distribution was favoured over the normal distribution for analysis of development time and wing length because (a) it does not predict negative values (the log link function also facilitates compliance with the assumptions of the Gamma distribution by prohibiting negative values) and (b) it accommodates data skew.

Models were run for  $5 \times 10^4$  iterations with a burn-in of  $5 \times 10^3$ . Four chains were run and posteriors were accepted only if the Gelman-Rubin diagnostic was  $< 1.02$  for all parameters, indicating that between-chain convergence had been achieved. Model fits for larval survival, larval development time and wing length – as well as 95% credible intervals (CIs) – were derived from posterior distributions of model parameters. Further details on the methodology for this is described Appendix B.2.



## **Results**

### **Larval survival**

Model selection favoured a model including food treatment and density as covariates for both the per pot and per capita survival data. Therefore

$$Y_i = \alpha_1 D_i + \alpha_2 F_i \quad (3.14)$$

$$Z_i = \gamma_1 D_i + \gamma_2 F_i \quad (3.15)$$

in Equations (3.4) and (3.5).

All parameter estimates are presented in Appendix B.3. Predicted and observed larval survival probabilities at all empirically measured food and density conditions are shown in Appendix B.4. Bayesian beta-binomial inverse-logit link GLM fits showed that increased larval density inhibited larval survival in the per pot feeding experiment. With per pot food at 16.50 mg, the model predicted a survival probability of 0.96 (95% CI: 0.94, 0.98) with density at 100 larvae per litre, which reduced to 0.07 (95% CI: 0.03, 0.12) at 1000 larvae per litre. In contrast, the per capita feeding experiment exhibited increased survival at higher densities across all feeding conditions. With per capita feeding at 0.30 mg per larvae, the model predicted a survival probability of 0.23 (95% CI: 0.19, 0.28) at 100 larvae per litre, which increased to 0.63 (95% CI: 0.53, 0.74) at 1000 larvae per litre. The inverse relationships between survival and larval density under the two different feeding regimes is further demonstrated using surface plots in Figure 3. 1, where larval survival was calculated according to Equation (3.4) and Equation (3.14) for unmeasured food and density conditions. In addition, parameter  $\alpha_1$  was positive ( $1.90 \times 10^{-3}$ , 95% CI:  $1.27 \times 10^{-3}$ ,  $2.59 \times 10^{-3}$ ) for the per capita feeding data and negative ( $-6.64 \times 10^{-3}$ , 95% CI:  $-8.07 \times 10^{-3}$ ,  $-5.52 \times 10^{-3}$ ) for the per pot feeding data. Estimates of

$\alpha_1$  also show that density had a stronger association with survival probability for the per pot data than for the per capita data; the absolute value of  $\alpha_1$  was larger for the per pot data than for the per capita data. Figure 3. 2 shows larval survival in each food condition for the per capita feeding experiment. Figure 3. 3 shows larval survival in each food condition for the per pot feeding experiment.

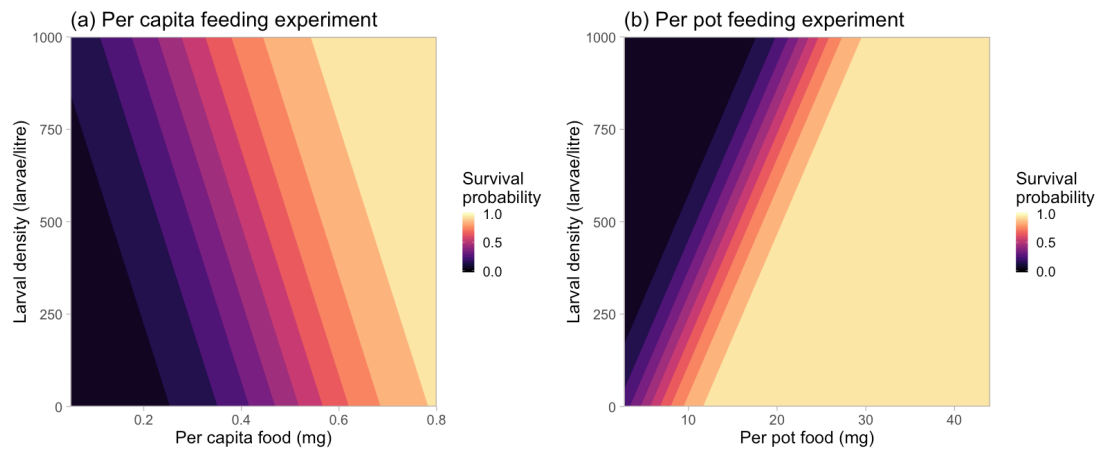


Figure 3. 1. Predicted survival probabilities for combinations of larval density and food availability under a (a) per capita feeding regime and a (b) per pot feeding regime. Models were used to predict survival probabilities for unmeasured combinations of larval density and food availability using Equation (3.4) and Equation (3.14). Colours represent the survival probability and contour lines delineate changes in the survival probability. The inverse association between density and survival probability under per capita and per pot feeding regimes is evident by comparison of subfigures (a) and (b).

## Larval development time

For the analysis of larval development time, model selection favoured a model including food treatment, density and an interaction term between food and density as covariates for both the per pot and per capita data. Therefore

$$X_i = \eta_1 D_i + \eta_2 F_i + \eta_3 D_i F_i \quad (3.16)$$

in Equation (3.9). Parameter estimates are shown in Appendix B.3 and predicted and observed development times in Appendix B.5.

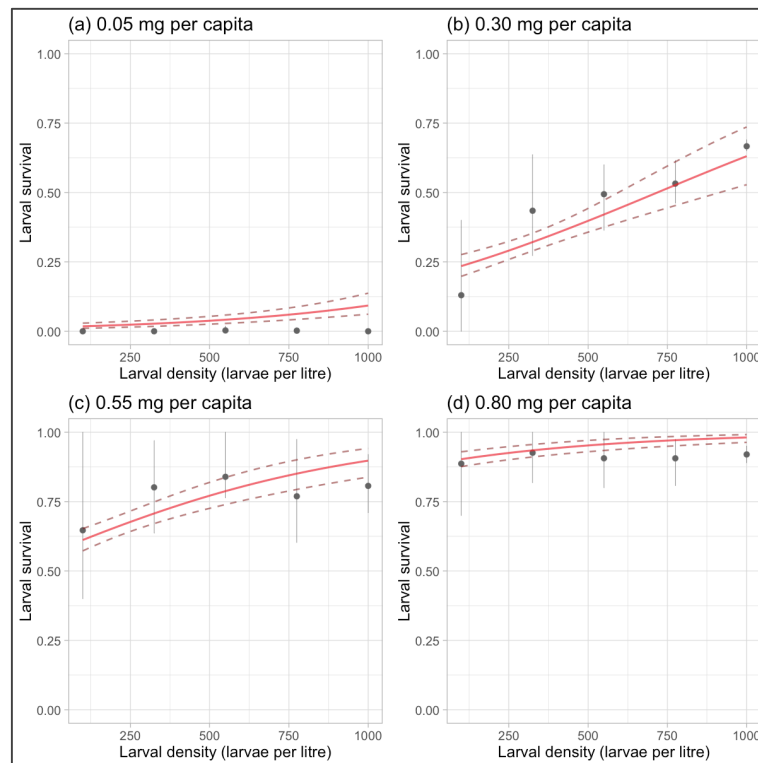


Figure 3. 2. Survival probability of *Ae. aegypti* in per capita feeding experiments with (a) 0.05, (b) 0.30, (c) 0.55 and (d) 0.80 mg of food per capita. Points display the mean survival probability for each density condition and error bars represent the range of per-pot survival proportions at each density condition. Each subplot displays beta-binomial inverse logit-link Bayesian GLM fits with 95% credible intervals.

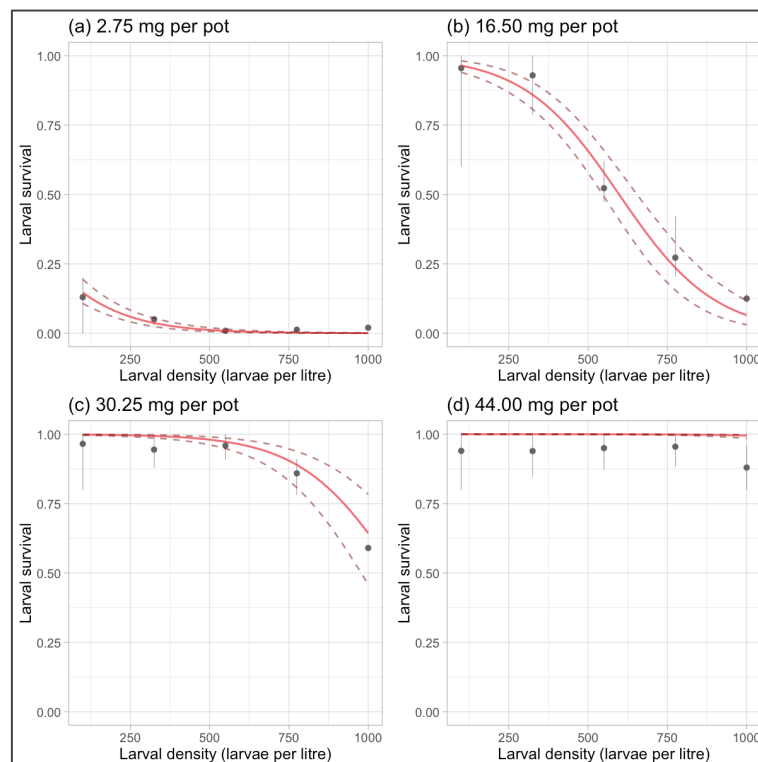


Figure 3. 3. Survival probability of *Ae. aegypti* in per-pot feeding experiments with (a) 2.75, (b) 16.50 (c) 30.25 and (d) 44.00 mg of liver powder per pot. Points display the mean survival probability for each density condition and error bars represent the range of per-pot survival proportions at each density condition. Each subplot displays beta-binomial inverse logit-link Bayesian GLM fits with 95% credible intervals.

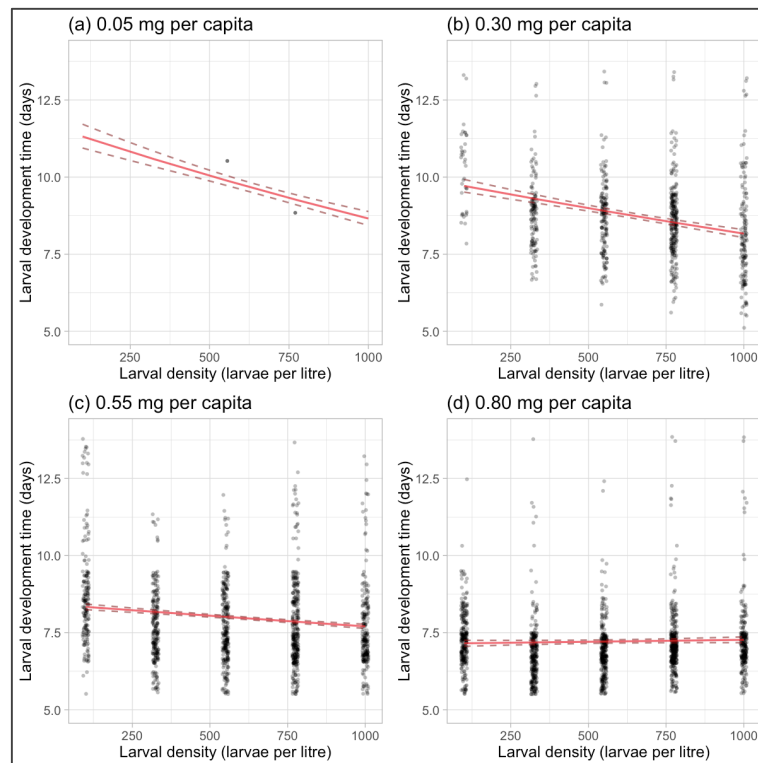


Figure 3. 4. Development time (days from hatch to pupation) of *Ae. aegypti* in per capita feeding experiments with (a) 0.05, (b) 0.30, (c) 0.55 and (d) 0.80 mg of food per capita. Points represent the development times of individual larvae that reach pupation. A jitter has been applied to data points to improve data visualisation. Each subplot displays a Gamma log-link Bayesian GLM with 95% credible intervals.

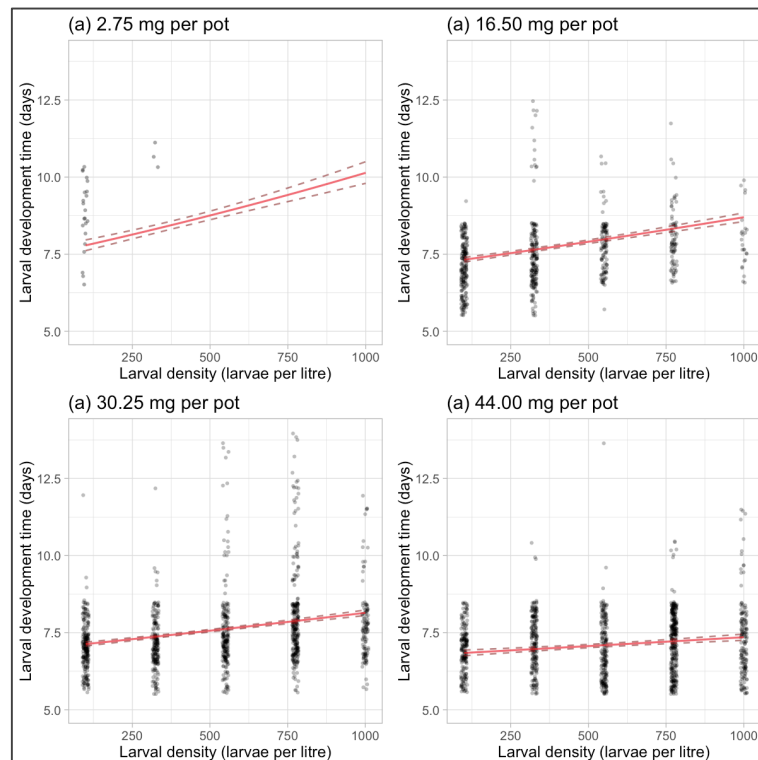


Figure 3. 5. Development time (days from hatch to pupation) of *Ae. aegypti* in per pot feeding experiments with (a) 2.75, (b) 16.50, (c) 30.25 and (d) 44.00 mg of food per pot. Points represent the development times of individual larvae that reach pupation. A jitter has been applied to data points to improve data visualisation. Each subplot displays a Gamma log-link Bayesian GLM with 95% credible intervals.

Figure 3. 4 and Figure 3. 5 display development times for per pot and per capita experiments respectively with Gamma-distributed log-link Bayesian GLM fits and 95% CIs. Points represent the development times of individual larvae that reach pupation. Increased larval density incurred longer development times in the per pot feeding experiment, although the effect was small. At 16.50 mg/pot, mean *Ae. aegypti* larval development time was predicted to increase from 7.32 (95% CI: 7.24, 7.40) days at 100 larvae/litre to 8.70 (95% CI: 8.56, 8.84) days at 1000 larvae/litre. In contrast, increased larval density led to shorter development times in the per capita feeding experiment. At 0.30 mg/larva development time was predicted to decrease from 9.71 (95% CI: 9.51, 9.92) days to 8.17 (95% CI: 8.04, 8.30) days. The only exception was 0.80 mg/larva where the predicted development time increased by 0.11 days between 100 and 1000 larvae/litre. Contour plots further demonstrating the inverse relationships between development time and larval density between the two experimental designs can be observed in Appendix B.5. Parameter estimates also demonstrate the inverse association of density with development time for per capita and per pot feeding:  $\eta_1$  was negative for the per capita feeding data ( $0.32 \times 10^{-3}$ , 95% CI:  $-0.38 \times 10^{-3}$ ,  $-0.26 \times 10^{-3}$ ) and positive for the per pot feeding data ( $0.30 \times 10^{-3}$ , 95% CI:  $0.24 \times 10^{-3}$ ,  $0.35 \times 10^{-3}$ ) as shown in Appendix B.3.

### **Emerged adult wing length**

Wing length data were not analysed for the lowest feeding conditions in either experiment due to low numbers of surviving larvae yielding insufficient adult sample sizes. Data for the remaining three food conditions with Gamma-distributed log-link GLM fits and 95% CIs can be observed in Figure 3. 6 and Figure 3. 7 for the per capita and per pot feeding experiments, respectively. Model selection using the DIC

favoured a model including food treatment and density as covariates for both the per capita and per pot data. Therefore

$$Q_i = \delta_1 D_i + \delta_2 F_i \quad (3.17)$$

in Equation (3.12). Parameter estimates are shown in Appendix B.3 and predicted and observed wing lengths in Appendix B.6.

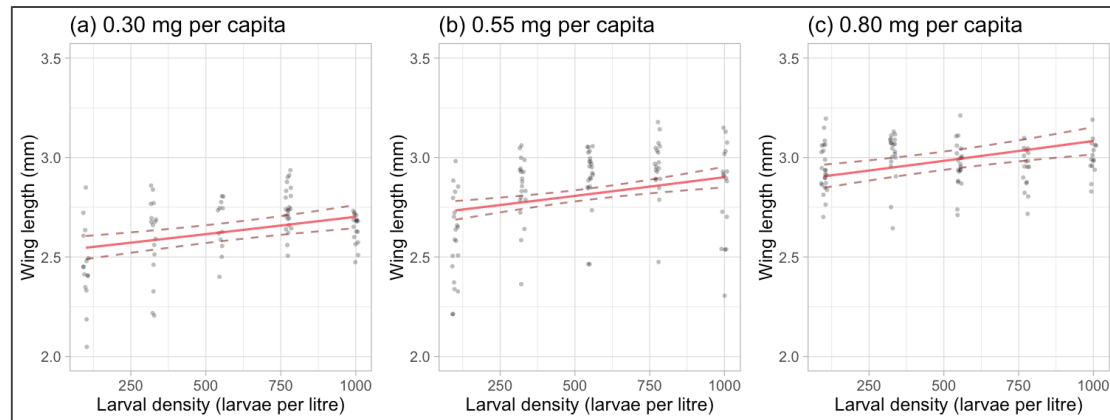


Figure 3. 6. Emerged adult *Ae. aegypti* wing length for the per capita feeding experiment at (a) 0.30, (b) 0.55 and (c) 0.80 mg of food per capita. Points represent the wing length of individual emerged adults. Only one wing was measured per mosquito. Subplots display Bayesian Gamma log-link GLM fits with 95% credible intervals. Data for the lowest food condition (0.05 mg/larva) were not collected due to the low survival rate at this treatment condition yielding insufficient sample sizes.

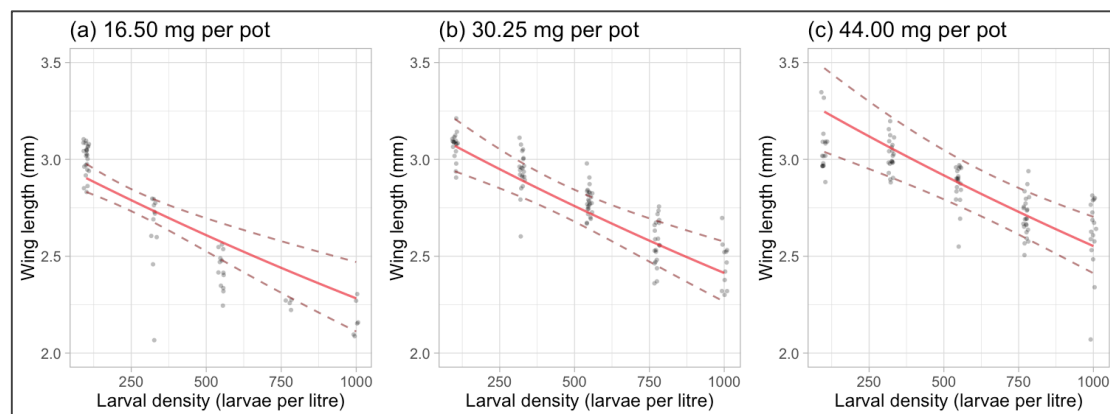


Figure 3. 7. Emerged adult *Ae. aegypti* wing length for the per pot feeding experiment at (a) 16.50, (b) 30.25 and (c) 44.00 mg of food per pot. Points represent the wing length of individual emerged adults. Only one wing was measured per mosquito. Subplots display Bayesian Gamma log-link GLM fits with 95% credible intervals. Data for the lowest food condition (2.75 mg/pot) were not collected due to the low survival rate at this treatment condition yielding insufficient sample sizes.

A negative association between larval density and adult wing length was observed in the per pot feeding experiment. A positive association was observed in the per capita feeding experiment. The association between density and adult wing length was stronger under per pot feeding: the absolute value of  $\delta_1$  was larger for the per pot data ( $-2.67 \times 10^{-4}$ , 95% CI:  $-3.67 \times 10^{-4}$ ,  $-1.67 \times 10^{-4}$ ) than the per capita data ( $5.66 \times 10^{-5}$ , 95% CI:  $2.50 \times 10^{-5}$ ,  $8.87 \times 10^{-5}$ ). This is further illustrated in Appendix B.6 using contour plots.

### **Consideration of per pot feeding data on a per capita scale**

Feeding data for the per pot feeding experiment were converted to a per capita scale to investigate further whether the observed negative association between density and larval survival in the per pot data was an artefact of limited per capita food availability at high densities. The per pot food quantity was divided by the number of larvae per pot to obtain per capita food availability. Survival probability in the transformed data was analysed using a beta-binomial inverse-logit link Bayesian GLM (as already described – see Methods above). Parameter estimates and CIs are displayed in Appendix B.3. Model predicted survival probabilities for combinations of per capita food availability and density are shown in Figure 3. 8(a). When transformed to a per capita scale, results from analysis of per pot survival data resembled those from the per capita feeding experiment (see Figure 3. 1). Per capita model predictions and transformed per pot model results (on per capita scale) were compared as shown in Figure 3. 8(b). The maximum difference in predicted survival probability was 0.17 while the mean difference was 0.06. Predictions from the model fitted to transformed per pot data were consistently higher than those from the true per capita data. The largest difference in predicted survival probability was observed for

low larval densities between  $\sim 0.4$ - $0.8$  mg/larva. This occurred because it was the region of parameter space with fewest sampling points when the per pot feeding experiment data were transformed to a per capita scale. Further explanation is given in Appendix B.7.

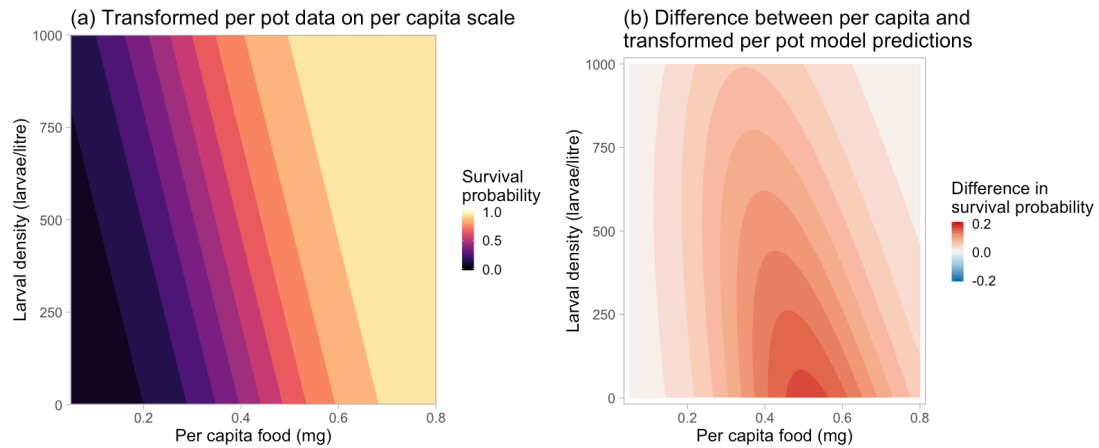


Figure 3. 8. Analysis of per pot data transformed to a per capita scale by dividing the per pot food quantity by the number of larvae in the pot. Subfigure (a) shows the model predicted survival probabilities for a Bayesian beta-binomial inverse-logit link GLM fitted to per pot data transformed onto a per capita scale. Subfigure (b) shows the difference in predicted survival probability between models fitted to (i) per pot data transformed to a per capita scale and (ii) true per capita experimental data. If the difference in survival probability is positive, predictions from model (i) are higher. If the difference in survival probability is lower, predictions from model (ii) are higher.



## **Discussion**

The idea that factors other than density are critical in the regulation of animal populations has roots in the work of Andrewartha and Birch (Andrewartha and Birch, 1954) among others (Chitty, 1960; Watson, 1989). In insects, Andrewartha and Birch (1954) observed that populations grew and declined in environmentally favourable and unfavourable times, irrespective of density (Andrewartha and Birch, 1954). Here, we have demonstrated the crucial importance of nutritional availability for density dependence in *Ae. aegypti*. Although we have focussed on nutrition, various other mechanisms of density dependence have been suggested across species including site-dependence (Nevoux et al., 2011; Rodenhouse et al., 2003), interference (Fernández-Bellon et al., 2016) and mutualism (Jha et al., 2012), demonstrating that density dependence is a complex bundle of mechanisms rather than a functional relationship between population density and growth. Therefore, mechanistic empirical studies are crucial to understand population regulation irrespective of the mechanism or taxa. Such studies are currently regrettably sparse in mosquito ecology.

The idea that animal populations may be limited in a bottom-up manner by environmental heterogeneity rather than top-down from their density is not a new one. White (2001) proposed that “if populations are not regulated ‘from above’ but limited ‘from below’, there is no need to invoke density dependence at all” (White, 2001). Nutritional availability has been observed to affect animal populations in terms of their individual development and population-level persistence (Crates et al., 2016; Hooper et al., 2003) and has also been suggested as a mechanism of density dependence in a handful of species such as Arctic charr (Amundsen et al., 2007) and guillemots (Ashbrook et al., 2010) among others (Ashbrook et al., 2010; Nevoux et

al., 2011) and has been observed to modify the outcome of density dependence in mosquitoes larvae (Juliano, 1998; Legros et al., 2009; Washburn et al., 1991). However, mechanistic empirical studies have not yet clarified the role of nutritional availability for density dependence in mosquito larvae. Mechanistic studies in a small number of species, such as zebrafish *D. rerio*, have shown that controlling for per capita food availability negates any observed effect of density. This suggests that density dependence is an artefact of food availability for this species (Hazlerigg et al., 2012). We used the mosquito *Ae. aegypti* to test the hypothesis that density dependence can operate via decreased per capita food availability due to increased numbers of competitors at high population densities in mosquito larvae. Our study resulted in two primary findings. First, our results supported the hypothesis that density dependence is a product of per capita nutritional availability for *Ae. aegypti*. Second, we observed increased survival, development rate and wing length at high densities when larvae were fed per capita. This second, unprecedented finding suggests that there were other, undocumented mechanisms occurring which benefitted mosquito larvae at high densities when per capita nutritional availability was held constant. Below, we discuss each of these findings and present hypotheses for promoted larval development at high densities in the per capita experiments.

In mosquitoes, the nomenclature of density dependence has been a subject of focus due to its importance in mathematical models of mosquito population dynamics and mosquito-borne disease transmission (Dye, 1984; Legros et al., 2009; Powell et al., 2018; Southwood et al., 1972). A handful of studies have suggested mechanisms by which density may affect larval development, such as competition for resources (Couret et al., 2014; Farjana et al., 2012; Jannat and Roitberg, 2013), habitat turbidity (Chirebyu and Chimbari, 2015) and cannibalism (Koenraadt et al., 2004; Porretta et

al., 2016; Reisen and Emory, 1976) among others. However, very few studies have sought to isolate any of these mechanisms by critical empirical investigation.

With regard to nutritional availability, there is overwhelming evidence that per capita food availability significantly affects larval development in multiple mosquito species (Araújo et al., 2012; Arravillaha and Barrera, 2004; Farjana et al., 2012; Merritt et al., 1992; Padmanabha et al., 2011). Westby and Juliano (2017) highlight the importance of per capita nutrient availability for mosquito larvae by demonstrating that prior exploitation of aquatic larval habitats by non-overlapping cohorts increases resource competition (Westby and Juliano, 2017). Per capita nutritional availability has also been observed to affect malaria transmission capacity (Moller-Jacobs et al., 2014; Shapiro et al., 2016). Despite this, studies of density dependence in mosquitoes have adopted diverse and inconsistent feeding regimes including oak leaves (*Quercus virginiana*) (Reiskind and Lounibos, 2009) and fish food (Agnew et al., 2002; Banerjee et al., 2017; Gilles et al., 2011; Schneider et al., 2000) at varying quantities, with some studies adjusting food quantities for the number of individuals (Jannat and Roitberg, 2013; Schneider et al., 2000) and others feeding larvae fixed amounts unadjusted for the number of individuals (Agnew et al., 2002; Couret et al., 2014; Gilles et al., 2011; Reiskind and Lounibos, 2009) or feeding *ad libitum* (Banerjee et al., 2017; Muriu et al., 2013). Some existing studies have even sought to eliminate the effects of nutritional availability. For example, Jannat and Roitberg (2013) and Schneider (2000) fed larvae on a per capita basis, thereby implicitly assuming that density either acts directly upon development, for example by chemical interference, or acts indirectly via a mechanism other than per capita nutritional availability (Jannat and Roitberg, 2013; Schneider et al., 2000). In response to the confusion, Gimmig (2002) proposes that “under [a per capita feeding regime], density-dependent effects

would not be expected unless [mosquito] larvae somehow interfere with each other at high densities” (Gimnig et al., 2002). Both White (2004) and Gimnig (2002) acknowledge that density *per se* may not have a substantial effect upon populations but does so by engaging in mechanisms such as resource limitation (Gimnig et al., 2002; White, 2004).

We observed that the negative associations between larval density and (a) larval survival, (b) larval development rate and (c) emerged adult wing length were eliminated - indeed, the associations changed from negative to positive - when nutritional availability was held constant per capita. This clearly shows that the larval rearing conditions adopted in studies of density dependence in mosquitoes are highly impactful; measures of population regulation are a proportional response to environmental variability. This conclusion need not be limited to the study of mosquitoes.

Most crucially for the study of mosquitoes, our results demonstrate that the effect of larval density assumed in many studies where per capita nutritional availability is not held constant occurs due to increased resource competition at high densities. When per pot feeding data were converted to a per capita scale, the observed relationship between larval density and survival resembled our observations from the true per capita data; a positive association between density and survival was confirmed (see Figure 3. 8).

The negative effect of high density on life-history parameters in the per pot experiment is in line with the current literature, which has emphasised detrimental effects of density upon larval development. However, the positive associations between larval density and (a) larval survival, (b) larval development rate and (b) adult wing length under per capita feeding were unprecedented and imply other

mechanisms that interplay with larval density. The results were also contrary to existing studies adopting per capita feeding (Alcalay et al., 2018a). We briefly highlight several hypotheses for promoted mosquito development at high densities in the per capita experiment. First, greater numbers of conspecifics may increase the propensity for cannibalism of dead larvae, which may act as a food source, resulting in improved development (Koenraadt et al., 2004; Porretta et al., 2016; Reisen and Emory, 1976). Cannibalism in *Ae. aegypti* was first recorded by MacGregor (1915) and has since been observed in *Aedes*, *Culex* and *Anopheles* species (Edgerly et al., 1999; Koenraadt and Takken, 2003; MacGregor, 1915; Muturi et al., 2010). Larval density and the duration of contact between individuals have both been observed to affect cannibalistic behaviour in mosquito larvae (Koenraadt and Takken, 2003; Reisen and Emory, 1976). Holding per-capita nutritional availability constant may allow the effects of cannibalism at high densities to become more evident.

Second, stressed conditions early in the larval lifespan may encourage adaptive responses that promote development. In some insect species hunger stress has been observed to induce physiological countermeasures that improve the insect's ability to endure nutritional shortages (Zhang et al., 2019). In honeybees (*Apis mellifera*), for example, periods of starvation resulted in physiological changes such as improved glycogen storage among others, which facilitated survival in nutrient-poor environments (Y. Wang et al., 2016). Pea aphids produce more offspring following exposure to high densities of conspecifics (Grantham et al., 2016). Adaptive response to stressed conditions have been observed in other species such as the least killifish (*Heterandria formosa*), where mothers respond to environmental challenges by hormonally or nutritionally enhancing offspring fitness for the environment (Leips et al., 2009). While behavioural plasticity to predation stress has been observed in *Aedes*

mosquitoes (van Uitregt et al., 2011), it is not immediately clear by what mechanism mosquito larvae would have adapted to stress in our study, as hunger stress should be constant across all density conditions in the per capita experiment. Further investigation is needed to consider adaptive responses to stress in *Ae. aegypti*.

Third, there may be chemical, social or behavioural effects of higher densities that result in physiological benefits. Larval aggregation commonly occurs in many insect species (Taylor, 1961) and can confer behavioural and physiological benefits which promote larval development, provided that the benefits of aggregation are not outweighed by the costs of competition (Cornell et al., 1987; Durisko and Dukas, 2013). For example, Morimoto et al. (2018) observed complex interactions between larval density, foraging behaviour and development in polyphagous fruit flies (*Bactrocera tryoni*), observing that larval aggregation resulted in consistently higher body mass, but that very high larval densities resulted in increased dispersion of larvae (Morimoto et al., 2018). It is possible that higher densities of *Ae. aegypti* larvae in the per-capita experiment induced chemical, behavioural or social benefits which promote larval development and survival. Further studies are needed to examine alternative mechanisms that may contribute to elevated larval fitness at high densities under constant per capita nutritional conditions.

Faster development times in mosquito larvae have consistently been associated with larger adult body sizes (Couret et al., 2014; Ross et al., 2014). Further, adult body size is an indicator of adult mosquito fitness, for example in terms of fecundity (Armbruster and Hutchison, 2002) or longevity (Barreux et al., 2018), although the latter relationship can be environmentally dependent. We observed notable effects of per capita nutritional availability on adult wing length, indicating that nutritional conditions experienced by *Ae. aegypti* larvae have carryover effects into adulthood;

similar carryover effects have been documented for other environmental factors and mosquito species (Dickson et al., 2017; Evans et al., 2018; Ezeakacha and Yee, 2019). Our study did not separate emerged adult mosquitoes by date of pupation; therefore, it was not possible to determine whether the fastest pupating adults in each pot were larger compared to their conspecifics. This would be interesting to consider because it is not yet clear whether the fastest pupating mosquitoes in a cohort have an innate fitness advantage or whether they were simply fortunate enough to encounter sufficient nutritional resources before other larvae. Further investigation could explore the relationships between life history traits measured in this study.

In Chapter 2, a numeric constant,  $\lambda$ , controlled the strength of density dependence in the context of precipitation as detailed in Equation (3.1). This parameter did not vary spatiotemporally. Other mathematical models of mosquito populations have used similar methods to account for density dependence (Beck-Johnson et al., 2013; Erickson et al., 2010). Ewing et al. (2017) and Smith et al. (2013) incorporate numeric constants ( $\delta_\pi$  and  $\psi$  respectively) that cause larval mortality to increase as a function of the current larval density (Ewing et al., 2016; Smith et al., 2013). Neither of these parameters depends upon environmental variables. The results of this study show clearly that the strength of density dependence – i.e. the value of  $\lambda$ ,  $\delta_\pi$  or  $\psi$  – depends on features of the environment, specifically nutritional availability. In addition, there is little consistency in the literature on the mechanisms denoted by density dependence parameters. Ewing et al. (2017) cite predation as the “main source of population regulation” (Ewing et al., 2016). Beck-Johnson et al. (2013) do not specify a mechanism but state that additional mortality arises “because of the effects of density dependence” (Beck-Johnson et al., 2013). Erickson et al. (2010) impose a carrying capacity to account for “inter- and intra-specific competition” (Erickson et

al., 2010). In short, mathematical ecologists are not in consensus on the role played by density dependence terms in their models. Future mathematical models of mosquito population dynamics should consider that numeric constants controlling the strength of density dependence might be context dependent and environmentally driven functions of density dependence may be more appropriate.

We have demonstrated that density dependence in *Ae. aegypti* is an artefact of variation in per capita nutritional availability, highlighting the importance of environmental variability for density dependence. Our results imply that population regulation is a proportional response to environmental variability. Nutritional availability as a mechanism of density dependence has been demonstrated in zebrafish *D. rerio* (Hazlerigg et al., 2012) and algae *C. reinhardtii* (Borlestean et al., 2015) as well as for *Ae. aegypti* in the context of the current study. It is possible that nutritional availability is an important mechanism of density dependence for other species as well. A number of other mechanisms of density dependence such as site dependence, mutualism and interference have been suggested for a range of species (Fernández-Bellon et al., 2016; Jha et al., 2012; Nevoux et al., 2011; Rodenhouse et al., 2003). In mosquitoes, seasonality and sensitivity to other environmental features has been well documented (Araújo et al., 2012; Arravillaha and Barrera, 2004; Farjana et al., 2012; Merritt et al., 1992; Padmanabha et al., 2011; Tsai et al., 2018). Therefore, nutritional availability is unlikely to be the only mechanism of density dependence operating in mosquitoes. Collectively, uncertainty on the mechanisms of density dependence in mosquitoes inhibits our ability to predict population responses to environmental change (Krebs, 1995). Empirical studies should seek to characterise density dependence in mosquitoes by employing further mechanistic study designs across a variety of environmental conditions.



## **Data availability**

Data are available on the Open Science Framework (OSF) with identifier <https://osf.io/bjyxq/>.



# Chapter 4

## Environmental heterogeneity influences *Aedes polynesiensis* mosquito density in French Polynesia

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## **Abstract**

**Background:** The mosquito *Aedes polynesiensis* is found in Pacific islands and territories where it transmits arboviruses and parasites. As land-use changes rapidly, it is paramount to understand the effects of environmental heterogeneity on mosquitoes. However, few models of mosquito population dynamics have considered environmental heterogeneity or dispersal behaviours.

**Methods:** We present an integrative methodology to address this. Our methodology had two main stages. (1) Field and remote sensing data were used to estimate spatial heterogeneity in environmental suitability for mosquitoes. (2) We developed a model of mosquito population dynamics to predict mosquito distributions over a heterogeneous landscape and compare dispersal behaviours. We used motu Tautau, French Polynesia, as a case study to demonstrate the utility of this methodological approach and validate models using field data. *Ae. polynesiensis* rely upon land crab *Cardisoma carnifex* burrows for oviposition in French Polynesia; environmental suitability was therefore defined as *C. carnifex* burrow density.

**Results & Conclusions:** Our methodology accurately detected micro-regions with large *Ae. polynesiensis* populations, facilitated by high *C. carnifex* burrow density. We observed that preferential dispersal towards oviposition sites promoted larger population sizes than non-preferential dispersal, but did not offer greater resilience to environmental change. Decreased environmental suitability for *Ae. polynesiensis* resulted in spatially non-linear effects upon the mosquito distribution. Mosquito control strategies must carefully balance spatial effects with net effects.



## **Introduction**

### **The role of environmental heterogeneity**

Spatial heterogeneity in mosquito populations and mosquito-borne infections arises due to, among other reasons, variation in habitat quality, habitat quantity, host density, temperature or rainfall (Martens & Hall, 2000; Mbogo *et al.*, 2003; Sattler *et al.*, 2005; Yohannes *et al.*, 2005; Hay *et al.*, 2009; Chaves *et al.*, 2011). Mosquito persistence is linked to human land-use changes such as agriculture, urbanisation and deforestation (Morse, 1995; Gubler, 1998; Patz *et al.*, 2000; Foley *et al.*, 2007; Vittor *et al.*, 2009). Models of mosquito behaviour in response to environmental heterogeneity are vital to inform mosquito control strategies as rapid land-use change occurs globally (Lambin & Meyfroidt, 2011). However, the majority of models describing mosquitoes and mosquito-borne disease assume spatially homogeneous transmission and rarely consider mosquito dispersal, host dispersal or environmental heterogeneity (Grenfell & Dobson, 1995; Torres-Sorando & Rodríguez, 1997; Smith *et al.*, 2004; Acevedo *et al.*, 2015). Herein, we address this problem by integrating field sampling, remote sensing and mathematical modelling to consider the effects of environmental heterogeneity and mosquito dispersal on spatial mosquito distributions.

It is important to distinguish two ways in which mosquito population sizes can be limited. First, mosquito population sizes are limited by the capacity of individual aquatic habitats to support larval mosquito populations. As highlighted in Chapter 3, this can occur through nutritional availability. Second, mosquito population sizes are limited by the number of individual aquatic habitats within a landscape. Greater

propensity of a landscape to retain water increases the environmental carrying capacity for mosquito larvae by providing more oviposition sites. The quantity of oviposition sites has been shown to influence adult mosquito population sizes (Yohannes *et al.*, 2005; Gu *et al.*, 2006; de Abreu *et al.*, 2015). In particular, urban areas have consistently been shown to have large numbers of aquatic habitats for mosquito larvae due to the availability of artificial containers (Derraik, 2005; Thongsripong *et al.*, 2013; Li *et al.*, 2014; Mattah *et al.*, 2017).

Several models of mosquito population dynamics have incorporated precipitation and its capacity to influence the environmental carrying capacity, including the model employed in Chapter 2 (White *et al.*, 2011; Tran *et al.*, 2013; Jia *et al.*, 2016; Wang *et al.*, 2016; North & Godfray, 2018). However, spatial variation in the number of aquatic habitats created or sustained by precipitation has not been comprehensively examined in mathematical models of mosquito populations. Jia *et al.* (2016) note that “..the actual effect of precipitation should be carefully weighted through rigorous field observations before any attempt to quantify [the strength of its effect]” (Jia *et al.*, 2016).

Herein we present a methodological approach for quantifying larval aquatic habitats in a heterogeneous landscape. We further apply a stage-structured population dynamics model and consider the effects of environmental heterogeneity and environmental change upon mosquito distributions. We offer a novel improvement to existing studies by integrating field data with mathematical modelling to consider spatial variation in the environmental carrying capacity for mosquito populations.



## **The *Aedes polynesiensis* mosquito**

Our methodology was applied to the mosquito species *Aedes polynesiensis*. This species of the *Aedes* genus is found only on a handful of South Pacific islands (Belkin, 1962). Like *Ae. aegypti*, *Ae. polynesiensis* is a competent vector for arboviruses such as chikungunya, dengue and Zika (Roth *et al.*, 2014; Richard *et al.*, 2016; Beck *et al.*, 2019) and is the primary vector of *Wucheria bancrofti* (Spururida: Onchocercidae), the causative agent of lymphatic filariasis (Russell *et al.*, 2005; Hapairai *et al.*, 2014). *Ae. polynesiensis* primarily use land crab, *Cardisoma carnifex*, burrows for oviposition in French Polynesian atolls (Bonnet & Chapman, 1958; Lardeux *et al.*, 1992, 2002b). *C. carnifex* dig burrows to the water table where mosquito larvae are protected in a freshwater chamber. Burrows remain active for ~25 days which is sufficient for larval emergence (Micheli *et al.*, 1991). Reliance upon *C. carnifex* burrows as a primary larval habitat renders *Ae. polynesiensis* an excellent study species to consider the importance of aquatic habitat availability as burrows are easily quantifiable. In addition, 141 species of mosquito are dependent on crab burrows for oviposition globally, making our findings widely applicable (Bruce-Chwatt & Fitz-John, 1951; Bright & Hogue, 1972; Day, 2016).

## **Mosquito dispersal**

In addition to determining the environmental carrying capacity, the quantity and availability of aquatic larval habitats influences mosquito dispersal behaviour (Le Menach *et al.*, 2005). *Ae. aegypti* are known to disperse in search of suitable oviposition sites and hosts (Service, 2004; de Abreu *et al.*, 2015). A small number of studies have examined *Ae. polynesiensis* dispersal (Mercer *et al.*, 2012). Hapairai et

al. (2013) used mark release recapture (MRR) experiments to estimate dispersal distances of *Ae. polynesiensis* in French Polynesia (Hapairai *et al.*, 2013a). They demonstrated consistent male dispersal patterns and distances between release locations but found that female dispersal behaviour varied by release location. These results suggest that either (a) the female dispersal response to environmental heterogeneity is stronger than for males or (b) males respond to different environmental cues that are more homogeneously distributed throughout the landscape. The importance of mosquito dispersal behaviour for population dynamics has received limited attention in entomological literature (Lutambi *et al.*, 2013). Lutambi *et al.* (2013) modelled mosquito dispersal in hypothetical heterogeneous environments and found the spatial distribution of resources to be highly influential upon adult mosquito dynamics (Lutambi *et al.*, 2013). A small number of other mosquito modelling studies have incorporated migration or dispersal effects (Yakob & Yan, 2010; Dufourd & Dumont, 2013; Manyombe *et al.*, 2017; North & Godfray, 2018), most of which use a meta-population approach. However, few of these incorporate environmental heterogeneity between patches and fewer still use field data to do so. In light of the above considerations, we constructed a model capable of capturing mosquito dispersal behaviours over a heterogeneous and dynamic landscape. Our methodology is a unique improvement on existing models as it incorporates field data to characterise environmental suitability.

## Outline

We used motu Tautau, French Polynesia, as a study site, where *C. carnifex* burrows are the primary oviposition site for *Ae. polynesiensis* mosquitoes. Our methodological approach had two major objectives:

### (1) Estimation of spatial heterogeneity in *C. carnifex* burrow density

Field sampling was conducted to characterise the distribution of *C. carnifex* burrows on motu Tautau. Field data were used to train and validate machine-learning algorithms. Subsequently, machine-learning algorithms were applied to remote sensing data to estimate the spatial distribution of *C. carnifex* burrows used by *Ae. polynesiensis* for oviposition.

### (2) Modelling *Ae. polynesiensis* in a heterogeneous environment

A mathematical model of mosquito population dynamics was applied to the estimated spatial distribution of *C. carnifex* burrows to consider the effects of spatial heterogeneity upon mosquito density. Lutambi et al.'s (2013) model of mosquito dispersal was adapted for *Ae. polynesiensis* and two dispersal behaviours were compared (Lutambi *et al.*, 2013). The effects of different patterns of environmental change upon mosquito populations were considered. The model was validated by comparison to trap data.

## **Methods**

### **Study site**

We used motu Tautau, Taha'a, French Polynesia, as a case study. 'Motus' are small, sand islands on the outer coral reef of atolls or islands in the process of becoming atolls. Motu Tautau's location on Taha'a island's outer reef is shown in Figure 4. 1(a) and Figure 4. 1(b). In the absence of land mammals, competitors or predators on motu Tautau, *C. carnifex* are exceptionally abundant and support large *Ae. polynesiensis* populations (Alexander, 1979; Fratini *et al.*, 2011). Modelling mosquito populations on motu Tautau is of particular interest as it is the target of a *Wolbachia* mosquito control program conducted by Institut Louis Malardé (<https://www.ilm.pf>) (O'Connor *et al.*, 2012), although these control methods were not yet fully implemented at the time of field sampling.

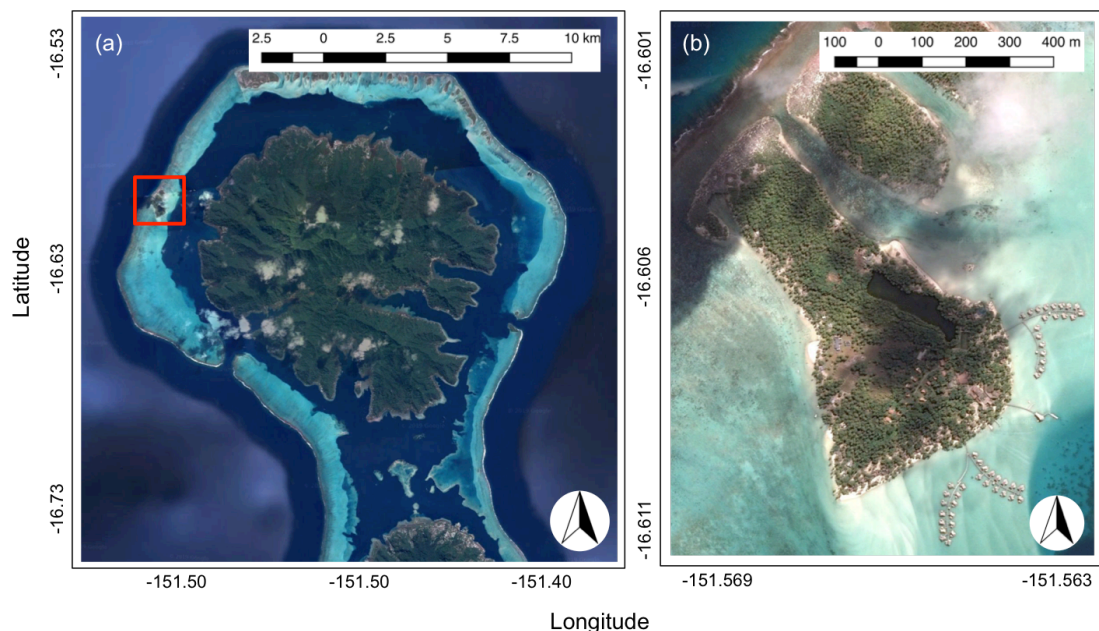


Figure 4. 1. Maps displaying (a) the location of motu Tautau on Taha'a's outer coral reef and (b) motu Tautau, where luxury hotel development is clearly visible on the motu's South end. In the South and Southwest of the motu there are staff living facilities and a small number of independent residents. The north section of the motu is mostly forested and free from substantial human development. Images are taken from Google Earth V 7.3.2. Taha'a, French Polynesia. 16°37'00"S 151°30'00"W. Image © 2019 DigitalGlobe. [17 April 2019]

## **Estimation of spatial heterogeneity in *C. carnifex* burrow density**

### ***Mosquito trapping data***

Taha'a has a warm tropical climate of ~22-31°C and experiences heavy rainfall in the wet season between November and March. Adult mosquito trap data from BG-Sentinal (BGS) traps using BG-Lures (Biogents AG, Regensburg, Germany) (Brelsfoard & Dobson, 2012; O'Connor *et al.*, 2012; Hapairai *et al.*, 2013b) were available weekly between 20-Aug-2018 and 15-Oct-2018 at 12 locations on motu Tautatu. Data were collected by Institut Louis Malardé in preparation for a *Wolbachia* mosquito control program. Within their protocol, traps were hung from tree branches ~20-50 cm from the ground. Engine grease was applied to the rope to prevent ant predation. Traps were run for the same 24-hour cycle each week. Collected mosquitoes were frozen and counted by sex and species.

### ***Crab burrow extraction***

Use of *C. carnifex* burrows by *Ae. polynesiensis* for oviposition was confirmed by burrow extraction. Burrows were sampled within a 30 m radius of four traps. 15 burrows were successfully sampled at each location. Not every extraction was successful due to the labyrinthine complexity of many burrows and the compromised structural integrity of the burrows in soft sand. The presence of other possible oviposition sites at each location was recorded. Examples of *C. carnifex* burrows and additional oviposition sites are shown in Figure 4. 2.

Water was extracted using 3 m of hosing and a hand pump with two check valves. The hose was inserted into the burrow and water was pumped into 10 L buckets. Water volume was measured using a 1 L measuring cylinder. Samples were left for 30 minutes to allow suspended sediment to settle. Water was dispensed gradually in small quantities into a 20×30 cm white plastic box illuminated with a flashlight and larvae were counted. The presence of copepods or other aquatic organisms was recorded and differences in copepod presence between sampling locations was assessed using  $\chi^2$  testing. Copepods predate heavily on mosquito larvae and have been suggested as a control strategy (Schaper, 1999; Awasthi *et al.*, 2015; Benelli *et al.*, 2016; Udayanga *et al.*, 2019). The diameter of each burrow on its largest axis was recorded and one-way ANOVA was used to test for variation between locations. Linear regression with likelihood-ratio test (LRT) model selection was used to determine associations between burrow volume and (a) burrow diameter and (b) the number of larvae extracted.

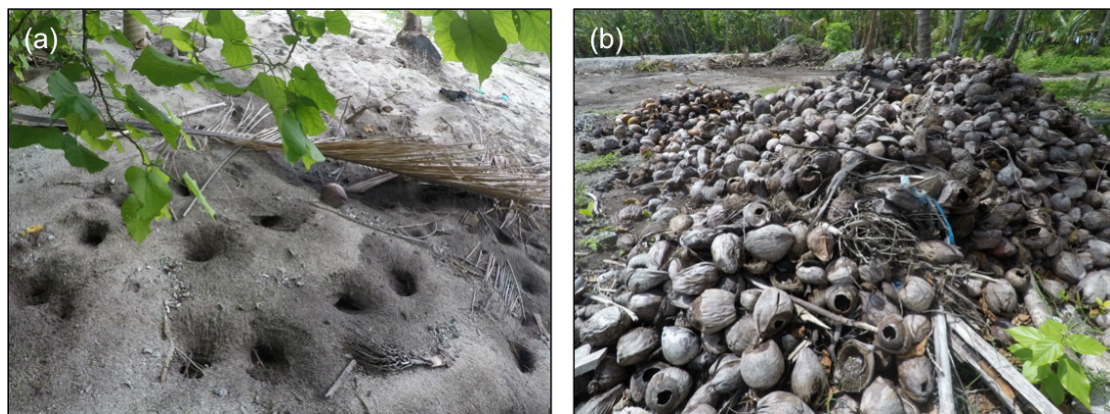


Figure 4. 2. Examples of (a) *C. carnifex* burrows on motu Tautau and (b) other potential oviposition sites. Used coconut husks are discarded in large quantities areas of construction or waste removal on motu Tautau. Collected water in these husks may provide suitable larval habitats for *Ae. polynesiensis*.

### ***Cartography***

Motu Tautau covers  $\sim 0.25 \text{ km}^2$ . A grid of sampling points at distances of  $\sim 100 \text{ m}$  (116 total sampling points) was defined encompassing the whole island. At each point, the number of burrows within a  $10 \text{ m}$  radius was recorded and converted to burrow density (burrows per  $100 \text{ m}^2$ ). The diameters of 20 burrows selected at random within a  $10 \text{ m}$  radius of the sampling point were recorded. Land cover at each point was classified as forest, exposed rock, beach, residential/hotel, freshwater lake or industrial/construction.

### ***Remote sensing***

11-band remote sensing data were downloaded from NASA's Landsat 8 from 16<sup>th</sup> July 2018 (the closest available date to field sampling (November 2018) with  $< 20\%$  cloud cover). Data were pre-processed using QGIS version 2.18 and the SCP plugin (QGIS Development Team, 2019). Dark Object Subtraction (DOS1) atmospheric correction was applied to obtain surface reflectance (Chavez, 1996). Pre-processed data were cropped to the study area ( $-151.574$  to  $-151.556$  longitude and  $-16.614$  to  $-16.597$  latitude).

For land cover classification, three land cover classes – easily identifiable from maps – were added to those from cartographical data to account for ocean water types: deep ocean, lagoon and exposed coral reef. A spectral signature using the 11-band Landsat 8 raster stack was estimated for each land cover class from collected field data using the SCP plugin. Euclidian Minimum Distance land classification was used to estimate the land cover class for the entire clipped map (Wacker & Landgrebe, 1972; Richards,

1993). The sensitivity and specificity of the classification algorithm were calculated for each land cover class.

### ***Spatial distribution oviposition sites***

Random forest machine learning algorithms were used to predict *C. carnifex* burrow density on motu Tautau from 11-band Landsat 8 data. Analyses were conducted using the randomForest package for R version 3.5.2 (Breiman, 2001; Liaw & Wiener, 2002; R Core Team, 2018). Individual regression trees within a single random forest model use  $m$  bootstrapped samples with replacement of the training data,  $D$ , and each split uses a subset of the predictor variables (Breiman, 2001). As such, random forests internally cross-validate and reduce individual variable dominance and over-fitting. Random forests were particularly appropriate for the given study because they do not require prior information about the association between Landsat 8 data and *C. carnifex* burrow presence or density. Model hyper-parameters and further details of the random forest methodology are given in Appendix C.1.

Random forest models were applied in a two-stage approach as detailed below. Both models used the 11-band Landsat 8 data at each grid cell as the predictor variables.

(1) Random forest classification with binary *C. carnifex* presence/absence as the response variable. Random forest classification yielded two data subsets:  $\Phi_0$  and  $\Phi_1$  where *C. carnifex* are absent and present, respectively and  $\Phi_0 \subset D$ ,  $\Phi_1 \subset D$  and  $\Phi_0 \cup \Phi_1 = D$ . Cohen's  $\kappa$  was used to determine the ability of random forest classification to improve upon an expected level of classification accuracy under random chance for *C. carnifex* presence/absence (Landis & Koch, 1977). The importance of each



Landsat 8 band for random forest classification was considered using the mean decrease in Gini index.

(2) Random forest regression with *C. carnifex* burrow density (burrows/100 m<sup>2</sup>) as the response variable. Burrow density in grid cells where *C. carnifex* were estimated to be absent from random forest classification ( $\Phi_0$ ) was set to zero following random forest regression. Predicted burrow densities were converted to the number of burrows in each cell. Pseudo- $R^2$  values were used to evaluate random forest regression. Feature importance was assessed for random forest regression using the decrease in model accuracy (measured by the mean squared error) when the focal trait is randomised.

## **Modelling *Ae. polynesiensis* dynamics in a heterogeneous environment**

### ***Ae. polynesiensis* dynamics without dispersal**

A model of *Ae. polynesiensis* population dynamics was applied to random forest estimates of burrow density. The model comprised of a grid with each cell,  $(i, j)$ , corresponding to a 15×15 m Landsat 8 cell. Male and female mosquitoes were modelled separately due to different dispersal behaviours and mortality rates (Hapairai *et al.*, 2013a); low recapture rates of male *Ae. polynesiensis* and *Ae. aegypti* compared to females suggest a severely shorter male lifespan (McDonald, 1977; Muir & Kay, 1998; Mercer *et al.*, 2012; Hapairai *et al.*, 2014). The model was as follows:

$$\frac{dJ_{i,j}}{dt} = (1 - c) b \sigma_{i,j} F_{i,j} - \mu_{J_{i,j}} J_{i,j} - p J_{i,j} \quad (4.1)$$

$$\frac{dF_{i,j}}{dt} = g p J_{i,j} - \mu_F F_{i,j} \quad (4.2)$$

$$\frac{dM_{i,j}}{dt} = g p J_{i,j} - \mu_M M_{i,j} \quad (4.3)$$

where  $J$  is the number of juvenile mosquitoes (encompassing egg, larval and pupal stages),  $F$  is the number of female adult mosquitoes and  $M$  is the number of male adult mosquitoes.  $c$  is the number of burrows colonised by copepods;  $b$  is the fecundity (eggs laid per unit time);  $\mu_J$  is the juvenile death rate;  $g$  is the gender emergence ratio;  $p$  is the pupation rate;  $\mu_F$  is the adult female death rate;  $\mu_M$  is the adult male death rate. All model parameters, their values and sources are shown in Table 4. 1. Our model retained males for two reasons. First, the gender ratio in trap data was unequal (see Results) and, as such, our model framework incorporated gender-specific dispersal behaviours and mortality rates to examine whether gender-biased mosquito populations in the field could arise from these mechanisms. Second, males contribute to the total number of mosquitoes in traps and these data were used for model validation. The model implicitly assumed that eggs were distributed equally among burrows and that 100% of eggs laid in copepod-infested burrows died (Schaper, 1999; Awasthi *et al.*, 2015; Benelli *et al.*, 2016; Udayanga *et al.*, 2019).  $\sigma_{i,j}$  was a binary parameter governing oviposition such that

$$\sigma_{i,j} = \begin{cases} 1 & \text{if } \alpha_{i,j} > 0 \\ 0 & \text{if } \alpha_{i,j} = 0 \end{cases} \quad (4.4)$$

where  $\alpha_{i,j}$  is the number of crab burrows in cell  $(i, j)$ . Larval mortality was described as follows:

$$\mu_{J_{i,j}} = \frac{\kappa J_{i,j}}{\alpha_{i,j} (1-c)} \quad (4.5)$$

where  $\kappa$  is a numeric constant. Further discussion of density-dependent mortality in our model is given in Appendix C.2. Derivation of equilibrium values and demonstration of model stability are shown in Appendix C.3. All model analysis and

simulations were performed in R version 3.5.2 using a Runge-Kutta 4 algorithm (R Core Team, 2018).

### ***Ae. polynesiensis* dynamics with dispersal**

We adapted the discrete-space dispersal model developed by Lutambi et al. (2013), where a comprehensive description of the methodology is available (Lutambi *et al.*, 2013). Dispersal was a Markov process because the mosquito distribution at time  $t+1$  was determined only by the state of the system at time  $t$ . Males and females have been observed to disperse different distances in *Ae. polynesiensis* and *Ae. aegypti* with females dispersing further (Sheppard *et al.*, 1969; McDonald, 1977; Muir & Kay, 1998; Hapairai *et al.*, 2013a). Gender-dependent dispersal parameters,  $D_M$  and  $D_F$  were defined for male and females respectively:

$$D_M = \frac{D_M^*}{A} \text{ and } D_F = \frac{D_F^*}{A} \quad (4.6)$$

where  $A$  is the area of each Landsat 8 grid cell (225 m<sup>2</sup>) and  $D_M^*$  and  $D_F^*$  are the distance travelled per unit time (m<sup>2</sup>day<sup>-1</sup>) by male and female mosquitoes, respectively.

Let  $\Pi$  be the set of all cells and  $(i, j)$  be a cell within  $\Pi$ . Eight cells surround each cell to form a neighbourhood,  $n_{i,j}$

$$n_{i,j} = \left\{ \begin{array}{l} (i-1, j-1), (i-1, j), (i-1, j+1), (i, j-1), (i, j+1), \\ (i+1, j-1), (i+1, j), (i+1, j+1), (i, j) \end{array} \right\} \quad (4.7)$$

Dispersal from a cell,  $(i, j)$ , was dependent only on the state of cells within  $n_{i,j}$  because it is not thought that mosquitoes can perceive targets beyond their immediate proximity (e.g. >20 m) (Gillies & Wilkes, 1969; Bidlingmayer, 1994). Recall that  $n_{i,j}$

is cell  $(i, j)$  and its eight neighbours.  $n_{i', j'}$  is cell  $(i', j')$  and its eight neighbours, one of which is  $(i, j)$ .  $\chi$  is a cell within  $\Pi$  and  $\chi'$  is a cell neighbouring  $\chi$ . The notation of  $\chi, \chi', (i, j)$  and  $(i', j')$  is sufficient to describe every possible relationship between cells as shown in Figure 4. 3. The following notation was used to describe dispersal:

$\alpha_\chi$  = number of burrows in cell  $\chi$

$\alpha_{n_{i,j}}$  = number of burrows in  $n_{i,j}$

$\alpha_{\chi'}$  = number of burrows in cell  $\chi'$

$\alpha_{n_{i',j'}}$  = number of burrows in  $n_{i',j'}$

$\bar{\alpha}_{\chi \in n_{i,j}}$  = proportion of burrows in  $n_{i,j}$  which are in  $\chi \in n_{i,j}$

$\bar{\alpha}_{\chi' \in n_{i,j}}$  = proportion of burrows in  $n_{i,j}$  which are in  $\chi' \in n_{i,j}$

$\bar{\alpha}_{\chi \in n_{i',j'}}$  = proportion of burrows in  $n_{i',j'}$  which are in  $\chi \in n_{i',j'}$

$\bar{\alpha}_{\chi' \in n_{i',j'}}$  = proportion of burrows in  $n_{i',j'}$  which are in  $\chi' \in n_{i',j'}$

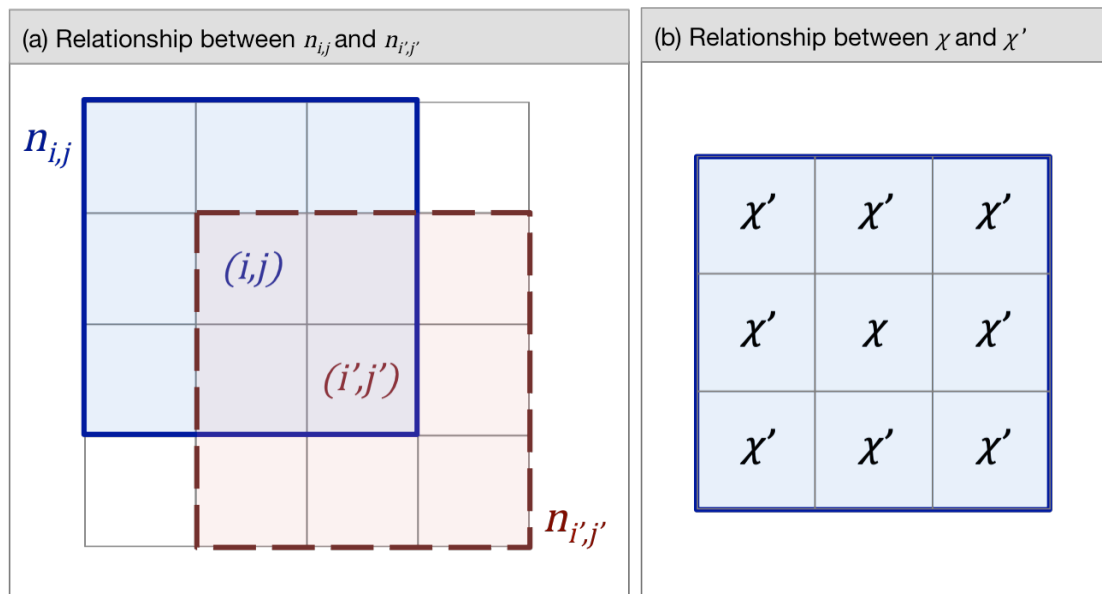


Figure 4. 3. Illustration of the relationships between cells based on their notation. Subfigure (a) illustrates the relationship between cells  $(i, j)$  and  $(i', j')$  which are within neighbourhoods  $n_{i,j}$  and  $n_{i',j'}$  respectively. Subfigure (b) illustrates the relationship between  $\chi$  and  $\chi'$  where  $\chi$  is a cell within  $\Pi$  (the set of all cells), and  $\chi'$  is a cell neighbouring  $\chi$ .

The total number of burrows in a neighbourhood was calculated by

$$\alpha_{n_{i,j}} = \sum_{\chi \in n_{i,j}} \alpha_{\chi} \quad \text{and} \quad \alpha_{n_{i',j'}} = \sum_{\chi \in n_{i',j'}} \alpha_{\chi} \quad (4.8)$$

The proportion of burrows in a group of cells,  $n_{i,j}$ , which are in  $\chi \in n_{i,j}$  was calculated by

$$\bar{\alpha}_{\chi \in n_{i,j}} = \frac{\alpha_{\chi}}{\alpha_{n_{i,j}}} \quad (4.9)$$

where

$$\sum_{\chi \in n_{i,j}} \bar{\alpha}_{\chi \in n_{i,j}} = 1 \quad (4.10)$$

Similarly

$$\bar{\alpha}_{\chi' \in n_{i,j}} = \frac{\alpha_{\chi'}}{\alpha_{n_{i,j}}} \quad (4.11)$$

$$\bar{\alpha}_{\chi \in n_{i',j'}} = \frac{\alpha_{\chi}}{\alpha_{n_{i',j'}}} \quad (4.12)$$

$$\bar{\alpha}_{\chi' \in n_{i',j'}} = \frac{\alpha_{\chi'}}{\alpha_{n_{i',j'}}} \quad (4.13)$$

To counteract edging effects, female mosquitoes did not migrate into neighbouring cells over oceans or lakes (i.e. where there were no *C. carnifex* burrows). The rate of movement out of a cell,  $(i, j)$ , into a neighbouring cell,  $\chi' \in n(i, j)$ , was defined by

$$\beta_{[(i,j) \rightarrow \chi']} = \begin{cases} De^{-\lambda(\bar{\alpha}_{\chi \in n_{i,j}} - \bar{\alpha}_{\chi' \in n_{i,j}})} & \text{if } \alpha_{\chi'} > 0 \\ 0 & \text{if } \alpha_{\chi'} = 0 \end{cases} \quad (4.14)$$

and the rate of movement into a cell was

$$\beta_{[\chi' \rightarrow (i,j)]} = \begin{cases} De^{-\lambda(\bar{\alpha}_{\chi' \in n_{i',j'}} - \bar{\alpha}_{\chi \in n_{i',j'}})} & \text{if } \alpha_{\chi} > 0 \\ 0 & \text{if } \alpha_{\chi} = 0 \end{cases} \quad (4.15)$$

where  $D \in \{D_M, D_F\}$  and  $\lambda$  is a dimensionless, constant parameter for the decay function. If  $(\bar{\alpha}_{\chi \in n_{i,j}} - \bar{\alpha}_{\chi' \in n_{i,j}}) = 0$  then adult mosquitoes disperse non-preferentially between all neighbouring cells. In this case, Equations (4.14) and (4.15) become

$$\beta_{[(i,j) \rightarrow \chi']} = \begin{cases} D & \text{if } \alpha_{\chi'} > 0 \\ 0 & \text{if } \alpha_{\chi'} = 0 \end{cases} \quad (4.16)$$

$$\beta_{[\chi' \rightarrow (i,j)]} = \begin{cases} D & \text{if } \alpha_{\chi} > 0 \\ 0 & \text{if } \alpha_{\chi} = 0 \end{cases} \quad (4.17)$$

Some cells on land were predicted to have a *C. carnifex* burrow density of zero using random forests. As defined above, our model prevented mosquito dispersal to cells with no burrows. Therefore, a negligible error term sampled from a Poisson distribution (mean = 2) was added to the predicted burrow density in each cell on land, to ensure that all cells on land had  $\alpha > 0$ . This prevented mosquitoes becoming trapped in small areas due to their inability to migrate over surrounding land.

### ***Two models of mosquito dispersal behaviour***

Field evidence suggests that male *Ae. polynesiensis* dispersal behaviours are less influenced by environmental heterogeneity than females (Hapairai *et al.*, 2013a).

Therefore, the rate of change of male mosquito populations was defined as:

$$\frac{dM_{i,j}}{dt} = g p J_{i,j} - \mu_M M_{i,j} - \left( \sum_{\chi' \in n_{i,j}} D_M \right) M_{i,j} + \left( \sum_{\chi' \in n_{i,j}} D_M M_{\chi'} \right) \quad (4.18)$$

Two models of female mosquito dispersal were compared. Equations (4.1) and (4.18) remained constant in both models.

The preferential dispersal model assumed that female mosquitoes disperse seeking oviposition sites and that  $D = D_F$ :

$$\frac{dF_{i,j}}{dt} = g p J_{i,j} - \mu_F F_{i,j} - \left( \sum_{\chi' \in n_{i,j}} \beta_{[(i,j) \rightarrow \chi']} \right) F_{i,j} + \left( \sum_{\chi' \in n_{i,j}} \beta_{[\chi' \rightarrow (i,j)]} F_{\chi'} \right) \quad (4.19)$$

The non-preferential dispersal model assumed the female adult mosquitoes disperse non-preferentially:

$$\frac{dF_{i,j}}{dt} = g p J_{i,j} - \mu_F F_{i,j} - \left( \sum_{\chi' \in n_{i,j}} D_F \right) F_{i,j} + \left( \sum_{\chi' \in n_{i,j}} D_F F_{\chi'} \right) \quad (4.20)$$

### ***Comparison of model estimates with trap data***

The estimated number of adult mosquitoes in the neighbourhood  $n_{i,j}$  of a trap, located in  $(i, j)$  is contained by

$$\bar{A}_{i,j} = \sum_{\chi' \in n_{i,j}} A_{\chi'} \quad (4.21)$$

where  $A_{i,j} = F_{i,j} + M_{i,j}$ . The median predicted population size across the neighbourhoods of all 12 traps is

$$\varpi = med\{\bar{A}_{i_1,j_1}, \bar{A}_{i_2,j_2}, \dots, \bar{A}_{i_{12},j_{12}}\} \quad (4.22)$$

The median number of mosquitoes captured across all BGS traps is  $\omega$ . A scaling factor,  $\Psi = \omega/\varpi$ , was used to re-project model estimates to facilitate comparison with trap data by applying  $\Psi$  to the model estimates at each trap:  $\{\Psi \bar{A}_{i_1,j_1}, \Psi \bar{A}_{i_2,j_2}, \dots, \Psi \bar{A}_{i_{12},j_{12}}\}$ . The absolute difference between rescaled model estimates and BGS trap data was used as a comparative measure.

### ***Environmental change due to larval source management***

The effect of changes in environmental suitability was considered in the context of larval source management (LSM). LSM is a vector control strategy, which removes potential oviposition sites to disrupt the mosquito life cycle (World Health Organization, 2013). Decreased environmental suitability due to LSM was defined as

$$\alpha^{\Lambda} = \begin{cases} (1 - \varepsilon)\alpha^{\Lambda} & \text{if } t \geq T \\ \alpha^{\Lambda} & \text{if } t < T \end{cases} \quad (4.23)$$

where  $\varepsilon$  is LSM efficacy (the proportion of *C. carnifex* burrows removed),  $\Lambda$  is LSM coverage (a set of cells with length,  $\theta$ , where LSM is implemented) and  $T$  is the time of intervention, which was set to occur once the model without LSM had reached stable equilibrium. Although our model simulates LSM, the formulation in Equation (4.23) is not limited to the effects of human intervention. Our model could indicate the effects other processes that decrease environmental suitability for *Ae. polynesiensis*, including changes in *C. carnifex* behaviour, land cover or local water quality, where  $\varepsilon$  and  $\theta$  represent the intensity and scale of environmental change, respectively.

Two spatial patterns of LSM were considered. First, targeted LSM defined  $\Lambda$  as the  $\theta$  cells with largest *Ae. polynesiensis* population at dispersal model equilibrium. Second, untargeted LSM defined  $\Lambda$  as  $\theta$  cells randomly sampled from the set of all cells. Parameter  $\varepsilon$  was varied between 0.05 and 0.95 and  $\theta$  was varied between 50 and 300 on iterative model runs. Examples of the LSM coverage grids with different values of  $\theta$  are shown in Appendix C.4. The model was run to equilibrium for each combination of  $\varepsilon$  and  $\theta$  for preferential and non-preferential dispersal models and the change in *Ae. polynesiensis* population size was recorded. For untargeted LSM, the



model was run for 20 bootstraps for each combination of  $\varepsilon$  and  $\theta$  taking a different random sample of  $\theta$  cells to avoid sampling bias. The net reduction in *Ae. polynesiensis* population size at equilibrium across bootstrapped simulations was recorded.

Table 4. 1. Descriptions, values and sources of key model parameters.

| Parameter | Description                                 | Value                                              | Units             | Source and Notes                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            |
|-----------|---------------------------------------------|----------------------------------------------------|-------------------|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| $\alpha$  | Number of <i>C. carnifex</i> burrows        | N/A                                                | burrows           | Estimated from random forest models using field data (see Methods).                                                                                                                                                                                                                                                                                                                                                                                                                                                                         |
| $c$       | Proportion of burrows inhabited by copepods | 0.475                                              | N/A               | Field data (see Results)                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    |
| $\sigma$  | Binary parameter controlling oviposition    | 0 if $\alpha_{i,j} = 0$<br>1 if $\alpha_{i,j} > 0$ | N/A               | N/A                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         |
| $b$       | Adult fecundity                             | 1.62                                               | day <sup>-1</sup> | No published data for <i>Ae. polynesiensis</i> ; <i>Ae. aegypti</i> data used. Joy et al. (2014) observed ~55 eggs/mosquito over four lifetime reproductive cycles in the laboratory (Joy et al., 2014). Eggs day <sup>-1</sup> calculated by $1/\theta$ where $\theta$ is <i>Ae. aegypti</i> lifespan in the laboratory. Literature review of lab-reared <i>Ae. aegypti</i> yielded $\theta = 33.95$ (Beeuwkes et al., 1933; McMeniman et al., 2009; Beilhe et al., 2012; Goindin et al., 2015; Chadee et al., 2017; Muttis et al., 2018). |
| $\mu_J$   | Juvenile mortality                          | See Equation (4.5)                                 | N/A               | N/A                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         |
| $\kappa$  | Density-dependent mortality constant        | $8.5 \times 10^{-4}$                               |                   | Estimate. See Appendix C.2. for more information.                                                                                                                                                                                                                                                                                                                                                                                                                                                                                           |
| $g$       | Gender emergence ratio                      | 0.5                                                | N/A               | An equal emergence ratio of male:female adult mosquitoes was assumed                                                                                                                                                                                                                                                                                                                                                                                                                                                                        |
| $p$       | Larvae to adult emergence rate              | 0.12                                               | day <sup>-1</sup> | No published data for <i>Ae. polynesiensis</i> . Estimated for a mean temperature of 27°C in <i>Ae. aegypti</i> (Yang et al., 2011).                                                                                                                                                                                                                                                                                                                                                                                                        |
| $\mu_F$   | Female adult mortality                      | 0.11                                               | day <sup>-1</sup> | $1/\tau_F$ where $\tau_F$ is the estimated average female lifespan (see below).                                                                                                                                                                                                                                                                                                                                                                                                                                                             |
| $\mu_M$   | Male adult mortality                        | 0.32                                               | day <sup>-1</sup> | $1/\tau_M$ where $\tau_M$ is the estimated average male lifespan (see below).                                                                                                                                                                                                                                                                                                                                                                                                                                                               |
| $\tau_F$  | Mean adult female stage duration            | 9.14                                               | days              | No published data for <i>Ae. polynesiensis</i> in wild populations; <i>Ae. aegypti</i> data used. Lab data not used due to artificially extended lifespans (Muir & Kay, 1998). Mean estimated lifespan from mark-release-recapture experiments used (McDonald, 1977; Muir & Kay, 1998; de Azambujo Garcia et al., 2016). In cases where studies reported daily survival rates, $S$ , mean longevity calculated by $1/S$ .                                                                                                                   |
| $\tau_M$  | Mean adult male stage duration              | 3.09                                               | days              | No published data for <i>Ae. polynesiensis</i> in wild populations; <i>Ae. aegypti</i> data used. Lab data not used due to artificially extended lifespans (Muir & Kay, 1998). Mean estimated lifespan from mark-release-recapture experiments used (McDonald, 1977; Muir & Kay, 1998; de Azambujo Garcia et al., 2016). In cases where studies reported daily survival rates, $S$ , mean longevity calculated by $1/S$ .                                                                                                                   |

|           |                                        |       |                                   |                                                                                                                                         |
|-----------|----------------------------------------|-------|-----------------------------------|-----------------------------------------------------------------------------------------------------------------------------------------|
| $\tau_I$  | Mean juvenile stage duration           | 9.86  | days                              | The mean of female and male emergence times taken from Mercer (1999); male and female times were comparable (Mercer, 1999).             |
| $D_F^*$   | Female diffusion coefficient           | 24.77 | m <sup>2</sup> time <sup>-1</sup> | Hapairai et al. (2013) observed mean of 123.87 m dispersal for female <i>Ae. polynesiensis</i> over five days (Hapairai et al., 2013a). |
| $D_M^*$   | Male diffusion coefficient             | 21.56 | m <sup>2</sup> time <sup>-1</sup> | Hapairai et al. (2013) observed mean of 107.68 m dispersal for male <i>Ae. polynesiensis</i> over five days (Hapairai et al., 2013a).   |
| $A$       | Area of study cell                     | 225   | m <sup>2</sup>                    | Each LandSat 8 grid cell was 15×15 m.                                                                                                   |
| $\lambda$ | Constant dimensionless decay parameter | 1     | N/A                               | Estimate. See Lutambi et al. (2013) for further specification (Lutambi et al., 2013).                                                   |

## Results

### *Ae. polynesiensis* distribution is spatially heterogeneous

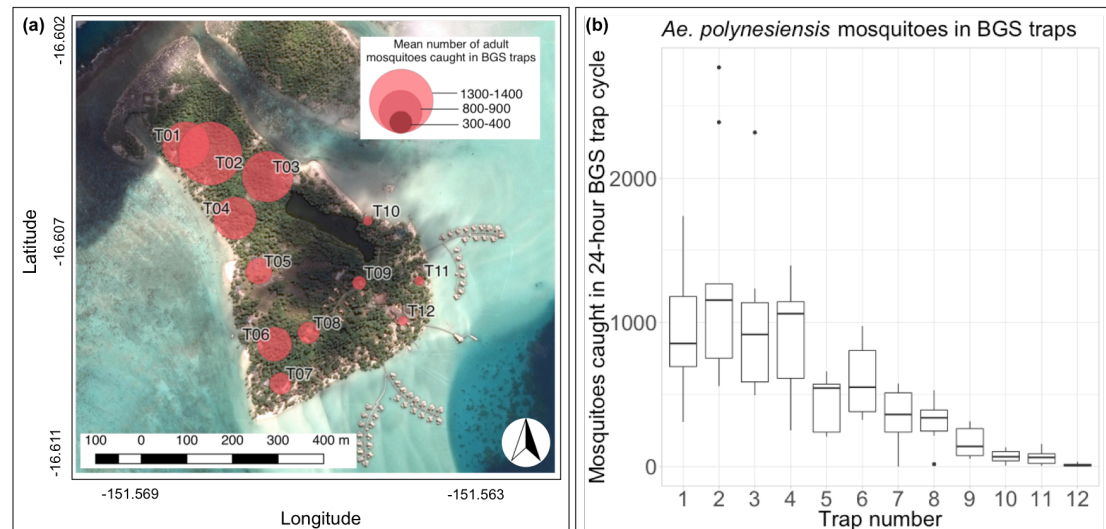


Figure 4. 4. *Ae. polynesiensis* mosquito numbers in BG-Sentinal (BGS) traps on motu Tautau between 20-Aug-2018 and 15-Oct-2018. The location of traps and their mean capture numbers are displayed in (a). Trap numbers of the 12 traps are denoted using T01-T12. The data spread is demonstrated in (b). Trap data were collected by Institut Louis Malardé.

*Ae. polynesiensis* accounted for >99.5% of mosquitoes in BGS traps. *Aedes aegypti* accounted for 0.02% and *Culex quinquefasciatus* for 0.46%. Only 3.7% of all captures were male mosquitoes. Mean captures in each trap and trap locations on motu Tautau are shown in Figure 4. 4(a) and the data spread is demonstrated in Figure 4. 4(b). There were no notable trends with time. Trap two saw the highest *Ae. polynesiensis* numbers per 24-hour cycle: 1,334 mosquitoes on average and a maximum of 2,767 on 10-Sept-2018. These numbers indicate very large *Ae. polynesiensis* populations; only between 17 and 241 mosquitoes per 24-hour cycle have been observed using the same equipment in parts of French Polynesia and other

South Pacific islands (Hapairai *et al.*, 2013c, 2015). Large *Ae. polynesiensis* populations appear endemic on Taha'a's motus; On nearby motu Taomaro, MRR experiments estimated *Ae. polynesiensis* population densities of 6,055 per hectare for the dry season and 18,860 per hectare for the wet season (Mercer *et al.*, 2012).

## **Larger *C. carnifex* burrows support more *Ae. polynesiensis***

### **larvae**

Burrows were sampled around traps T02, T03, T08, T09. Copepods were found in 47.5% of burrows. There was no dependency between copepod presence and trap number ( $\chi^2=0.741$ ,  $p=0.864$ ). Larvae were absent in 100% of burrows containing copepods; the two species did not cohabit. Burrow volume varied significantly between trap numbers but burrow diameter did not ( $p=0.017$  and  $p=0.132$  respectively, one-way ANOVA).

There was a positive linear relationship between burrow diameter and burrow volume ( $p<0.001$ ). Inclusion of trap number as a categorical covariate did not improve model fit ( $p=0.058$ , LRT). There was a positive relationship between burrow volume and the number of larvae extracted ( $p<0.001$ ) and between burrow diameter and the number of larvae extracted ( $p=0.01$ ). Trap number as a categorical covariate did not improve model fit in either instance. Larval density (larvae/litre) did not vary significantly between locations ( $p=0.123$ , one-way ANOVA). In burrows without copepods, the mean larval density was 7 larvae/litre and the mean number of larvae extracted was 51. Plotted data, model fits and parameter estimates are shown in Appendix C.5.

## Oviposition site availability is spatially heterogeneous

Predicted and observed land cover classes on motu Tautau are shown in Figure 4. 5. The mean specificity and sensitivity of the classifier across land cover classes were 92% and 51%, respectively. The confusion matrix of predicted and observed land cover types is shown in Appendix C.6.

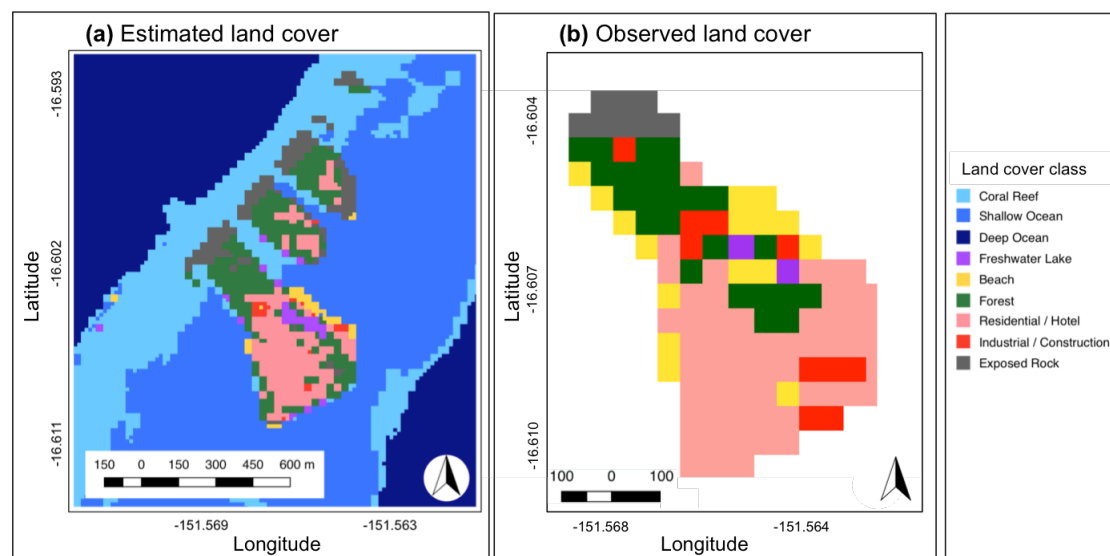


Figure 4. 5. Land cover classes on motu Tautau and surrounding area (a) estimated from Euclidian Minimum Distance land cover classification and (b) observed from field sampling. Subfigure (a) is at a resolution of 15×15 m and subfigure (b) is at a resolution of 100×100 m.

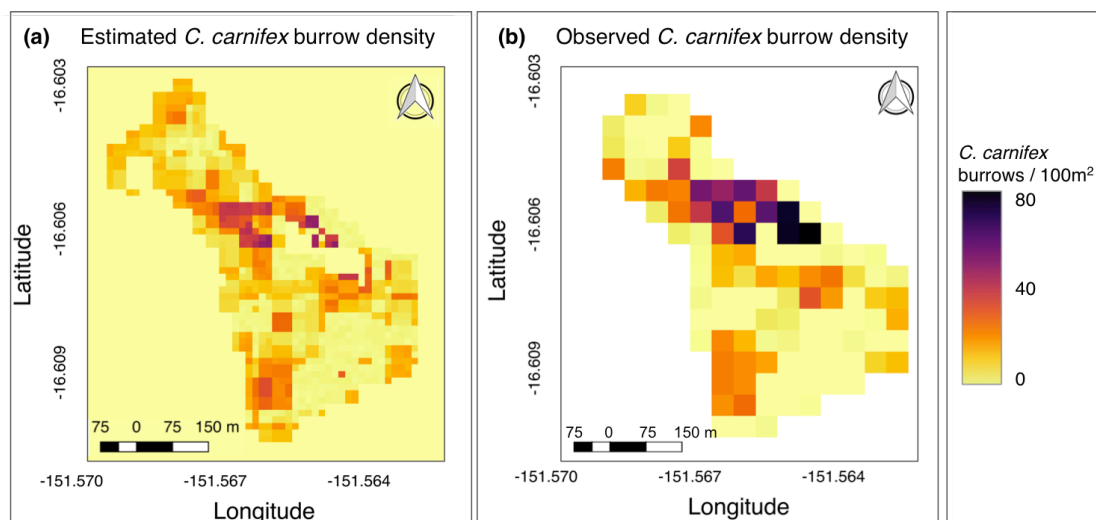


Figure 4. 6. Spatial distribution of *C. carnifex* burrows on motu Tautau (a) predicted using random forests and (b) observed from field sampling. Subfigure (a) is at a resolution of 15×15 m and subfigure (b) is at a resolution of 100×100 m.

The observed and estimated *C. carnifex* burrow distributions are shown in Figure 4. 6. For random forest classification of *C. carnifex* presence/absence, Cohen's  $\kappa$  was 0.28, indicating that Landsat 8 reflectance offers an improvement in classification accuracy over random chance (Landis & Koch, 1977). The confusion matrix used to calculate Cohen's  $\kappa$  is shown in Appendix C.7.

For regression trees of *C. carnifex* burrow density, the pseudo- $R^2$  was 0.19 which is relatively low, although it should be noted that random forests were able to capture the main features of the spatial distribution (Figure 4. 6) despite some error in the exact numbers of *C. carnifex* burrows estimated. The mean "Out-of-bag" (OOB) error in predicted burrow density was 12.56 burrows/100 m<sup>2</sup>. Further information on random forest methodology and feature importance plots are shown in Appendices C.1 and C.7. Random forest regression incurred mild smoothing, overestimating at low and underestimating at high burrow densities as shown in Appendix C.7.

### **Model estimates approximate trap data**

The predicted spatial distribution of *Ae. polynesiensis* (male and female combined) for non-preferential and preferential dispersal models is shown in Figure 4. 7. Preferentially migrating *Ae. polynesiensis* populations (male and female combined) were 1.34 fold higher than non-preferentially migrating mosquitoes. Larval populations were 1.33 fold higher for preferentially compared to non-preferentially dispersing mosquitoes. The average male percentage of the *Ae. polynesiensis* population was 30.6% for preferential and 35.6% for non-preferential dispersal models.

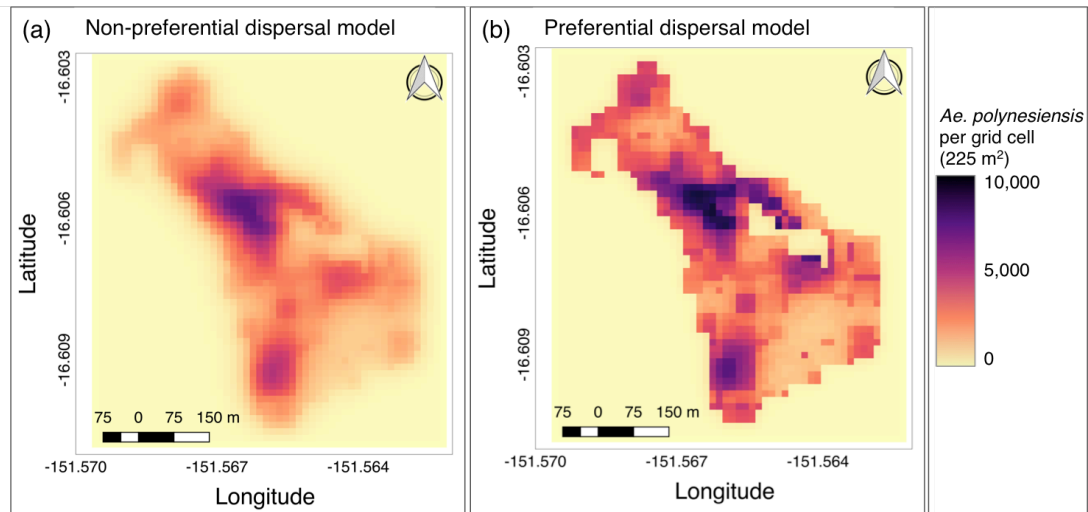


Figure 4. 7. Predicted distribution of *Ae. polynesiensis* adult mosquitoes (male and female) on motu Tautau for the (a) non-preferential and (b) preferential female dispersal models.

A comparison of preferential and non-preferential dispersal model results with BGS trap data is shown in Figure 4. 8. The median non-preferential dispersal model predictions,  $med(\Psi \bar{A}_{i,j})$ , in the neighbourhood,  $n_{i,j}$ , of each trap were marginally closer to the median observed mosquito numbers at each trap. The median difference between the number of trapped mosquitoes and model estimates was 199 for the preferential model and 162 for the non-preferential model. The trap with the largest absolute difference between model predictions and BGS trap data (trap T02 with an error of 597 and 599 burrows for non-preferential and preferential models, respectively) also had the largest error in the predicted *C. carnifex* burrow density out of all 12 traps (48.2 burrows / 100 m<sup>2</sup>).



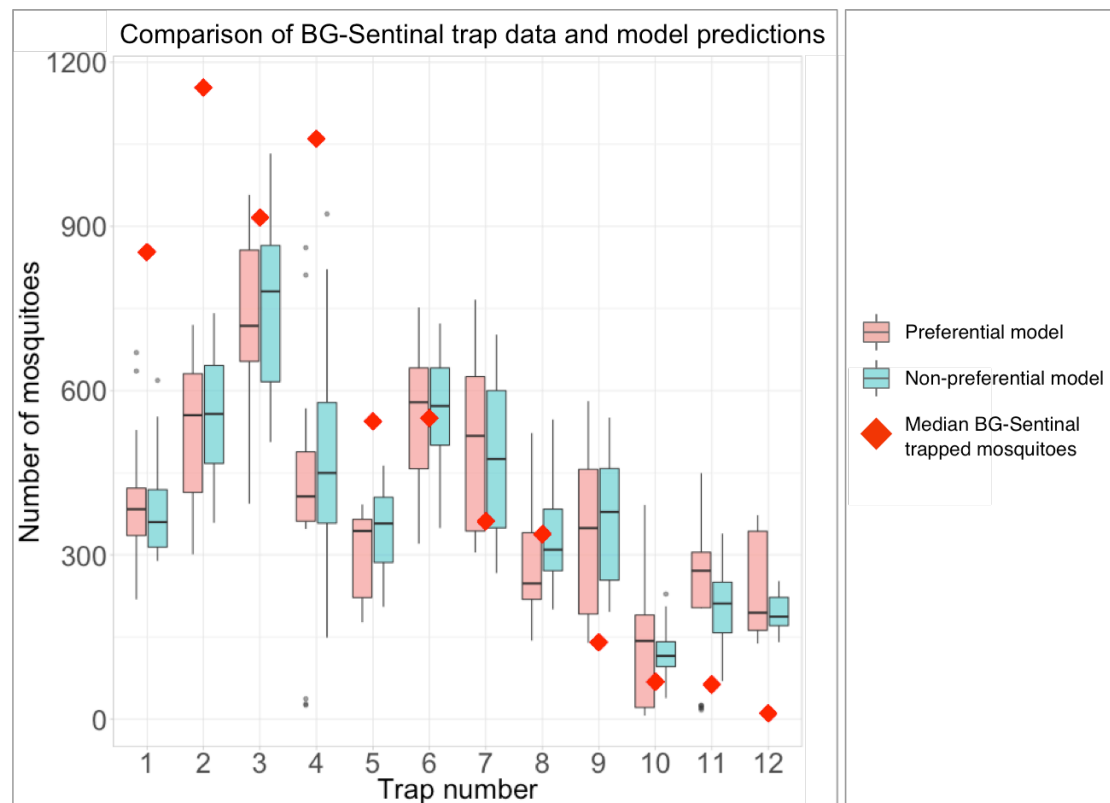


Figure 4. 8. Comparison of preferential and non-preferential dispersal models with the median number of caught adult *Ae. polynesiensis* in BGS traps.

## Environmental change has spatially non-linear effects

The net effects of each LSM strategy upon preferentially and non-preferentially dispersing *Ae. polynesiensis* populations were comparable. While targeted LSM consistently suppressed a greater net proportion of the *Ae. polynesiensis* population than untargeted LSM, the effect was small. In the preferential dispersal model, targeted LSM suppressed 3.2% (standard deviation (SD) = 1.7%) more of the *Ae. polynesiensis* population on average than non-targeted LSM for the parameter values of intervention coverage,  $\theta = \{50, \dots, 300\}$ , and efficacy,  $\varepsilon = \{0.05, \dots, 0.95\}$ . For non-preferential dispersal, targeted LSM suppressed 2.2% (SD = 1.1%) more of the population than non-targeted LSM. The net proportion of the *Ae. polynesiensis*

population suppressed across the parameter space,  $\theta = \{50, \dots, 300\}$  and  $\varepsilon = \{0.05, \dots, 0.95\}$ , for each dispersal behaviour and LSM strategy is shown in Appendix C.8.

Figure 4. 9 shows the change in the *Ae. polynesiensis* population as a result of targeted and untargeted LSM for preferential and non-preferential dispersal models. Although the net effects of targeted and non-targeted LSM strategies were comparable (as shown in Appendix C.8), each strategy had distinct, non-linear spatial effects upon the *Ae. polynesiensis* population. Targeted LSM had a negligible effect upon *Ae. polynesiensis* populations outside of the intervention zone (Figure 4. 9(a) and Figure 4. 9(c)). Whilst targeted LSM provided enhanced population suppression, its effects were restricted to an area localised around the target cells. In contrast, untargeted LSM provided a lower level of suppression across a wider geographic area. Figure 4. 10 shows the absolute difference in the proportion of the *Ae. polynesiensis* population suppressed between LSM strategies for  $\theta = \{50, 300\}$  and  $\varepsilon = \{0.50\}$ ; the outcomes for other values of  $\theta$  and  $\varepsilon$  are shown in Appendix C.8. Whilst targeted LSM was more effective than untargeted LSM in its local intervention zone, untargeted LSM quickly became more effective as the distance from targeted LSM intervention zones increased. Maps showing the distribution of LSM deployment sites used to generate the results shown in Figure 4. 9 and Figure 4. 10 are displayed in Appendix C.4.

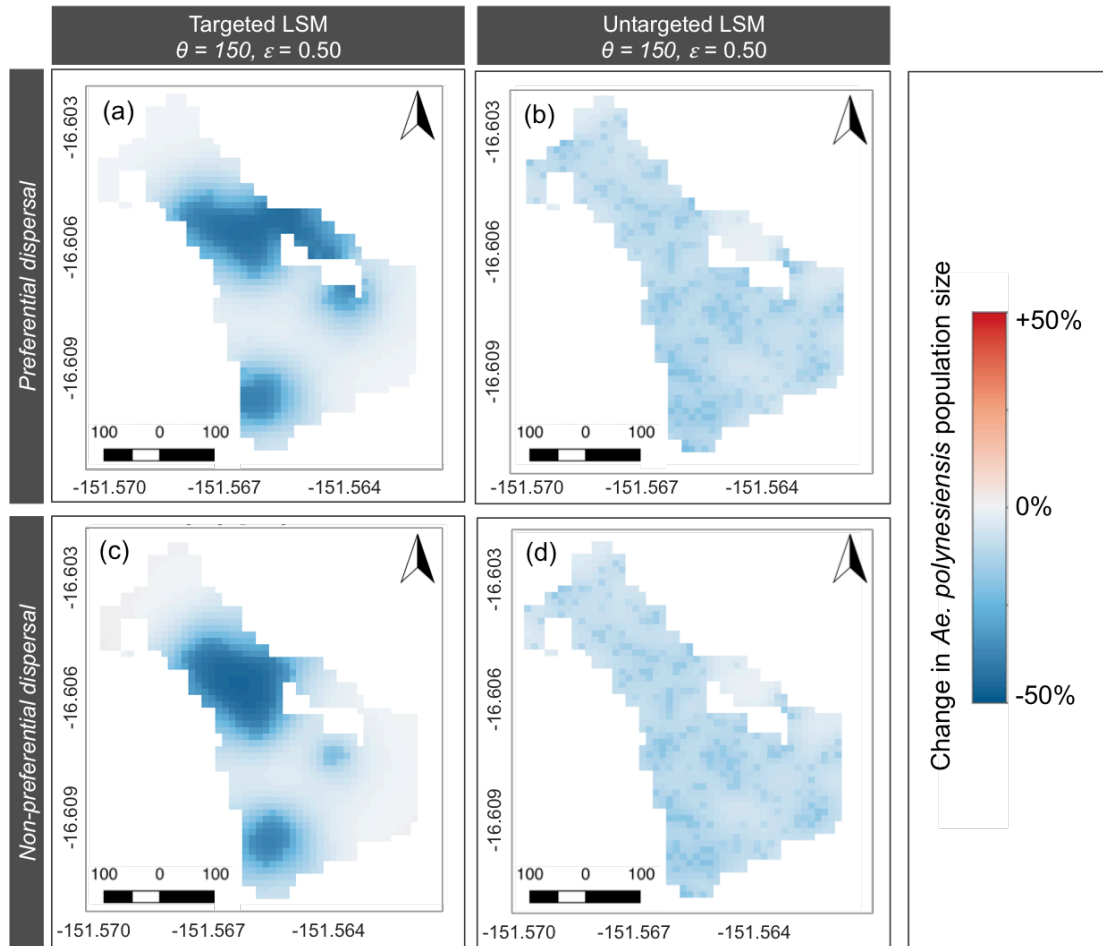


Figure 4. 9. The change in the *Ae. polynesiensis* population size in each grid cell following larval source management (LSM) intervention. Results are displayed for preferential dispersal (a)-(b) and non-preferential dispersal (c)-(d) using a targeted (a) & (c) and an untargeted (b) & (d) LSM intervention strategy. Results are displayed for a medium coverage, medium efficacy LSM intervention, where the LSM coverage in terms of the number of cells treated,  $\theta$ , is 150 and the LSM efficacy in terms of the proportion of burrows removed at each treated cell,  $\varepsilon$ , is 0.5. Whilst targeted interventions ((a) & (c)) result in larger local reductions in the *Ae. polynesiensis* population size, untargeted interventions ((b) & (d)) result in more spatially homogeneous reductions. The effects for preferential and non-preferential dispersal models were comparable.

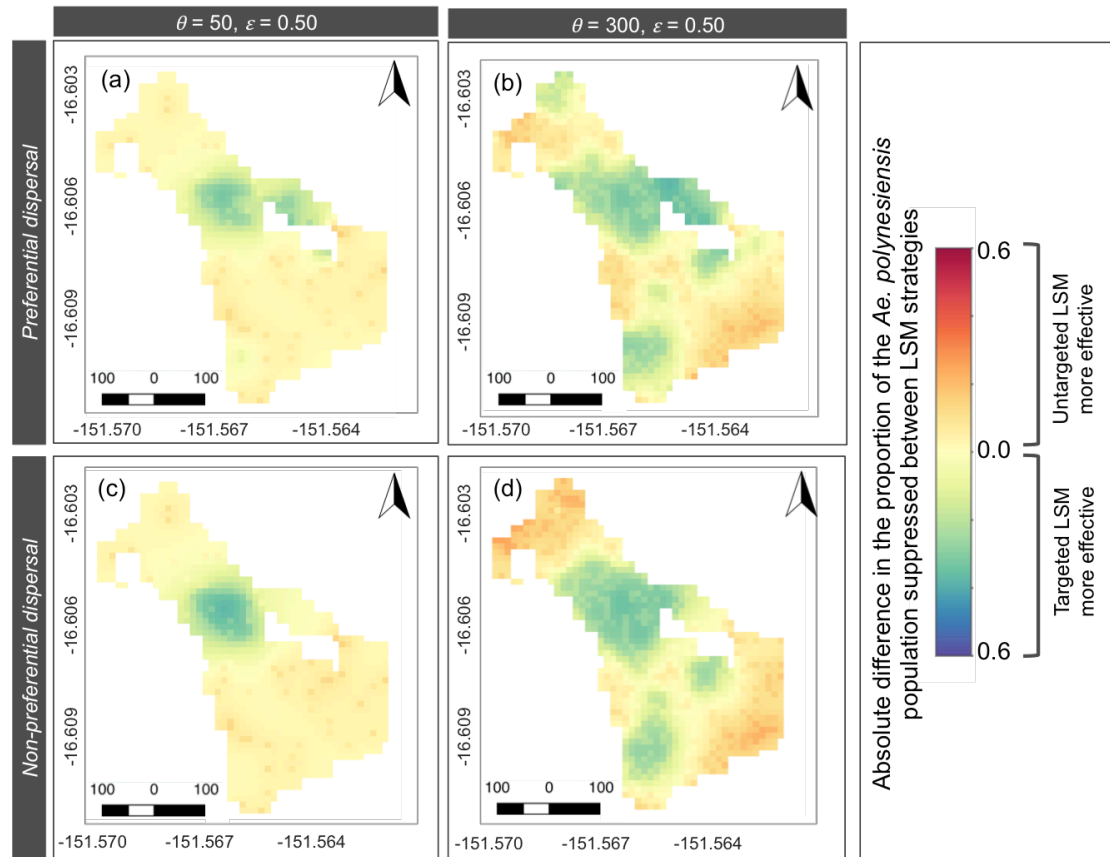


Figure 4. 10. The absolute difference between larval source management (LSM) strategies in the proportion of the *Ae. polynesiensis* population suppressed. Results are displayed for preferential dispersal (a)-(b) and non-preferential dispersal (c)-(d). Results are displayed for different values of LSM coverage in terms of the number of grid cells treated ( $\theta$ ) and LSM efficacy in terms of the proportion of *C. carnifex* burrows removed at treated grid cells ( $\varepsilon$ ). Subfigures (a) and (c) display low coverage, medium efficacy LSM with  $\theta = 50$  and  $\varepsilon = 0.5$ . Subfigures (b) and (d) display high coverage, medium efficacy LSM with  $\theta = 300$  and  $\varepsilon = 0.5$ . Orange/red colours indicate that untargeted LSM is more effective. Green/blue colours indicate that targeted LSM is more effective. Yellow indicates no substantial difference in the proportion of the population suppressed between LSM strategies.

## **Discussion**

### **Environmental heterogeneity**

Spatial heterogeneity has non-linear effects on mosquito populations by limiting the availability of resources (Lutambi *et al.*, 2013; Hiscox *et al.*, 2014). Spatial heterogeneity can also influence mosquito dispersal via host-seeking and oviposition site seeking behaviours (Le Menach *et al.*, 2005; Day, 2016). Complex and rapid land-use change is occurring globally (Lambin & Meyfroidt, 2011; IPCC, 2018). Consideration of spatial heterogeneity is therefore paramount in models of mosquito populations to predict the distributions of epidemiologically important species.

Existing models have considered the effects of spatially heterogeneous distributions of hosts (Cummins *et al.*, 2012; Shcherbacheva *et al.*, 2018) and oviposition sites (Smith *et al.*, 2004; Le Menach *et al.*, 2005; Lutambi *et al.*, 2013) upon mosquito dispersal behaviours. A small number of studies have considered spatial heterogeneity in other landscape elements such as wind (Dufourd & Dumont, 2013). Most studies have used hypothetical test cases to examine the dynamics of their models (Lutambi *et al.*, 2013). Therefore, it is not always clear how accurate theoretical models are in estimating mosquito responses to environmental heterogeneity in their natural habitat. We have offered a unique improvement on previous studies by using field data to motivate and validate our model. We have integrated field sampling, remote sensing and mathematical modelling to examine the spatial distribution of *Ae. polynesiensis* on motu Tautau, French Polynesia. Our study provides an example of a methodological pipeline applicable on larger scales to (a) estimate many types of

environmental heterogeneity and (b) consider the effects of environmental heterogeneity upon the behaviours of different mosquito species.

We found that oviposition site-seeking behaviour in female *Ae. polynesiensis* resulted in 1.46-fold larger *Ae. polynesiensis* populations on average compared to non-preferential dispersal behaviours. This is intuitive because non-preferential dispersal results in a lower probability that a habitable area will be encountered and colonised (Schowalter, 2006).

## Environmental change

The net proportion of the *Ae. polynesiensis* population suppressed by targeted and untargeted LSM strategies were comparable for preferentially and non-preferentially dispersing *Ae. polynesiensis* populations. This suggests that, although preferential dispersal was an advantageous ecological mechanism leading to larger *Ae. polynesiensis* population sizes, it did not offer substantial protection against environmental disruption. Targeted LSM offered a very marginal increase in the net proportion of the *Ae. polynesiensis* population suppressed compared to untargeted LSM. This result is consistent with previous models of mosquito control strategies. North et al. (2019) considered the effects of genetic mosquito control in West Africa and observed that a stratified release grid offered only a marginal increase in suppression than randomly selected release sites (95.9% compared to 93.6% suppression) (North *et al.*, 2019).

Although the net effects of LSM were comparable between strategies, targeted and untargeted LSM strategies had different, non-linear spatial effects upon mosquito population sizes. The largest per-grid-cell reductions in *Ae. polynesiensis* density

were achieved by targeted LSM. However, these reductions occurred on a local scale and failed to impact regions far from the intervention zone. By contrast, untargeted LSM resulted in smaller per-grid-cell reductions in *Ae. polynesiensis* density but these were distributed more heterogeneously through space. These results have considerable implications for mosquito control strategies, two of which are discussed below.

First, our results suggest that localised changes in habitat quality do not have downstream effects for mosquito populations outwith the vicinity of the localised change. For mosquito control strategies, this means that using net suppression as a target outcome is not necessarily a good metric because key areas may be completely unaffected by an intervention, despite large net effects. For example, on motu Tautatu, hotel infrastructure and residential housing are restricted to the South end of the island as shown in Figure 4. 1(b). Targeting LSM to regions with the largest *Ae. polynesiensis* populations resulted in the greatest net and per grid cell suppression effects. However, most of these effects were limited to areas on the North end of the motu; the South end was largely unaffected (Figure 4. 9(a) and Figure 4. 9(c)). Therefore, mosquito-human contacts might not be reduced as a result of poorly targeted LSM strategies; local and net effects must be carefully balanced by mosquito control strategies.

Second, our model did not detect increases in mosquito density anywhere in the study region following LSM. This might appear counterintuitive because one might expect that, under the assumption of preferential dispersal towards oviposition sites, mosquitoes would disperse away from treated areas seeking aquatic larval habitats, thereby increasing mosquito density in surrounding areas. Our results did not show this phenomenon because the models were at equilibrium prior to LSM intervention;

many cells were saturated at their environmental carrying capacity. Therefore, eggs laid by mosquitoes dispersing away from LSM intervention sites did not have a notable effect upon the *Ae. polynesiensis* population size because additional eggs exceeded the environmental carrying capacity, resulting in density-dependent larval mortality. Whether these dynamics hold in field environments depends upon the extent to which aquatic habitat carrying capacity is saturated under field conditions. Extraneous micro-environmental and micro-climatic variation may compromise the equilibration of larval populations at carrying capacity. Therefore, there is the potential for unintended increases in mosquito density in untreated areas if the environment is sufficiently unstable that mosquito populations do not equilibrate at carrying capacity.

## **Model validation**

The non-preferential dispersal model predicted patterns in *Ae. polynesiensis* density marginally closer to trapping data than the preferential model. However, it is not possible to conclude that non-preferential dispersal is the prevailing behaviour. Preferential and non-preferential models predicted disparate mosquito population sizes. Mosquito population size cannot be estimated from trap data without labour-intensive MRR studies (Pollock *et al.*, 1990), which have not been conducted on motu Tautau. Despite this, the importance of predicting spatial patterns – not sizes – of mosquito populations cannot be understated. It is visually evident by comparing Figure 4. 4(a) and Figure 4. 7 that our model accurately detects micro-regions with large *Ae. polynesiensis* populations. Spatial heterogeneity in animal populations arises from ensembles of complex mechanisms, which are difficult to empirically study.



Models with the capacity to incorporate species biology and behaviour facilitate the study of ecological mechanisms that manifest in spatial patterns.

## Limitations

*Ae. polynesiensis* population sizes were over- and under-estimated at some BGS traps as shown in Figure 4. 8. Three reasons for this are discussed below as limitations of the current model.

First, BG-Lures used by BGS traps could facilitate large trap counts in areas with few oviposition sites (i.e. traps T01 and T04) by attracting host-seeking mosquitoes from nearby high-density areas.



Figure 4. 11. Bromeliad plant observed during field sampling. Bromeliad phytotelmata are known to catch rainwater and provide suitable oviposition sites and larval habitats for multiple mosquito species. Bromeliads were observed to be widespread and dense in forested areas on motu Tautau.

Second, landscape features may offer additional oviposition sites heterogeneously distributed across motu Tautatu. For example, large numbers of discarded coconut husks were observed in industrial/construction sites on the north end of motu Tautau

(see Figure 4. 2(b)). Coconut shells are known to collect water and harbour mosquito larvae in French Polynesia (Richard & Cao-Lormeau, 2019). Bromeliad phytotelmata were widely present in forested areas on motu Tautau (as evidenced by Figure 4. 11) and are known breeding sites for *Ae. aegypti* and *Ae. polynesiensis* as well as other mosquito species (Marques *et al.*, 2012; Wilke *et al.*, 2018). In addition, proximity to the ocean may render some *C. carnifex* burrows too saline for oviposition (Lardeux *et al.*, 1992).

Third, errors in the prediction of *C. carnifex* burrow density may have influenced model estimates. Random forests cannot exploit trends in the data to predict outside of their training set, as they do not fit relationships between variables. Many implementations of random forests smooth the estimated response surface by averaging across trees (Wyner *et al.*, 2017). When field data recorded  $\leq 5$  burrows/100 m<sup>2</sup>, all random forest errors were positive (overestimation). At  $>5$  burrows/100 m<sup>2</sup>, all errors were negative (underestimation). The errors were also larger at the tails of the distribution of field data. The distribution of prediction errors is shown in Appendix C.7. Our dataset is relatively small and larger datasets may fare better at capturing tail ends of the distribution.

Exact spatial interpolation methods such as kriging or radial basis functions (RBFs) preserve observed data points and are able to capture trends in the data that random forests cannot (Mitas & Mitasova, 2005). However, interpolation may not be as effective as machine learning approaches for two reasons. (i) Machine-learning algorithms are able to utilise a wide range of data to infer nonlinearities between two sampling points whereas interpolation methods are limited to only the data given by the two sampling points. (ii) Quantification of oviposition sites is labour intensive. Interpolation methods may therefore be restricted to small-scale studies. Machine

learning algorithms facilitate prediction over large spatial areas without spatially consistent sampling. Exploration of the use of RBFs on the current dataset is shown in Appendix C.9.

Above I have discussed discrepancies between predicted mosquito densities and trap counts. A discrepancy between the observed and predicted gender distribution should also be noted. 3.7% of trapped mosquitoes were male. Our model predicted ~30-36% of mosquitoes to be male. This may have occurred because (i) differences in life history traits between females and males may be larger than suggested by the empirical literature, (ii) the gender emergence ratio of pupae may not be 1:1, or (iii) the trapping protocol may be biased towards trapping female mosquitoes. Further empirical work is needed to clarify these considerations.

## **Future work**

We note three main areas for future work. First, other mosquito dispersal behaviours – notably, host-seeking – are well documented and their inclusion would be a valuable contribution to our model (Bowen, 1991; Cummins *et al.*, 2012; Shcherbacheva *et al.*, 2018). However, additional data on the host distribution are required for this to be possible. Second, the diameter of burrows as a proxy for burrow volume was not used to control intra-burrow density-dependent mortality, despite the linear relationship observed between the two. This was because the prediction errors of random forest regression for burrow diameter were unsuitably large (data not shown). In addition, absence of rainfall time-series data means that the stability of the relationship between burrow diameter and volume cannot be certain. A larger, temporal training set may fare better. Third, our model does not incorporate *C. carnifex* dynamics. However,

Micheli et al. (1991) observed that *C. carnifex* and *Sesarma meinerti* burrow density remain relatively constant across time (Micheli *et al.*, 1991). Therefore, dynamic *C. carnifex* populations may not substantially influence model results.

## Conclusions

The primary goal of this study was to detail a methodological approach for incorporating environmental heterogeneity into mathematical models of mosquito ecology. Two secondary objectives were used to realise this goal. First, we aimed to predict spatial heterogeneity in *C. carnifex* burrow density. This was achieved by integrating field data and remote sensing using random forest models. Second, we aimed to model *Ae. polynesiensis* population dynamics in response to spatial heterogeneity in *C. carnifex* burrows. This was achieved using a mechanistic model of mosquito dispersal with oviposition site seeking behaviours. Our model demonstrated that changes in the environment inhabited by mosquitoes, such as LSM, have non-linear and spatially heterogeneous effects on *Ae. polynesiensis*. Therefore, mosquito control strategies must carefully balance spatial and net effects. Further adaptation of the integrative methodological pipeline we have presented could facilitate model application at larger spatial scales and for additional sources of environmental heterogeneity.

## **Data availability**

The Landsat 8 data that support the findings of this study are available to download from NASA's Earth Explorer portal at <https://earthexplorer.usgs.gov> and were accessed between March 2019 and July 2019. During preparation of this chapter for journal submission, field sampling data will be made available on the Open Science Framework (OSF) with identifier <https://osf.io/u87j9/>.

## **Code availability**

During preparation of this chapter for journal submission, a minimum working example of the custom algorithms used to conduct this research will be made available on the Open Science Framework (OSF) with identifier <https://osf.io/u87j9/>.



# Chapter 5

## Discussion

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## **Summary of chapters**

This thesis has considered the effects of environmental change on mosquito population dynamics and life history traits. In Chapter 2, I presented a temperature and precipitation driven mathematical model of *Aedes aegypti* population dynamics in response to climate change. I predicted that *Ae. aegypti* will benefit from climate change across most of Brazil. In some regions, seasonal patterns of mosquito density will be disrupted due to increasing aridity and temperatures exceeding the thermal maximum for *Ae. aegypti* survival. I placed the results of this model in an epidemiological context and predicted that the transmission potential of dengue fever will increase across most of Brazil.

Density dependence is an aggregate term capturing a suite of complex biological mechanisms and environmental factors. However, density-dependent effects on life history traits are commonly captured in mosquito population dynamics models by numeric constants. In Chapter 3, I presented a mechanistic empirical study of the effects of nutritional availability on *Ae. aegypti* larval density dependence. I compared feeding regimes that were adjusted and unadjusted for the number of larvae in a habitat. By comparing these feeding regimes, I demonstrated that density-dependent effects on larval development times, survival probabilities and adult wing lengths were modulated by nutritional availability.

In Chapter 4, I presented a methodological approach for estimating the spatial distribution of biologically relevant environmental factors for mosquito populations. I subsequently used a discrete-space dispersal model to estimate *Aedes polynesiensis* distributions across an environmentally heterogeneous landscape and considered the implications of environmental change for mosquito populations. The approach is

adaptable to other species and taxa. I demonstrated that environmental change had spatially non-linear effects on *Ae. polynesiensis* population sizes.

## **Broader implications**

### **Entomological surveillance**

*Ae. aegypti* and *Aedes albopictus* have evolved new oviposition behaviours and host preferences to adapt to rapid human encroachment into their ancestral habitat (Powell, 2013). Given the anthropophilic nature of these epidemiologically important mosquito species, consideration of anthropogenic variables is crucial for the accurate estimation of species distributions. In Chapter 2, I used municipal building index for *Ae. aegypti* from the Brazilian Ministry for Health (Secretaria de Vigilância Sanitária em Saúde, 2005) to capture the effects of anthropogenic variables on *Ae. aegypti* occurrence probability. Below, I consider two broader considerations for the use of entomological surveillance data in modelling studies.

First, there remain many prevailing questions regarding the geographical extent of epidemiologically important mosquito species. Studies of mosquito distributions can incur investigator subjectivity because habitat types are often classified in unstandardised, qualitative ways such as ‘suburban’, ‘agricultural’ or ‘urban’ (Derraik, 2005; Sattler *et al.*, 2005; Champion & Vitek, 2014), which limits comparability between studies. This lack of standardisation also means that habitat types are not classified in a way that captures the differences between them in an ecologically meaningful way, such as by larval habitat availability, host availability or

microclimate (Thiemann *et al.*, 2011; Li *et al.*, 2014; Murdock *et al.*, 2017). Studies of *Ae. aegypti* habitat preferences are typically limited to a few habitat types within reasonable access of research centres. Crucially, this limited geographic range of mosquito surveillance can incur sampling bias. The absence of *Ae. aegypti* in very rural or forested areas is either not recorded or the area not investigated. Evidence for *Ae. aegypti* absence in rural areas is weaker and less abundant than evidence for *Ae. aegypti* presence in urban areas. As a consequence, the strength of the relationship between anthropogenic factors and *Ae. aegypti* occurrence may be heavily diluted in many studies.

Second, entomological surveys on the scale of that conducted by the Brazilian Ministry for Health are rare and require mobilisation of large, centrally managed groups of people. Large-scale surveys are beyond the capabilities of most research groups. It is therefore important to incentivise governments and industries to participate in mosquito surveillance at the national level because these data are imperative to mobilise targeted health services. Fortunately, participation of large bodies in entomological research is beginning to occur. For example, Brazilian biotechnology and bioinformatics company, Ecovec (<http://ecovec.com/>), have begun conducting comprehensive entomological surveillance in Belo Horizonte and surrounding municipalities. Several national governments – such as the Australian Government – have also adopted national mosquito surveillance programs (van den Hurk *et al.*, 2012). However, the data from such programs are rarely publicly available, limiting research capacity. There is growing recognition of the issues of inaccessibility and lack of detailed meta-data in entomological research (Rund *et al.*, 2019), and there are an increasing number of online databases and depositories making entomological data searchable and accessible (Giraldo-Calderón *et al.*, 2015;

GBIF: The Global Biodiversity Information Facility, 2019). Compendiums of entomological data in online depositories, such as the *Aedes* species occurrence data compiled by Kraemer et al. (2015), are currently imperative for researchers to understand the distributions of epidemiologically relevant species (Kraemer *et al.*, 2015a). However, the sampling protocols used to collect the data collated within compendiums are far from standardised.

### **Changes in climatic cycles can disrupt ecosystems**

In Chapter 2, it was predicted that climate change will disrupt the seasonal dynamics of *Ae. aegypti* populations. This result has been echoed for many other species (Burkett *et al.*, 2005; Bronson, 2009; Burger *et al.*, 2012; Johansson *et al.*, 2012; Zhang *et al.*, 2017). In 2000, Rocky Mountain yellow-bellied marmots (*Marmota flaviventris*) were observed to be leaving hibernation over a month earlier than in previous decades (Inouye *et al.*, 2000). Across Europe, migratory bird species have temporally adjusted migration patterns due to changing temperatures; those that don't have seen the highest rates of population decline (Møller *et al.*, 2008).

Disruption of animal and plant phenology decouples population cycles that many species depend upon. For example, increasing temperatures in Greenland have resulted in a trophic mismatch between caribou migration and the emergence of vegetation that they rely on for food (Post & Forchhammer, 2007). As a result, young caribou have suffered increased mortality. Evidence suggests that changing climates might decouple budworm populations in Canada's boreal forests from the cycles of its parasitoid and avian predators with consequences for the health of forests that budworm feed upon (Mattson & Haack, 1987; Flemming & Volney, 1995). Whilst it

is important to establish the effects of climate change upon the biology of individual species, one must not lose sight of the role that each species plays in the wider, changing ecosystem. Chapter 4 presented one example of how the dependencies between species (*Ae. polynesiensis* and *Cardisoma carnifex*) could be modelled. Worryingly, environmental cues for reproduction or other life history events are unknown in many species (Bronson, 2009). Therefore, the true impact of climate change upon ecosystem function may not be fully understood until after the fact.

## **Density as a surrogate measure for mechanisms of population regulation**

Many studies have detected associations between population density and life-history traits. The most successful of these have typically occurred in large mammals (Fowler, 1981, 1987; Messier, 1991; Coulson *et al.*, 2001). Peeters *et al.* (2017) observed declines in population growth rate with increased population sizes of Svalbard reindeer (*Rangifer tarandus platyrhynchus*) (Peeters *et al.*, 2017). Albon *et al.* (1983) reported an association between density and fertility in red deer (Albon *et al.*, 1983). Associations between life-history traits and density have been observed in bighorn sheep (L'Heureux *et al.*, 1995; Portier *et al.*, 1998) and seals (Fowler, 1990; Svensson *et al.*, 2011) as well as smaller mammals, including voles (Hansen *et al.*, 1999; Stenseth *et al.*, 2003). For invertebrates, the detection of density dependence has historically been more contentious; many entomologists failed to observe associations between population size and population growth after decades of examining wild populations (Dempster, 1983; Stiling, 1987).

In Chapter 3, I highlighted that density dependence is really an aggregate term for multiple biological mechanisms involving environmental variables. Studies that aim to detect associations between population density and population growth actually use density as a surrogate measure for a suite of more complex ecological mechanisms. These mechanisms could include territoriality, disease, famine, drought or any other ecological process regulating a population. Whilst the use of density as a surrogate measure facilitates concise data analysis and mathematical models, it collapses complex mechanisms of population regulation into a single measure. I suggest that whether or not it is appropriate to use density in this way depends upon the ecology and environment of the species in question and note three main points of consideration.

1) The detectability of associations between density and population growth may be affected by environmental stability. Strong (1986) makes a compelling argument for this, and defines a ‘density vague’ region at medial densities below the environmental carrying capacity where there is no notable change in population growth (Strong, 1986). Strong notes that the population growth rate is “distinctly affected by density only at higher population levels [above carrying capacity]” (Strong, 1986). This is depicted in Figure 5. 1. In stable environments, population sizes can increase unhindered to equilibrate at a consistent environmental carrying capacity. Further increases in population density result in an adjustment of the rate of population growth to return populations to equilibrium. This is shown on in Figure 5. 1(a) where, if the population density exceeds the fixed carrying capacity, the population growth rate declines. In this case, it should be expected that density would be correlated with population growth. In contrast, in unstable environments, the carrying capacity is subject to change. Population densities are less likely to exceed the carrying capacity

because environmental instability prevents unhindered growth. Therefore, populations remain in the ‘density vague’ region, as shown in Figure 5. 1(b), where there is little association between density and population growth. For example, Coulson *et al.* (2001) found that the strength of associations with density in Soay sheep were functionally related to weather events (Coulson *et al.*, 2001). During phases of bad weather, “the [Soay sheep] population never reaches a large enough size for dramatic density-dependent declines to occur” (Coulson *et al.*, 2001). In other words, when the environment is unstable, populations remain in the ‘density vague’ region and density dependence is not detectable. As highlighted by Krebs (2002), the most appropriate response to this is not to abandon the concept of density-dependent population regulation, but to reconsider the phenomenon in a mechanistic way (Krebs, 2002).

2) The size and range of a species may affect the detectability of associations between population density and growth. Indeed, it has already been suggested that environmental change has a stronger association than density with population growth in smaller species (Stearns, 1992). For mosquitoes, the carrying capacity of the environment is highly spatially heterogeneous over small geographic scales, as demonstrated for *Ae. polynesiensis* in Chapter 4. Mosquitoes can oviposit in artificial containers, tree holes, rock holes, crab burrows and irrigation systems, all in close proximity and variable in quantity. Each habitat type has a different nutritional profile and therefore a different carrying capacity. In addition, adult mosquito migration distances are thought to be quite short (Gillies & Wilkes, 1969; Bidlingmayer, 1994; Hapairai *et al.*, 2010), making life history traits susceptible to micro-environments and micro-climates. It is perhaps unsurprising that the detection of patterns of density dependence in mosquitoes – and other insect species – has been challenging when the carrying capacity of their environment is not fixed but heavily fragmented. These

landscapes are, perhaps, incomparable to those exploited by large mammals, where individuals are not subject to variation at the micro-scale and the carrying capacity is more spatially homogeneous.

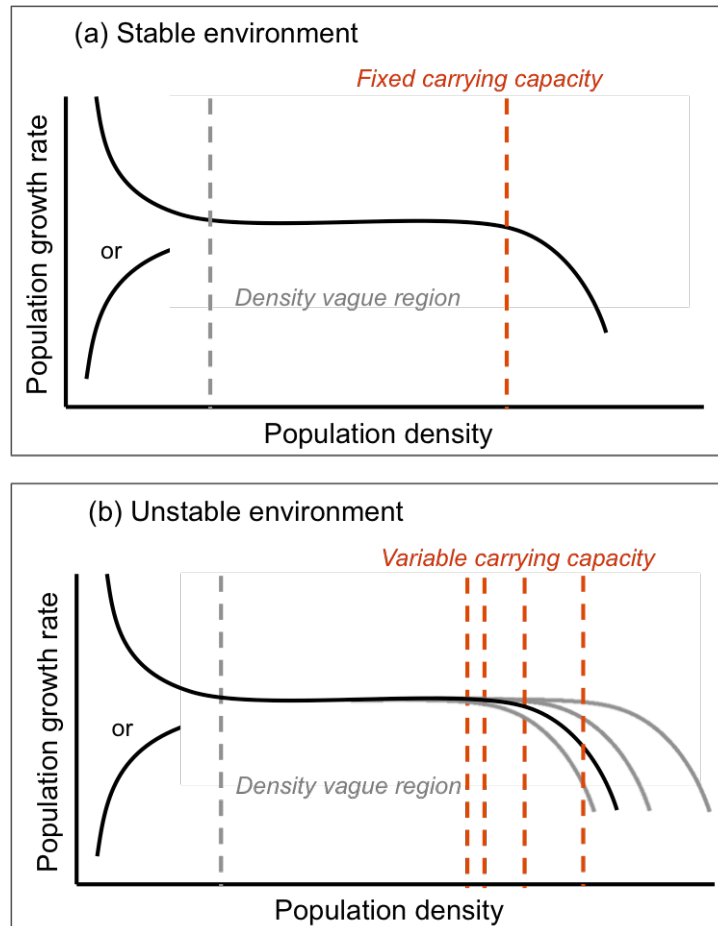


Figure 5. 1. Relationship between population density and the population growth rate. Figure is adapted from Strong (1986). Solid lines represent the association between population density and population growth. At low densities, population growth can either be positively or negatively associated with increasing density. Grey dashed lines indicate the lower limit of the 'density vague' region. Within this region, density has little or no association with population growth. Movement within this region is affected by external environmental factors. Red dashed lines on the right hand side represents the upper limit of the 'density vague' region and the environmental carrying capacity, as labelled. The carrying capacity corresponds to the largest possible population size than a given environment can support. Subfigure (a) represents a stable environment where the carrying capacity remains constant. Subfigure (b) represents an unstable environment where the carrying capacity is variable, as shown by multiple red dashed lines.

3) The length of a species' generation time relative to the sampling frequency can affect the likelihood of detecting associations between traits in one generation and a subsequent generation. Whether or not an observation is representative of underlying



population dynamics depends upon the time scales over which a population changes. If the time between samples is longer than the generation time, it cannot be easily concluded that the state of the current generation has arisen due to traits of the previous generation as opposed to unmeasured factors between samples. The importance of sampling frequency in mosquito ecology has been highlighted (Reisen & Pfuntner, 1987; Reisen & Lothrop, 1999; Reisen *et al.*, 1999, 2000; Zhang *et al.*, 2013), however most empirical studies have continued to carry out mosquito sampling with weekly frequency (Jian *et al.*, 2014).

I do not suggest that the use of density as a surrogate measure for more complex mechanisms should be rejected. However, the use of density as a surrogate measure should follow careful assessment of the ecology of the species under investigation. Density dependence theory that has been effective in large mammals is unlikely to be as successful in many invertebrates for the reasons outlined above. It should also be noted that climate and land use change are likely to unbalance previously stable environments. As a consequence, density may cease to be a reliable surrogate measure for ecological mechanisms in some species. There are multiple factors that contribute to population regulation, one of which is population density. The relative importance of population density for population regulation may change over time in response to environmental change and ecologists should be prepared to adopt new analytic methods in such an eventuality.

### **Spatially non-linear responses to environmental change**

In Chapter 4, I presented a discrete-space dispersal model of *Ae. polynesiensis* population dynamics in response to environmental heterogeneity in oviposition site

availability. A reduction in the number of oviposition sites had spatially non-linear effects upon mosquito population sizes depending upon whether the reduction was localised or randomly distributed through space. Whilst spatially localised reductions in oviposition site availability resulted in substantial local decreases in *Ae. polynesiensis* population sizes, these effects were spatially restricted. In contrast, randomly distributed reductions in oviposition site availability provided a lower level of suppression across a wider geographic area.

The spatially non-linear effects of environmental change upon population distributions have been documented for other species. For example, a reduction in Arctic sea ice has caused a decline in Pacific walrus (*Odobenus rosmarus divergens*) numbers in the deep waters of the Arctic Basin (Jay *et al.*, 2012). Elsewhere, Pacific walruses have begun congregating on shore in large numbers, a phenomenon that has not historically occurred (Fay *et al.*, 1984). Biota that are capable are expected to migrate in order to track the shift in climatic zones as a result of climate change in order to stay within a suitable habitat range (Hersteinsson & Macdonald, 1992; Hughes, 2000; Walther *et al.*, 2002; Chen *et al.*, 2011; Hetem *et al.*, 2014). Destruction of a habitat does not always entail the removal of the species. Numerous non-linear effects of habitat change can occur, including migration to new suitable habitats, overcrowding in remaining habitats or adaptation to environmental change. Adaptation to encroachment upon ancestral habitats has been observed in *Aedes* mosquitoes, as already noted (Powell, 2013).

The above considerations have important consequences for mosquito control programs. Environmental control programs such as larval source management (LSM), insecticidal spraying or copepod release may reduce population sizes at the

intervention site but have either no effect or unintended consequences elsewhere due to adaptation to new habitats or adoption of new dispersal behaviours.

## **Future directions**

### **Within-vector virus dynamics**

This thesis has focussed on the effects of environmental change upon mosquito ecology. The results have been placed in an epidemiological context, but the effects of environmental change upon mosquito-borne viruses and parasites themselves have not been discussed. Temperature is probably the most important extrinsic variable affecting the transmissibility of arboviruses (Mellor, 2000). Temperature affects mosquito longevity, thereby altering a mosquito's capacity to survive the extrinsic incubation period (EIP). Temperature is also thought to affect the replication and molecular dynamics of arboviruses (Lambrechts *et al.*, 2011; Samuel *et al.*, 2016) and the development rate of malaria parasites within the mosquito host (Paajimans *et al.*, 2012). The precise effects of temperature upon disease transmissibility are likely to vary with virus-vector combinations.

Comprehensive models of within-vector virus and parasite dynamics have been used to explore the effects of temperature upon transmission potential (Paajimans *et al.*, 2013). However, few models have considered the thermal responses of parasite and virus biology to climate change (Mordecai *et al.*, 2017) and fewer still have done so on a spatial scale. This could be a valuable extension to models such as that presented in Chapter 2.

## Interdisciplinary research

Empirical studies are indispensable for elucidating complex aspects of mosquito ecology and parameterising mathematical models. Likewise, mathematical models can re-interpret empirical data, provide new hypotheses to test empirically, and test hypotheses which are challenging to consider empirically. The integration of mathematical and empirical studies in mosquito ecology is crucial for a holistic understanding of the study system. Below I briefly discuss ways in which modellers and empiricists may be able to work in a more interdisciplinary manner in mosquito ecology.

First, empirical investigation has the capacity to fill many of the gaps encountered by mathematical modelling. As noted in Chapter 3, empirical studies of density dependence in mosquitoes adopt a diverse range of feeding regimes such as plant matter, fish food and liver powder (Schneider *et al.*, 2000; Agnew *et al.*, 2002; Reiskind & Lounibos, 2009; Gilles *et al.*, 2011; Banerjee *et al.*, 2017). Whilst it is important to understand the effects of different nutritional profiles, a lack of standardisation between studies makes data aggregation for parameterisation of mathematical models challenging. In addition, whilst some parameters in mosquito population models are well established, there is a distinct lack of empirical information for others, notably mosquito fecundity. Future empirical studies would be well placed to choose some of their focus by reference to what is both lacking and required to parameterise mathematical models.

Second, mathematical models must pay careful attention to the empirical literature in order to properly characterise mosquito ecology. Robust empirical investigation is paramount to understand complex aspects of mosquito ecology and test hypotheses

that mathematical studies cannot. Important ecological features such as host preferences (Lehane, 2005; Takken & Verhulst, 2013) and interspecific interactions (Juliano, 1998) have been detailed and described by empirical research, and have subsequently been integrated into informative mathematical models (Simpson *et al.*, 2012; Paton & Bonsall, 2019). However, this is not true of all ecological features in mosquitoes; as highlighted in Chapter 4, dispersal behaviours of mosquitoes are one phenomenon that has been comprehensively documented by empirical research (Reuben, 1987; Reiter *et al.*, 1995; Muir & Kay, 1998; Tsuda *et al.*, 2001; Winskill *et al.*, 2015) but not yet readily assessed by mathematical models (Lutambi *et al.*, 2013). Mathematical models must carefully consult the empirical literature to identify key ecological processes for their study question.

## **Integrated models**

As discussed above, environmental change is unlikely to act independently upon any given species without implications for the wider ecosystem. There are few models of mosquito populations that have considered the role of mosquitoes within their ecosystem.

The topic which has perhaps been most widely discussed is that of interspecific interactions between mosquito species (Juliano, 1998, 2009). The interaction between *Ae. aegypti* and *Ae. albopictus* has been of particular focus. These species are known to compete in the wild; indeed, *Ae. albopictus* have widely displaced *Ae. aegypti* in the USA (O'Meara *et al.*, 1995; Lounibos *et al.*, 2011). This interspecific competition gives rise to different patterns of coexistence and competitive exclusion (Lounibos & Juliano, 2018). The outcomes of interspecific competition are believed to be

environmentally dependent. A notable model of interaction between *Ae. aegypti* and *Ae. albopictus* was developed by Paton & Bonsall (2019), who observe that reproductive interference between the two species has epidemiological consequences which are modified by host availability (Paton & Bonsall, 2019). Costanzo et al. (2005) demonstrated that temperature can modify the outcome of interspecific competition between *Ae. aegypti* and *Ae. albopictus* (Costanzo *et al.*, 2005). However, the effects of climate and environmental heterogeneity for competitive outcomes in mosquitoes have not been comprehensively explored. Models considering these processes would be a valuable contribution to the field. The interaction of mosquitoes with other species such as predatory fish, copepods and other aquatic species that predate or compete with mosquito larvae could benefit from further empirical and theoretical research (Quiroz-Martínez & Rodríguez-Castro, 2007; Louca *et al.*, 2009; Dida *et al.*, 2015). Mosquitoes may be affected as much by the distribution of other species as they are by environmental factors.

## **Conclusion**

This thesis has explored the effects of environmental change upon mosquito populations using an interdisciplinary mathematical, laboratory and field approach. The findings suggest that changes in climate over the coming decades will facilitate higher *Ae. aegypti* mosquito population densities in most regions of Brazil, which will have epidemiological consequences for mosquito-borne disease. Changes in climate will also disrupt seasonal mosquito cycles, possibly decoupling them from other processes within their ecosystem. The importance of mechanistic empirical studies of mosquito life-history traits for accurate mathematical models has been emphasised;

laboratory results demonstrated that environmental factors such as nutrient availability have non-negligible effects on density dependence. Further, this thesis has presented a methodological framework for modelling mosquitoes in heterogeneous environments, which combines field data, remote sensing and mathematical modelling. The results showed that the spatial heterogeneity in the distribution of resources substantially influences mosquito distributions. In addition, environmental change was shown to have non-linear effects upon mosquito populations; therefore, mosquito control strategies must carefully balance spatial effects and net effects. Further work would be beneficial to integrate these results with epidemiological models and inform public health policy.





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# Appendices



# Appendix A

## Supplementary material for Chapter 2

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## **A.1. Derivation of survival equations**

The instantaneous, stage specific survival can be written as:

$$S_i(t) = e^{-\int_{t-\tau_i(t)}^t \mu_i(t) dt} \quad (\text{A.1})$$

where  $i = \{J, A\}$ ,  $J$  and  $A$  denote juvenile and adult mosquito populations, respectively,  $\mu_i(t)$  is the stage-specific mortality and  $\tau_i$  is the stage-specific development time. First, the derivative of Equation (A.1) is taken to give:

$$\frac{dS_i(t)}{dt} = S_i(t) \left[ \frac{d}{dt} \left( -\int_{t-\tau_i(t)}^t \mu_i(t) dt \right) \right] \quad (\text{A.2})$$

which is further evaluated as:

$$\frac{dS_i(t)}{dt} = S_i(t) \left[ \frac{d}{dt} (t - \tau_i(t)) \mu_i(t - \tau_i(t)) - \frac{dt}{dt} \mu_i(t) \right] \quad (\text{A.3})$$

and subsequently as:

$$\frac{dS_i(t)}{dt} = S_i(t) \left[ \left( 1 - \frac{d\tau_i(t)}{dt} \right) \mu_i(t - \tau_i(t)) - \mu_i(t) \right] \quad (\text{A.4})$$

Since  $\frac{d\tau_i(t)}{dt} = 1 - \left( \frac{g_i(t)}{g_i(t - \tau_i(t))} \right)$ , then this can be substituted into equation (A.4)

to give:

$$\frac{dS_i(t)}{dt} = S_i(t) \left[ \left( 1 - 1 + \frac{g_i(t)}{g_i(t - \tau_i(t))} \right) \mu_i(t - \tau_i(t)) - \mu_i(t) \right] \quad (\text{A.5})$$

which simplifies to

$$\frac{dS_i(t)}{dt} = S_i(t) \left[ \frac{g_i(t) \mu_i(t - \tau_i(t))}{g_i(t - \tau_i(t))} - \mu_i(t) \right] \quad (\text{A.6})$$

## **A.2. Temperature and precipitation variation**

Table A. 1. Parameter values and 95% confidence intervals for non-linear models describing the relationships between temperature and *Aedes aegypti* life history traits. Model forms are shown in Equations (2.8)-(2.14). It should be noted that for parameters taken for Mordecai et al. (2017) (adult fecundity and juvenile survival), 95% credible intervals are given due to the Bayesian framework used to derive parameters. 95% confidence intervals are not given for juvenile mortality because juvenile mortality was calculated using  $\mu_j(t) = \ln(S_j(t))/\tau_j(t)$  as per Equation (2.11) before fitting a polynomial function. The variability in  $\mu_j(t)$  is therefore captured by the 95% confidence intervals on parameters describing  $S_j(t)$  and  $\tau_j(t)$ . Where parameters are determined by equations in the main text, this is denoted by “Eq.” followed by the equation number as used in the main text for Chapter 2.

| Trait                                             | Parameter      | Value                  | 95% CI                |                       | Source                               |
|---------------------------------------------------|----------------|------------------------|-----------------------|-----------------------|--------------------------------------|
|                                                   |                |                        | 2.5%                  | 97.5%                 |                                      |
| Adult fecundity, $b$                              | $c_b$          | $8.56 \times 10^{-3}$  | $3.78 \times 10^{-3}$ | $1.41 \times 10^{-2}$ | [1] &<br>Eq. (2.8)                   |
|                                                   | $T_{0b}$       | 14.58                  | 8.08                  | 20.60                 |                                      |
|                                                   | $T_{Mb}$       | 34.61                  | 34.00                 | 35.77                 |                                      |
| Adult mortality, $\mu_A$                          | $k$            | 36.55                  | 32.27                 | 23.85                 | [2–10] &<br>Eq. (2.9)                |
|                                                   | $\gamma$       | 25.17                  | 23.85                 | 26.50                 |                                      |
|                                                   | $\sigma$       | 7.31                   | 5.90                  | 8.71                  |                                      |
| Juvenile development rate, $g_j$                  | $\beta_{0g}$   | 133.53                 | 113.45                | 153.61                | [2,7,17,18,<br>9–16] &<br>Eq. (2.10) |
|                                                   | $\beta_{1g}$   | -8.29                  | -9.90                 | -6.69                 |                                      |
|                                                   | $\beta_{2g}$   | 0.14                   | 0.10                  | 0.17                  |                                      |
| Juvenile survival, $S_j$                          | $c_s$          | $5.99 \times 10^{-3}$  | $6.82 \times 10^{-3}$ | $5.13 \times 10^{-3}$ | [1] &<br>Eq. (2.12)                  |
|                                                   | $T_{0s}$       | 13.56                  | 12.56                 | 14.51                 |                                      |
|                                                   | $T_{Ms}$       | 38.29                  | 37.54                 | 39.02                 |                                      |
| Juvenile mortality, $\mu_j$                       | $\beta_{0\mu}$ | $3.37 \times 10^{-3}$  | -                     | -                     | Eq. (2.13)                           |
|                                                   | $\beta_{1\mu}$ | $-5.88 \times 10^{-2}$ | -                     | -                     |                                      |
|                                                   | $\beta_{2\mu}$ | $4.05 \times 10^{-3}$  | -                     | -                     |                                      |
|                                                   | $\beta_{3\mu}$ | $-1.26 \times 10^{-4}$ | -                     | -                     |                                      |
|                                                   | $\beta_{4\mu}$ | $1.47 \times 10^{-6}$  | -                     | -                     |                                      |
| Density-dependent Juvenile mortality, $\delta(t)$ | $K$            | Eq. 14                 |                       |                       | [19] &<br>Eq. (2.14)                 |
|                                                   | $\lambda$      | $7.5 \times 10^8$      | 2.5                   | 7                     |                                      |
|                                                   | $\omega$       | 4                      | -                     | -                     |                                      |

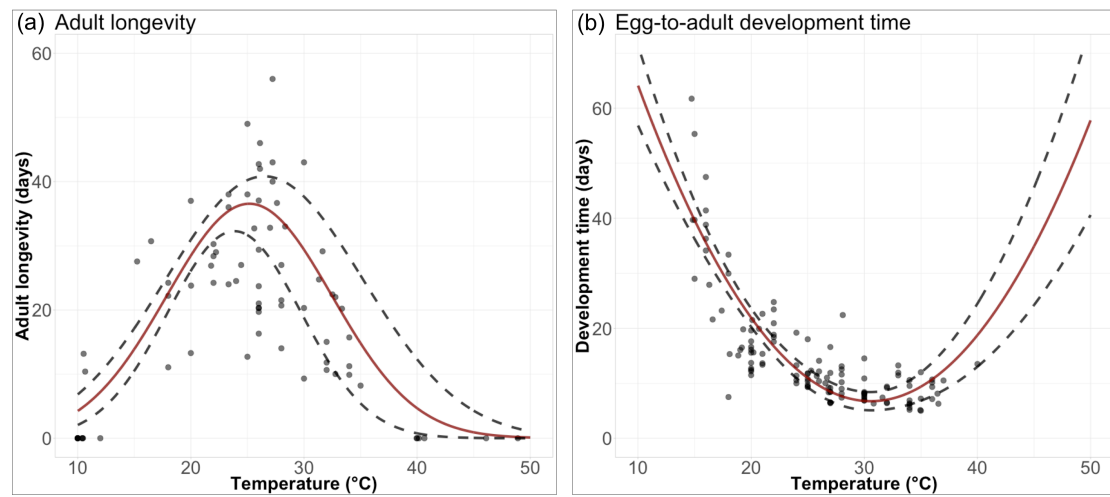


Figure A. 1. Fitted functions and 95% confidence intervals for associations between temperature and (a) adult longevity and (b) egg-to-adult development time. Plots of the fitted functional forms for adult fecundity and egg-to-adult survival can be found in Mordecai et al. (2017), Figure 1.

### **A.3. Juvenile density dependence**

We defined density-dependent juvenile mortality as a function of the existing juvenile density and of precipitation, with juvenile mortality increasing at high densities and low precipitation. This is a similar approach as has been adopted in existing modelling studies of the mosquito life cycle such as Ewing et al. (2016) who use a predator-prey relationship to stipulate increased larval mortality at high larval densities [20]. We observed that temperature alone was insufficient to prevent uncontrolled mosquito population growth in our model. This suggests that other ecological mechanisms are required by mathematical models to accurately predict mosquito dynamics. Many mechanisms of density dependence have been proposed for mosquito larvae including resource limitation, chemical interference and cannibalism [12,21,22]. Exploration of these mechanisms was beyond the scope of this paper; we used parameter  $\lambda$  to control the size of the carrying capacity, as influenced by precipitation, and therefore the density-dependent mortality at a given time. We conducted sensitivity analysis on parameter  $\lambda$  and observed that variation in this parameter affected the upper limit of predicted *Ae. aegypti* density but did not notably affect trends in *Ae. aegypti* density or ratios of *Ae. aegypti* density between time points or locations. Therefore our results expressed as percentage increase in *Ae. aegypti* density hold true, irrespective of the value of parameter  $\lambda$ . Mechanisms of density-dependent population regulation are further explored in Chapter 3.

#### **A.4. LIRAA sampling protocol**

*Ae. aegypti* occurrence data used in this study come from comprehensive entomological surveillance conducted by the Brazilian Ministry for Health. The sampling methodology followed the LIRAA protocol which is described by the Brazilian Ministry of Health [23–25]. LIRAA is used in all municipalities regardless of size. The sampling methodology for each municipality is determined according to the municipality population density and the number of buildings. Urban areas within municipalities were divided into strata with comparable socioeconomic characteristics to achieve homogeneity in each stratum. Strata have between 8,100-12,000 premises each depending on the municipality population density.

Samples were collected using a cluster sampling approach with blocks as a primary unit of sampling and buildings as a secondary unit. One can imagine LIRAA as establishing a spatial mesh with a block to be inspected at each intersection. Within the sampling block, buildings are inspected. Each block falls within a stratum. An independent sample is drawn from within each block, with the sample size being determined by the stratum size. In this way, LIRAA controls well for sampling effort.

The LIRAA protocol generates various indices describing levels of mosquito infestation [23–25]. We used the building index – the proportion of buildings infested – as a response variable to model *Ae. aegypti* occurrence probability due to spatial heterogeneity in anthropogenic variables.

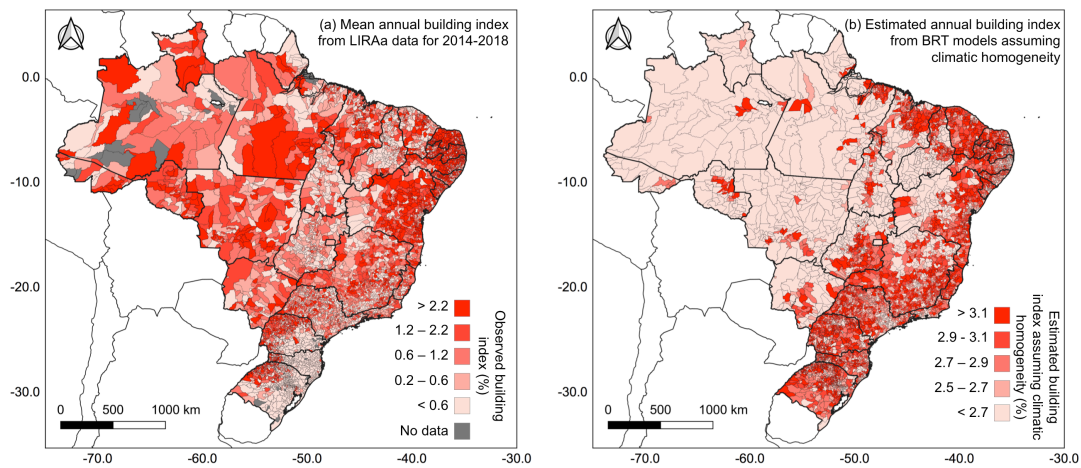


Figure A. 2. Subfigure (a) displays the median building index for the time period 2014-2018 from entomological surveillance data provided by the Brazilian Ministry for Health using the LIRAA sampling protocol. The building index is the percentage of sampled buildings found to be infested with *Ae. aegypti*. Subfigure (b) displays the estimated building index for 2018 using Boosted Regression Tree (BRT) models. When predicting the building index, climatic predictor variables were held constant in every municipality in order to separate the effects of anthropogenic variables from those of climate.

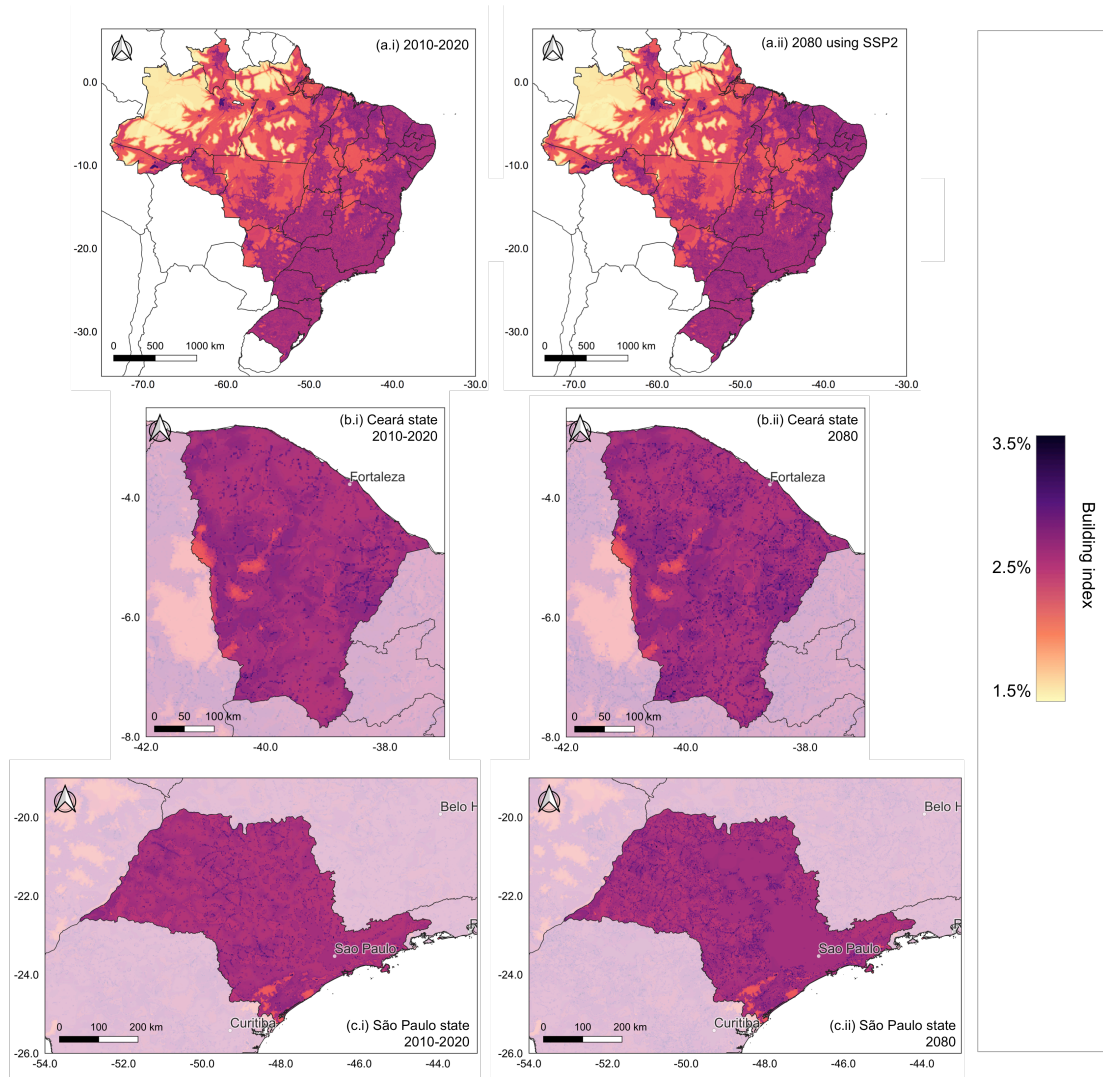


Figure A. 3. Estimated building index for (a) 2010-2020 and (b) 2080 for the whole of Brazil; (c) 2010-2020 and (d) 2080 for Ceará state; (e) 2010-2020 and (f) 2080 for São Paulo state. Comparing subfigures (a) and (b) there are few large-scale changes in the estimated range of *Ae. aegypti*. However, comparing subfigures (c) and (d) or subfigures (e) and (f), it can be observed that changes in population density and urban extent result in small-scale changes in *Ae. aegypti* occurrence probability (this is shown by an increase in the number of dark purple/black pixels).

## **A.5. Modified Chelton method for comparison of time series**

The modified Chelton method is outlined by Pyper and Peterman (1998) [26]. In brief, Pyper and Peterman adjusted Chelton's 1984 method [27] by specifying  $N^* - 2$  rather than  $N^*$  degrees of freedom. Pyper and Peterman (1998) observed that this approach offered improved balance between  $N^*$  and Type I error rates [26]. The degrees of freedom,  $N^*$ , was calculated by rearrangement of Equation (1) in Pyper and Peterman (1998) to give

$$N^* = \frac{N}{1 + 2 \sum_{j=1}^{\infty} \left( \frac{N-j}{N} p_{xx}(j) p_{yy}(j) \right)} - 2 \quad (\text{A.7})$$

where  $N$  is the sample size and  $p_{xx}(j)$  and  $p_{yy}(j)$  are the autocorrelations of two time series,  $x$  and  $y$ , at a lag,  $j$ .  $T$ -statistics were calculated by

$$t = r_{xy} \sqrt{\frac{N^*}{1 - r_{xy}^2}} \quad (\text{A.8})$$

where  $r_{xy}$  is the correlation between two time series,  $x$  and  $y$ .  $P$ -values were extracted from the  $t$ -statistics.



## **A.6. Calculation of $R_0$ for dengue fever**

The  $R_0$  of the two-compartment Ross-Macdonald model for dengue fever presented in Equations (2.15)-(2.16) in the main text can be determined as the determinant of the Jacobian matrix of the linearised system. From Equations (2.15)-(2.16), we can write the Jacobian as

$$R_0 = Det \begin{bmatrix} \frac{\partial H}{\partial V} & \frac{\partial H}{\partial V} \\ \frac{\partial V}{\partial H} & \frac{\partial V}{\partial V} \end{bmatrix} \quad (\text{A.9})$$

Then, calculating the partial derivatives:

$$R_0 = Det \begin{bmatrix} aBV(t)\frac{A^*}{2N^*} - r & aB\frac{A^*}{2N^*}(1 - H(t)) \\ aC(1 - V(t)) & aCH(t) - \mu_A^* \end{bmatrix} \quad (\text{A.10})$$

Assuming that dengue invades an entirely healthy population,  $H(t) \rightarrow 0$  and  $V(t) \rightarrow 0$ . The adult *Ae. aegypti* population,  $A(t)$ , human population,  $N(t)$ , and adult *Ae. aegypti* mortality,  $\mu_A(t)$ , are assumed to be at equilibrium ( $A(t) = A^*$ ,  $N(t) = N^*$  and  $\mu_A(t) = \mu_A^*$ ). Therefore  $R_0$  is described by

$$R_0 = Det \begin{bmatrix} -r & \frac{aBA^*}{2N^*} \\ aC & -\mu_A^* \end{bmatrix} \quad (\text{A.11})$$

The parameter estimates used to calculate the stability of the disease free state,  $R_0$ , are shown in Table A.2.

Table A. 2. Parameters, parameters values and their source for calculation of  $R_0$  for dengue fever.

| Parameter | Description                             | Value | Source |
|-----------|-----------------------------------------|-------|--------|
| $a$       | <i>Ae. aegypti</i> biting rate          | 0.50  | [28]   |
| $B$       | Vector to human transmission efficiency | 0.38  | [28]   |
| $C$       | Human to vector transmission efficiency | 0.38  | [28]   |
| $r$       | Human recovery rate                     | 0.17  | [28]   |

### A.7. Seasonal patterns in the *Ae. aegypti* distribution

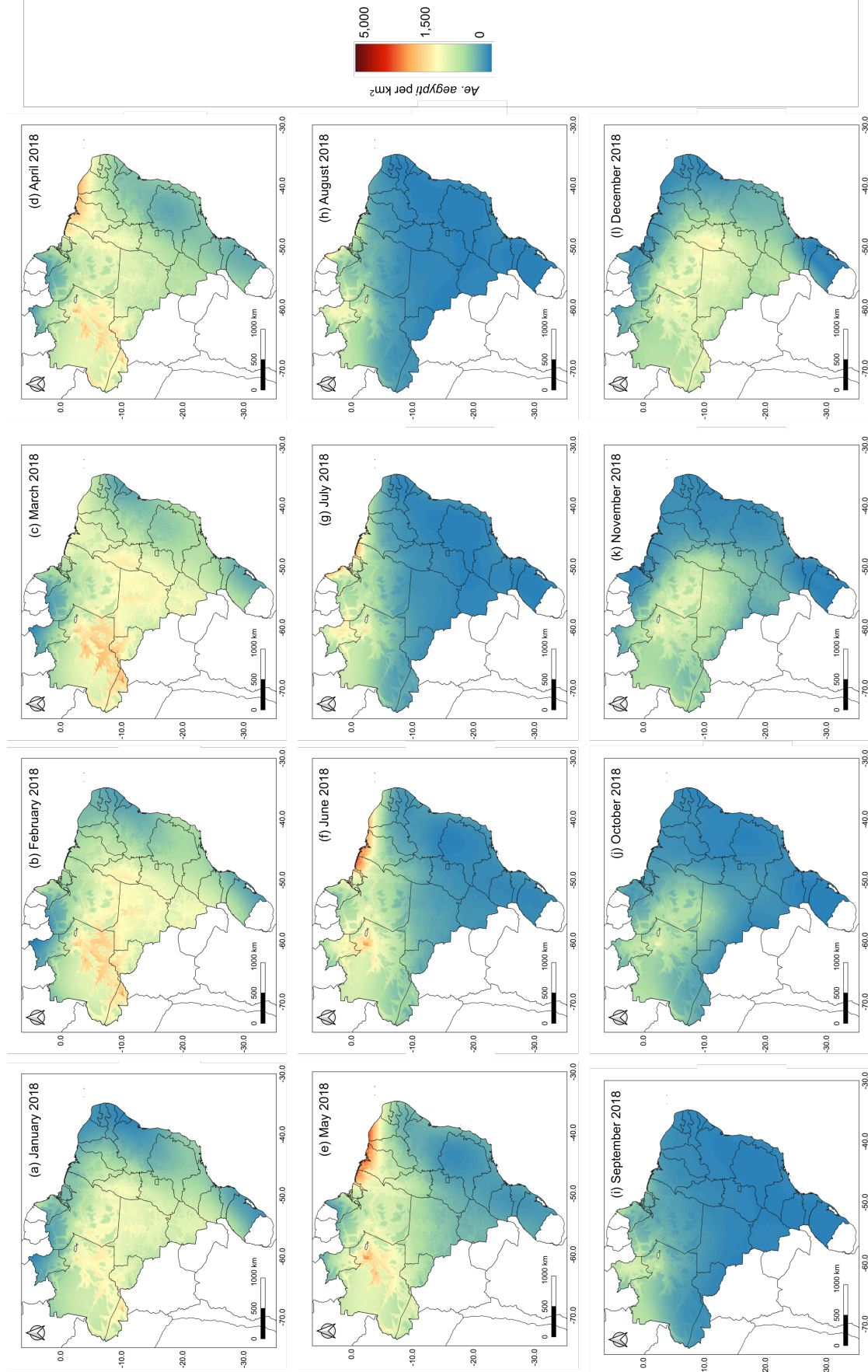


Figure A. 4. Estimated mean monthly *Ae. aegypti* density in 2018. Results are displayed for each month in subfigures (a)-(l). The x- and y-axes display the longitude and latitude, respectively.

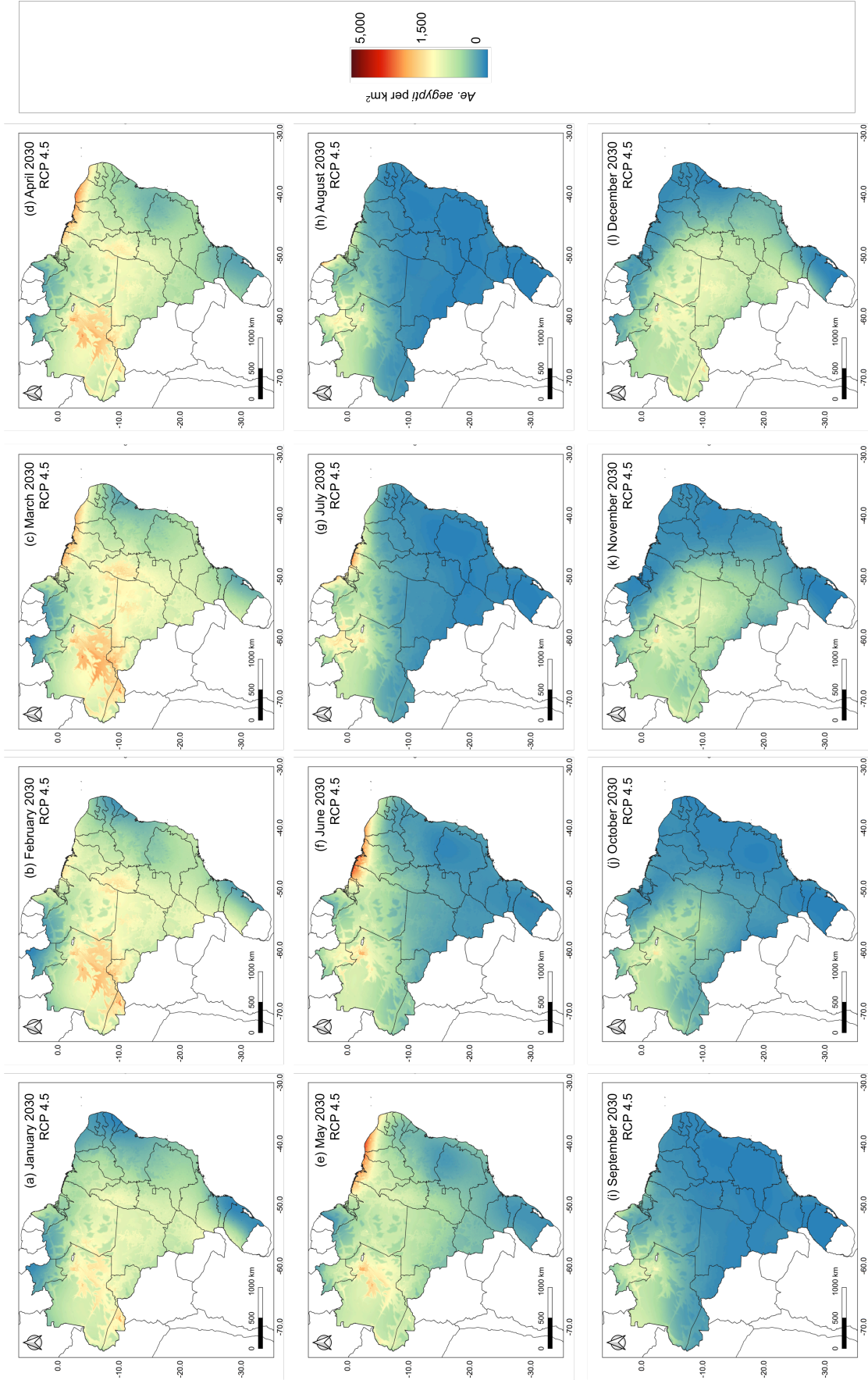


Figure A. 5. Estimated mean monthly *Ae. aegypti* density in 2030 for the RCP 4.5 climate projections. Results are displayed for each month in subfigures (a)-(l). The x- and y-axes display the longitude and latitude, respectively.

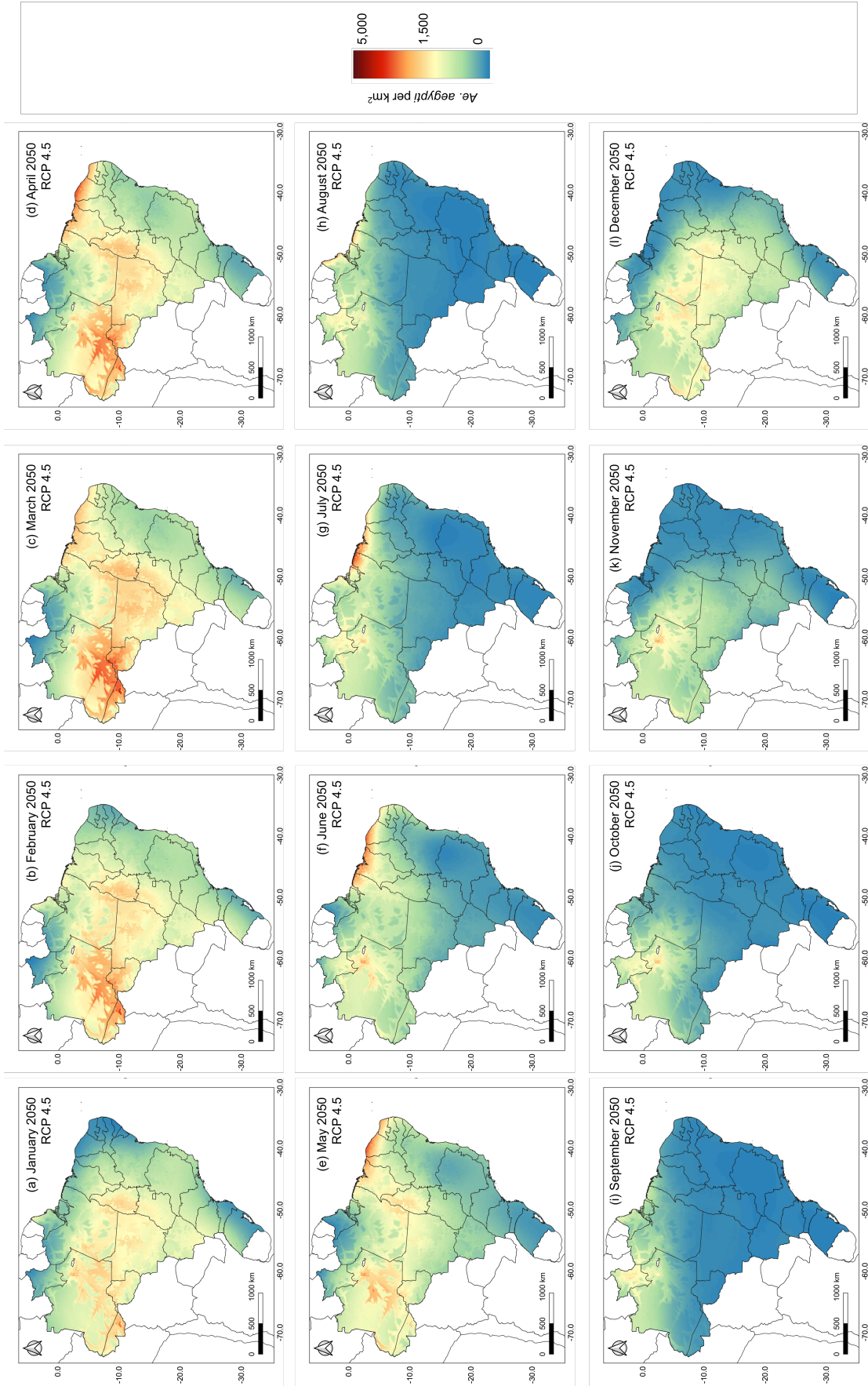


Figure A. 6. Estimated mean monthly *Ae. aegypti* density in 2050 for the RCP 4.5 climate projections. Results are displayed for each month in subfigures (a)-(l). The x- and y-axes display the longitude and latitude, respectively.



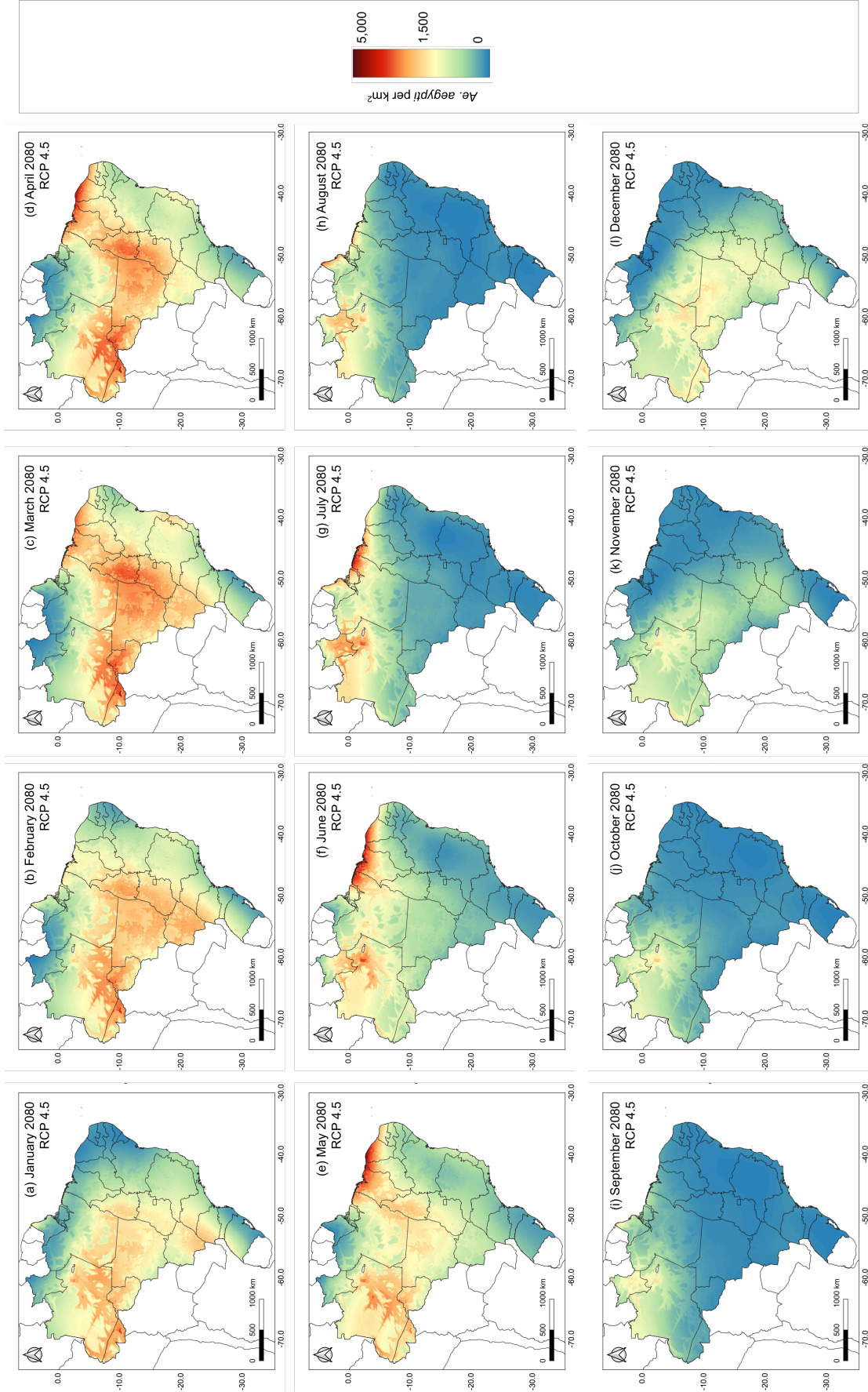


Figure A. 7. Estimated mean monthly *Ae. aegypti* density in 2080 for the RCP 4.5 climate projections. Results are displayed for each month in subfigures (a)-(l). The x- and y-axes display the longitude and latitude, respectively.

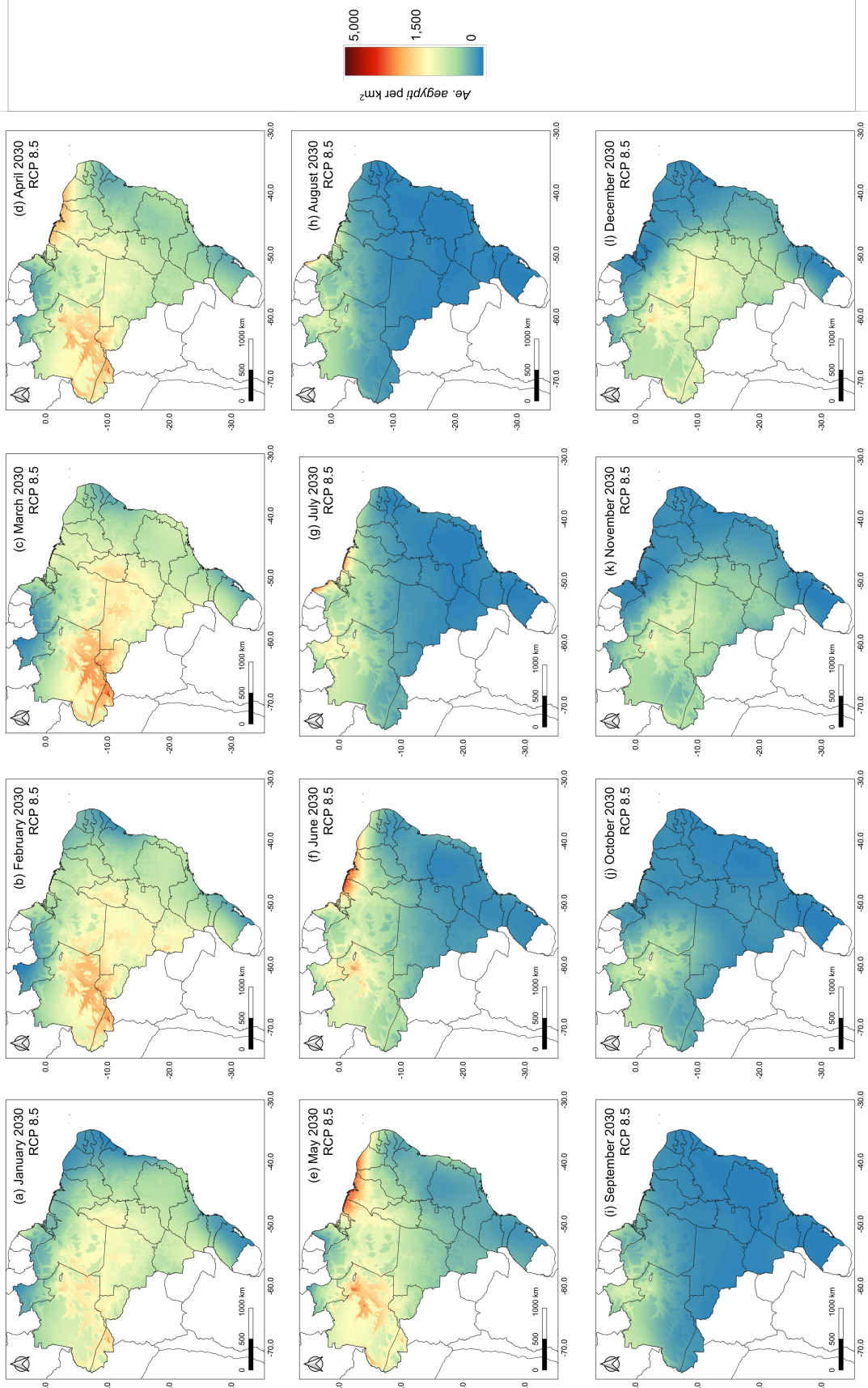


Figure A. 8. Estimated mean monthly *Ae. aegypti* density in 2030 for the RCP 8.5 climate projections. Results are displayed for each month in subfigures (a)-(l). The x- and y-axes display the longitude and latitude, respectively.

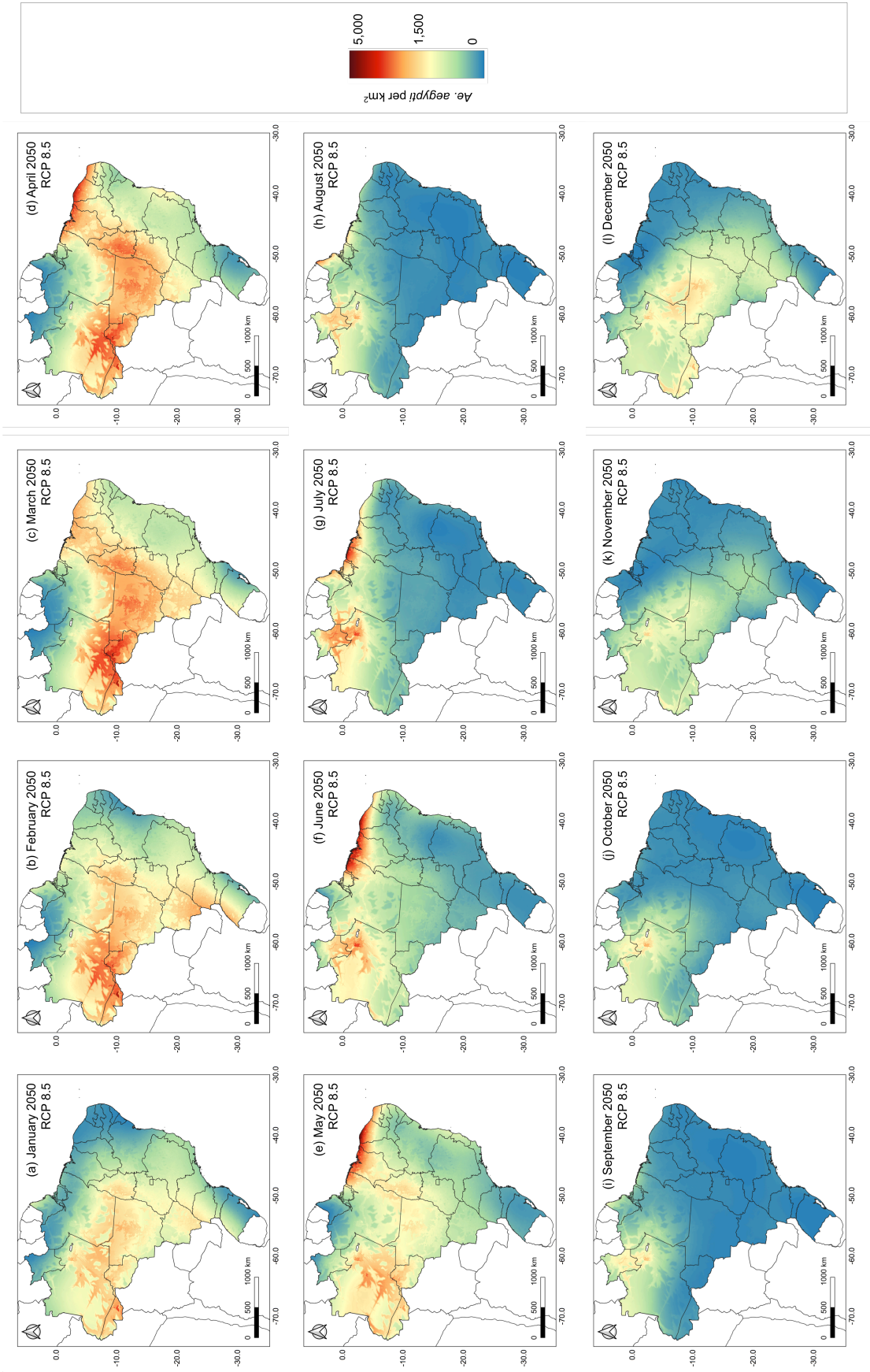


Figure A. 9. Estimated mean monthly *Ae. aegypti* density in 2050 for the RCP 8.5 climate projections. Results are displayed for each month in subfigures (a)-(l). The x- and y-axes display the longitude and latitude, respectively.



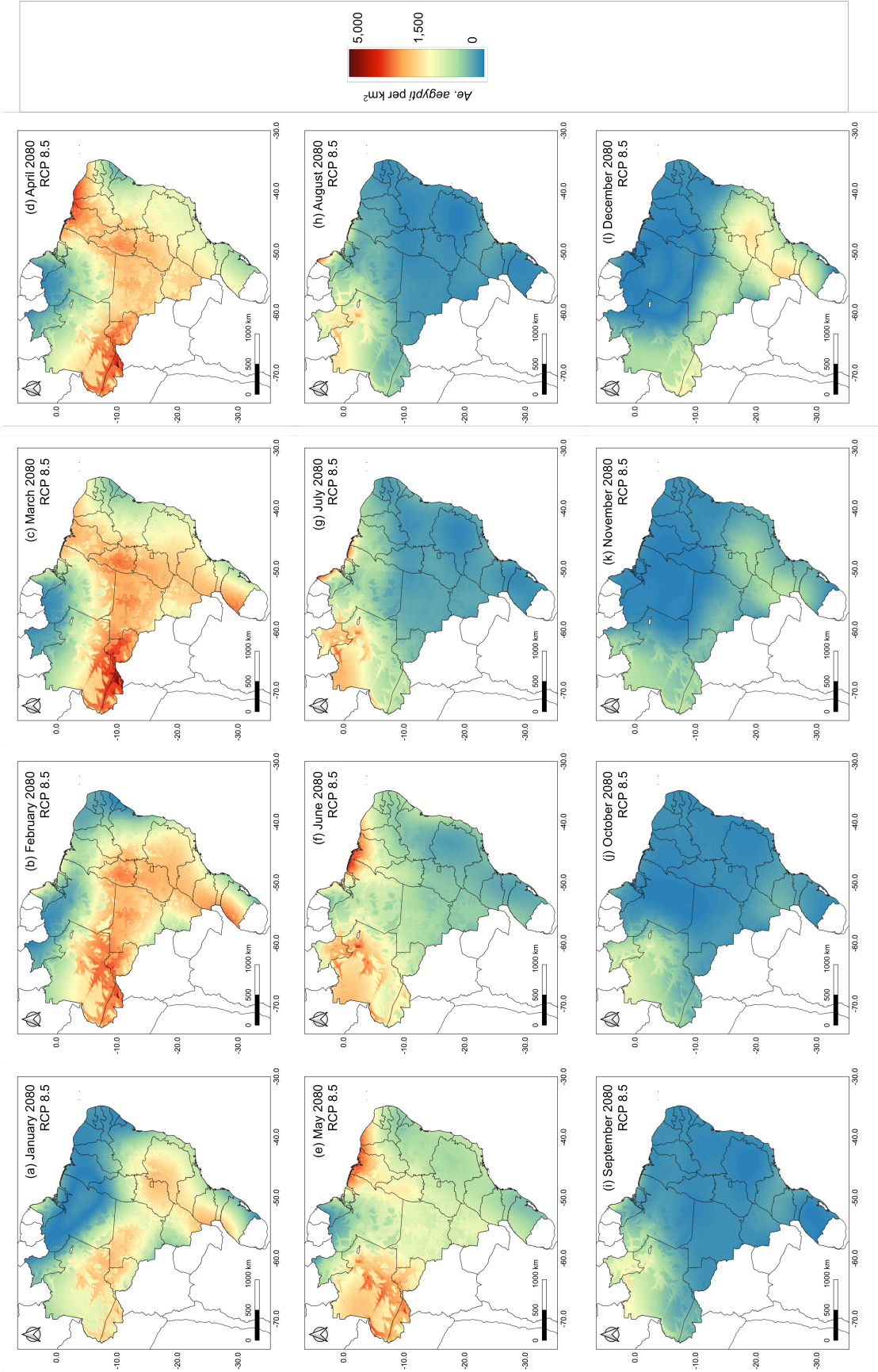


Figure A. 10. Estimated mean monthly *Ae. aegypti* density in 2080 for the RCP 8.5 climate projections. Results are displayed for each month in subfigures (a)-(l). The x- and y-axes display the longitude and latitude, respectively.



## **A.8. Change in mean annual *Ae. aegypti* density by region**

Table A. 3. Estimated fold-change in mean annual *Ae. aegypti* density for each official Brazilian region. Values represent the fold change in *Ae. aegypti* density compared with the annual mean in 2018. The mean annual *Ae. aegypti* density refers to the mean density across the whole year for the whole region. Values are displayed for RCP 4.5 and RCP 8.5 climate projections.

| Region       | Fold change in mean annual <i>Ae. aegypti</i> density from 2018 |         |         |         |         |         |
|--------------|-----------------------------------------------------------------|---------|---------|---------|---------|---------|
|              | 2030                                                            | 2030    | 2050    | 2050    | 2080    | 2080    |
|              | RCP 4.5                                                         | RCP 8.5 | RCP 4.5 | RCP 8.5 | RCP 4.5 | RCP 8.5 |
| North        | 1.03                                                            | 1.06    | 1.17    | 1.23    | 1.28    | 1.11    |
| Northeast    | 1.12                                                            | 1.08    | 1.48    | 1.55    | 1.66    | 1.61    |
| Southeast    | 1.25                                                            | 1.30    | 1.42    | 1.72    | 1.91    | 2.62    |
| Central-West | 1.06                                                            | 1.07    | 1.24    | 1.47    | 1.57    | 1.45    |
| South        | 1.10                                                            | 1.14    | 1.26    | 1.53    | 1.64    | 2.95    |

## **A.9. Change in mean annual *Ae. aegypti* density by state**

Table A. 4. Estimated fold change in mean annual *Ae. aegypti* density for each Brazilian state. Values represent the fold change in *Ae. aegypti* density from 2018. The mean annual *Ae. aegypti* density refers to the mean density across the whole year for the whole state. Values are displayed for RCP 4.5 and RCP 8.5 climate projections. States are displayed in alphabetical order.

| State               | Fold change in mean annual <i>Ae. aegypti</i> density from 2018 |         |         |         |         |         |
|---------------------|-----------------------------------------------------------------|---------|---------|---------|---------|---------|
|                     | 2030                                                            | 2030    | 2050    | 2050    | 2080    | 2080    |
|                     | RCP 4.5                                                         | RCP 8.5 | RCP 4.5 | RCP 8.5 | RCP 4.5 | RCP 8.5 |
| Acre                | 1.03                                                            | 1.16    | 1.29    | 1.42    | 1.47    | 1.68    |
| Alagoas             | 1.21                                                            | 0.87    | 2.06    | 1.90    | 1.75    | 1.68    |
| Ampá                | 1.00                                                            | 1.06    | 1.05    | 0.95    | 1.06    | 0.93    |
| Amazonas            | 1.06                                                            | 1.08    | 1.20    | 1.31    | 1.33    | 1.26    |
| Bahia               | 1.14                                                            | 1.21    | 1.56    | 1.70    | 1.88    | 2.08    |
| Ceaá                | 1.13                                                            | 0.96    | 1.36    | 1.46    | 1.54    | 1.27    |
| Distrito Federal    | 1.20                                                            | 1.20    | 1.43    | 1.63    | 1.90    | 2.15    |
| Espírito Santo      | 1.08                                                            | 1.25    | 1.32    | 1.62    | 1.95    | 2.04    |
| Goiás               | 1.15                                                            | 1.12    | 1.35    | 1.55    | 1.79    | 1.80    |
| Maranhão            | 1.04                                                            | 1.00    | 1.26    | 1.30    | 1.41    | 1.17    |
| Mato Grosso do Sul  | 1.03                                                            | 1.06    | 1.23    | 1.45    | 1.48    | 1.26    |
| Mato Grosso         | 1.03                                                            | 1.04    | 1.19    | 1.44    | 1.59    | 1.58    |
| Minas Gerais        | 1.28                                                            | 1.39    | 1.51    | 1.81    | 2.04    | 2.83    |
| Pará                | 1.00                                                            | 1.01    | 1.10    | 1.07    | 1.14    | 0.78    |
| Paraíba             | 1.23                                                            | 1.02    | 1.69    | 1.69    | 1.56    | 1.45    |
| Paraná              | 1.13                                                            | 1.10    | 1.25    | 1.61    | 1.76    | 2.56    |
| Pernambuco          | 1.18                                                            | 0.99    | 1.72    | 1.65    | 1.63    | 1.57    |
| Piauí               | 1.07                                                            | 1.03    | 1.37    | 1.40    | 1.54    | 1.39    |
| Rio de Janeiro      | 1.16                                                            | 1.19    | 1.25    | 1.34    | 1.46    | 2.06    |
| Rio Grande do Norte | 1.26                                                            | 1.05    | 1.62    | 1.74    | 1.60    | 1.32    |
| Rio Grande do Sul   | 1.12                                                            | 1.20    | 1.28    | 1.55    | 1.61    | 3.28    |
| Rondônia            | 1.03                                                            | 1.13    | 1.26    | 1.52    | 1.50    | 1.53    |
| Roraima             | 1.01                                                            | 0.99    | 1.05    | 1.16    | 1.17    | 1.16    |
| São Paulo           | 1.22                                                            | 1.10    | 1.25    | 1.59    | 1.66    | 2.33    |
| Santa Catarina      | 1.00                                                            | 1.07    | 1.18    | 1.36    | 1.47    | 2.82    |
| Sergipe             | 1.15                                                            | 0.86    | 2.03    | 1.91    | 1.90    | 1.74    |
| Tocantins           | 1.04                                                            | 1.04    | 1.29    | 1.31    | 1.45    | 1.17    |

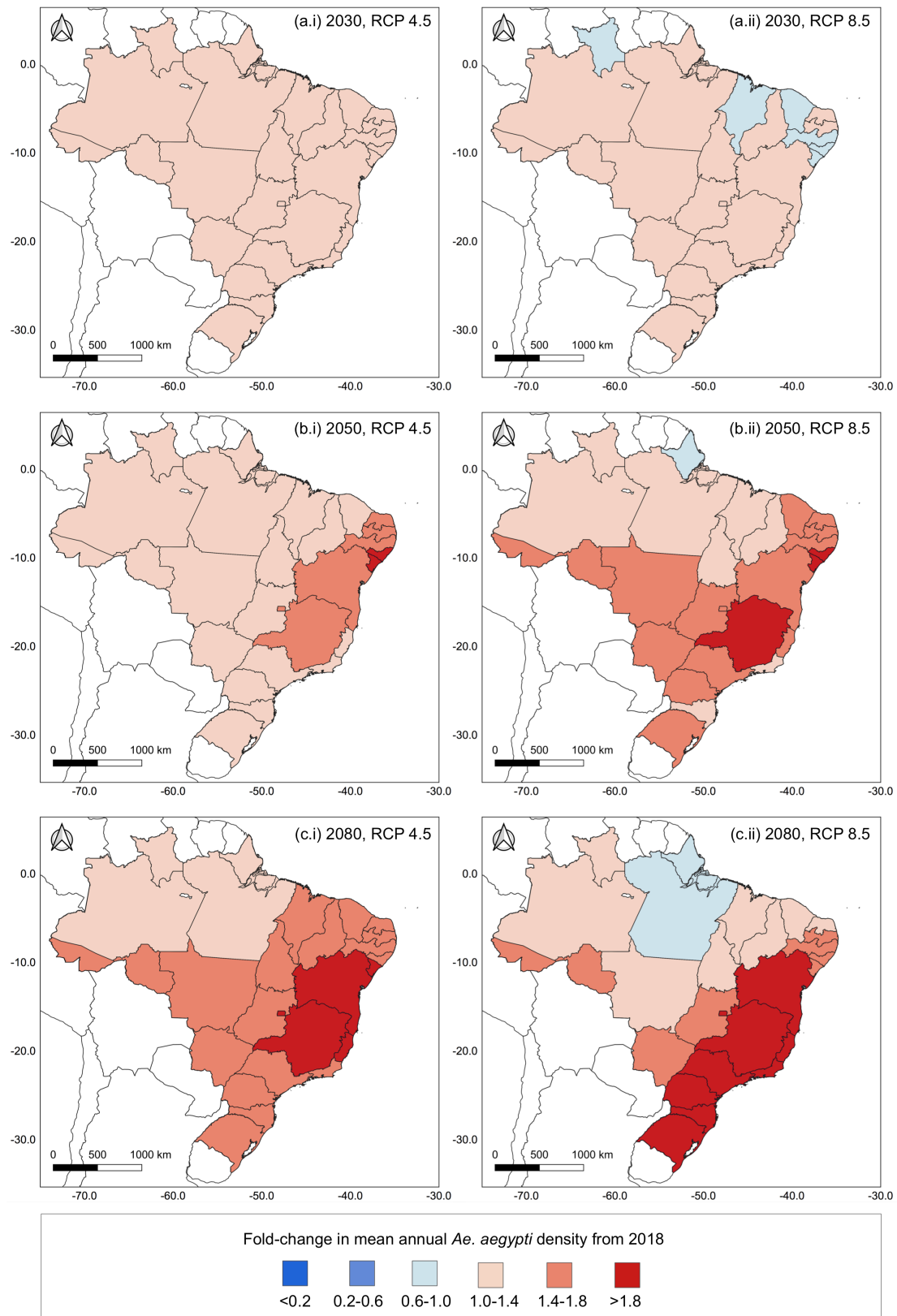


Figure A. 11. Estimated fold-change in mean annual *Ae. aegypti* density from 2018 in each Brazilian state. Fold-changes are shown for: 2030 for (a.i) RCP 4.5 and (a.ii) RCP 8.5; 2050 for (b.i) RCP 4.5 and (b.ii) RCP 8.5; 2080 for (c.i) RCP 4.5 and (c.ii) RCP 8.5 climate projections

## **A.10. Change in mean annual *Ae. aegypti* density in major cities**

Table A. 5. Estimated fold-change in mean annual *Ae. aegypti* density for Brazil's ten largest cities by population size. Values represent the fold change in *Ae. aegypti* density compared with the annual mean in 2018. The mean annual *Ae. aegypti* density refers to the mean density across the whole year. Values are displayed for RCP 4.5 and RCP 8.5 climate projections. Cities are displayed in order of their population size with the largest first.

| City           | Fold change in mean annual <i>Ae. aegypti</i> density from 2018 |                 |                 |                 |                 |                 |
|----------------|-----------------------------------------------------------------|-----------------|-----------------|-----------------|-----------------|-----------------|
|                | 2030<br>RCP 4.5                                                 | 2030<br>RCP 8.5 | 2050<br>RCP 4.5 | 2050<br>RCP 8.5 | 2080<br>RCP 4.5 | 2080<br>RCP 8.5 |
| São Paulo      | 1.11                                                            | 1.13            | 1.15            | 1.34            | 1.29            | 2.30            |
| Rio de Janeiro | 1.17                                                            | 1.23            | 1.25            | 1.39            | 1.48            | 2.05            |
| Brasília       | 1.18                                                            | 1.16            | 1.27            | 1.32            | 1.62            | 1.78            |
| Salvador       | 1.34                                                            | 1.11            | 1.64            | 1.95            | 2.23            | 2.17            |
| Fortaleza      | 0.97                                                            | 1.01            | 1.09            | 1.29            | 1.11            | 1.56            |
| Belo Horizonte | 1.18                                                            | 1.23            | 1.33            | 1.41            | 1.45            | 2.24            |
| Manaus         | 1.04                                                            | 1.08            | 1.15            | 1.17            | 1.19            | 0.94            |
| Curitiba       | 1.05                                                            | 1.20            | 1.12            | 1.26            | 1.32            | 2.45            |
| Recife         | 1.13                                                            | 1.01            | 1.39            | 1.56            | 1.32            | 1.85            |
| Goiânia        | 1.18                                                            | 1.16            | 1.27            | 1.32            | 1.62            | 1.78            |

## **A.11. Locations of Brazilian regions, states and cities**

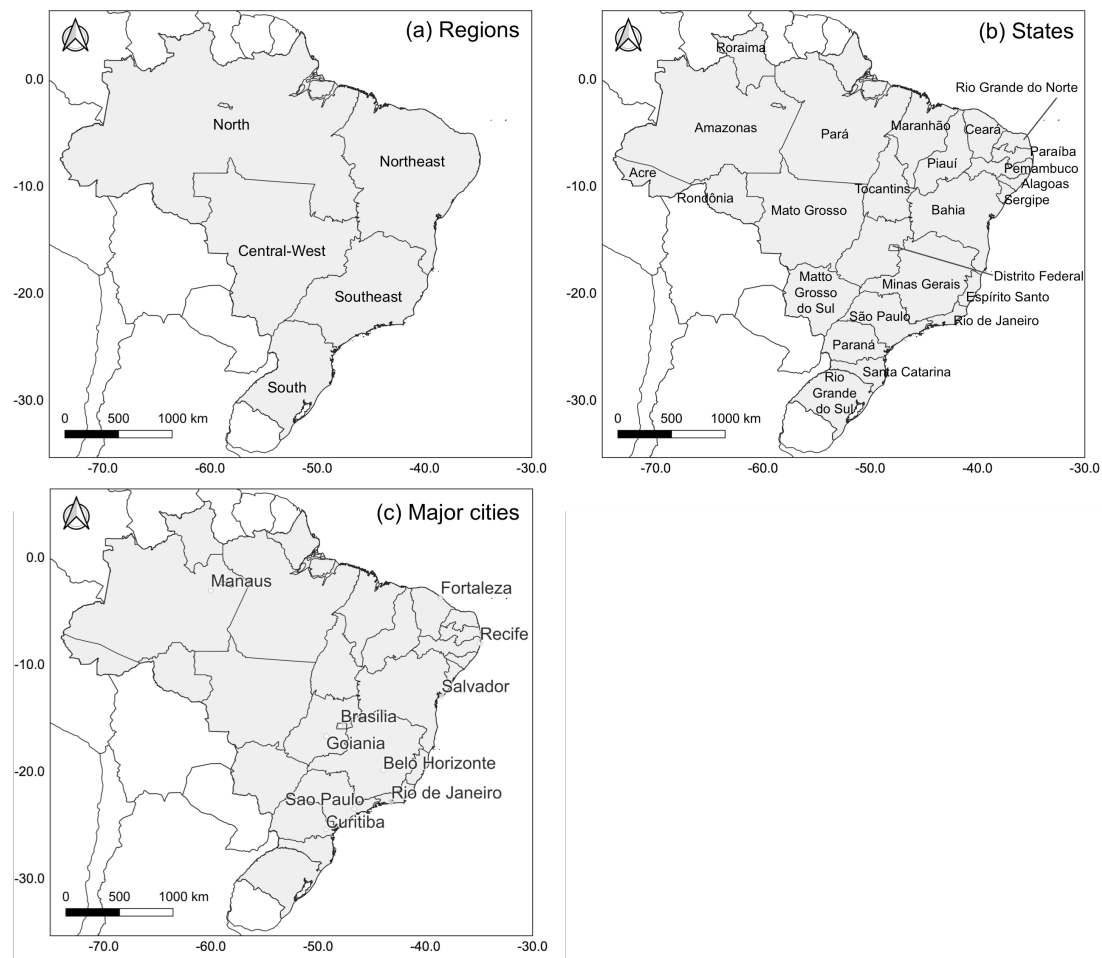


Figure A. 12. Locations of Brazilian (a) regions, (b) states and (c) ten largest cities by population size.

## **A.12. Estimated mosquito density trajectories**

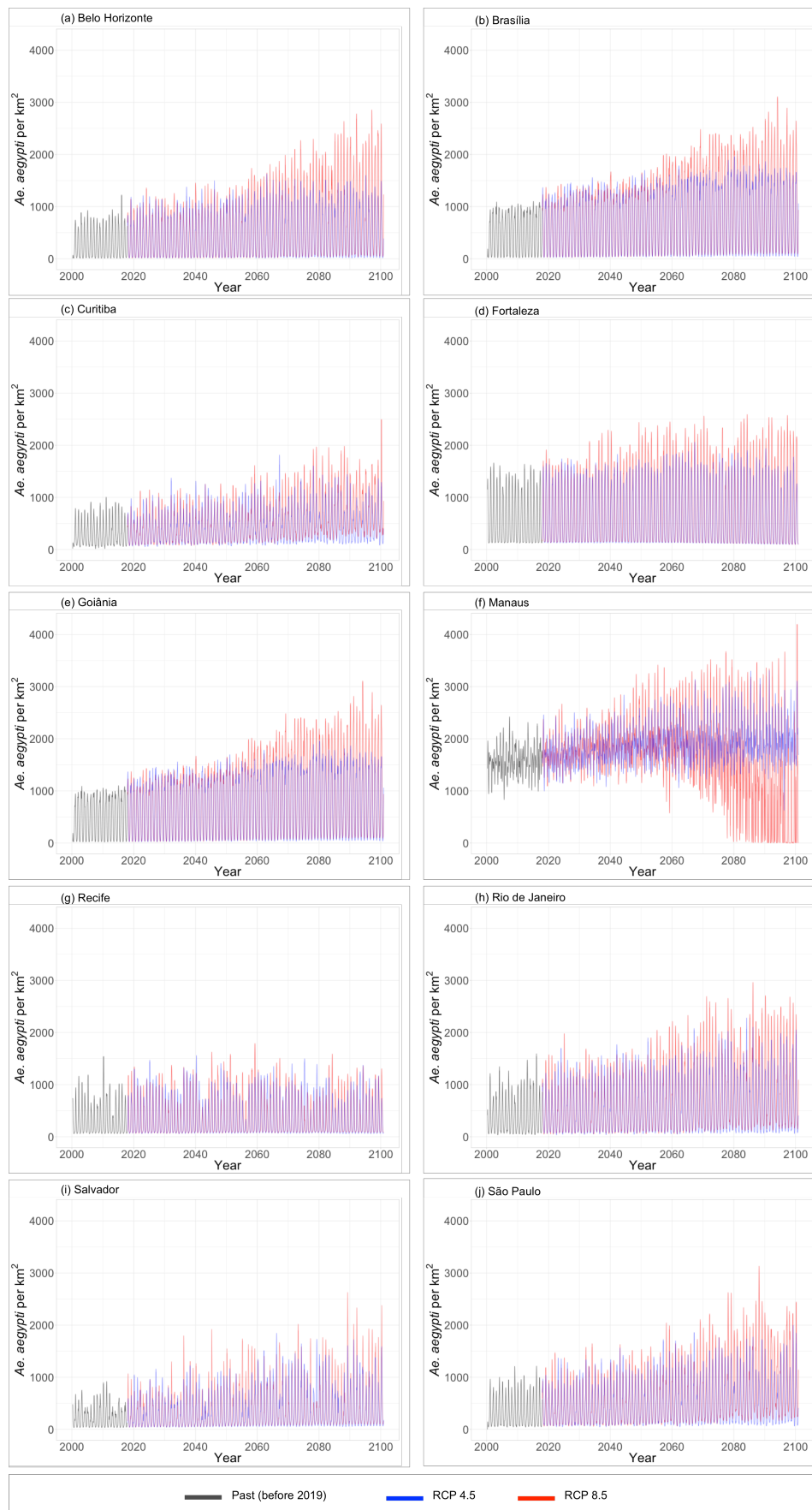


Figure A. 13. Estimated *Ae. aegypti* density (mosquitoes per km<sup>2</sup>) in for Brazil's ten largest cities by population size between 2000 and 2100. Estimates of historical mosquito densities are shown in grey and estimates of future densities are shown in blue and red for RCP 4.5 and RCP 8.5, respectively.

### **A.13. Validation of model predictions against time series**

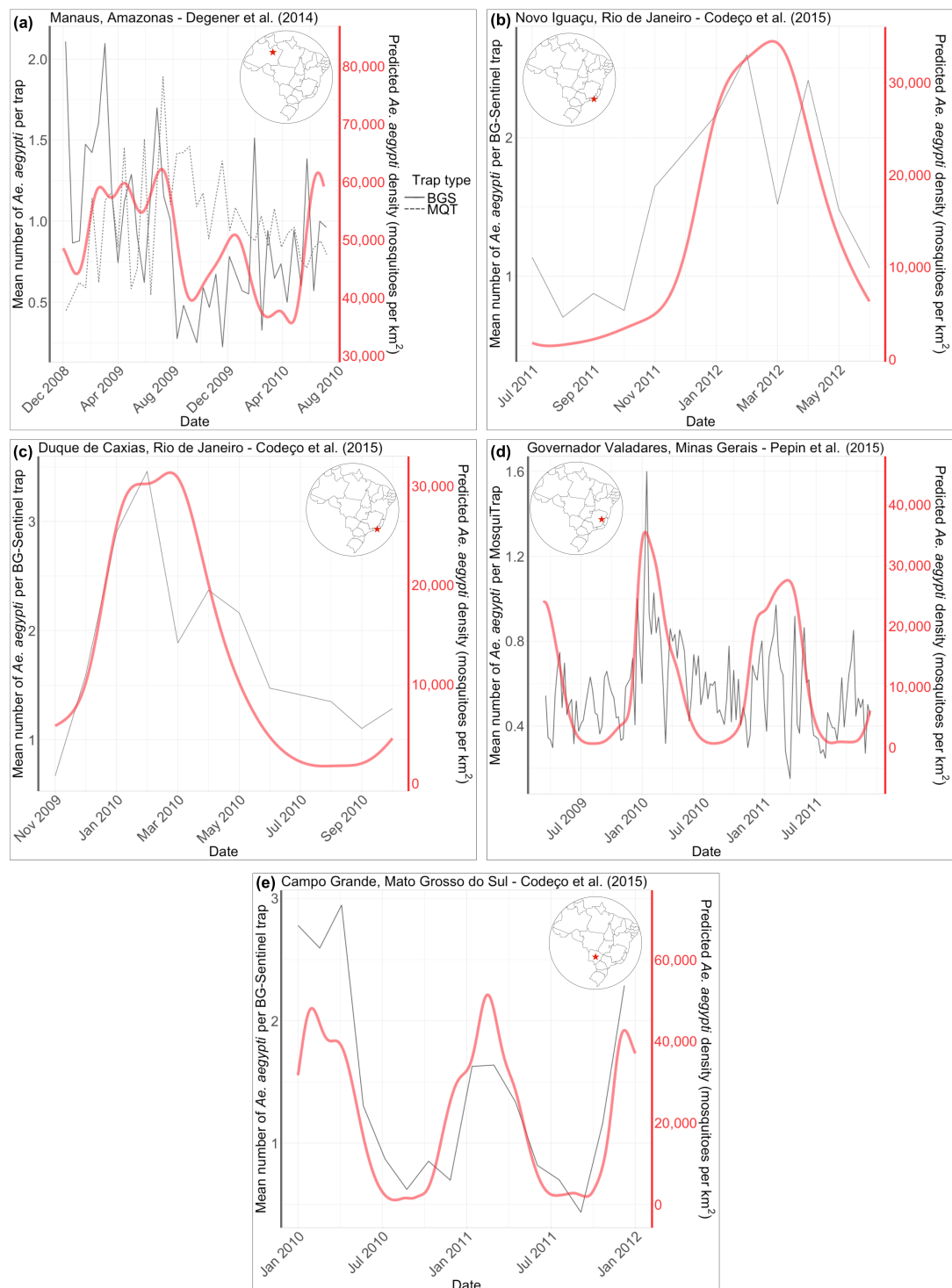


Figure A. 14. Comparison of existing time series of *Ae. aegypti* trap counts (grey lines) with model-predicted *Ae. aegypti* density (red lines) at five locations across Brazil. In combination with Figure (2.6) in the main text, these data represent all available *Ae. aegypti* time series compared with model estimates during the course of this study. Comparisons are shown for (a) Manaus, (b) Novo Iguaçu, (c) Duque de Caxias, (d) Governador Valadares and (e) Campo Grande. Time series were significantly correlated with model estimates in subfigures (b)-(e). In subfigure (a), model estimates were significantly correlated with BG-Sentinel trap data but not with MosquiTrap data. The data in these figures are adapted for presentation from Degener et al. (2014), Codeço et al. (2015) and Pepin et al. (2017) [29–31].

Table A. 6. Details of temporal data of *Ae. aegypti* used to validate model predictions. The location, citation and trap type for each dataset are shown. The  $r_{xy}^2$  value is the correlation coefficient for the modified Chelton method as detailed in Appendix A.5. The  $p$ -value indicates whether model estimates were significantly correlated with the time series data. Whether or not studies provide the raw time series data within their supplementary information is indicated; where raw data were not available, data were digitised from figures using WebPlotDigitizer, as detailed in the main text. The data source for each study is indicated. This specifies whether data taken from each study were generated by the study authors or obtained from a co-operative third party who have not made the data publicly available themselves.

| Location             | Study                               | Trap type   | $r_{xy}^2$ | $p$ -value | Number of traps | Raw data available? | Data source       |
|----------------------|-------------------------------------|-------------|------------|------------|-----------------|---------------------|-------------------|
| Manaus               | Degener et al. (2014) [29]          | BG-Sentinal | 0.20       | 0.05       | 24              | N                   | Author collection |
| Manaus               | Degener et al. (2014) [29]          | MosquiTrap  | 0.01       | 0.72       | 24              | N                   | Author collection |
| Campo Grande         | Codeço et al. (2015) [30]           | BG-Sentinal | 0.65       | 0.02       | 24              | N                   | Author collection |
| Parnamirim           | Codeço et al. (2015) [30]           | BG-Sentinal | 0.04       | 0.57       | 24              | N                   | Author collection |
| Duque de Caxias      | Codeço et al. (2015) [30]           | BG-Sentinal | 0.66       | 0.02       | 24              | N                   | Author collection |
| Novo Iguaçu          | Codeço et al. (2015) [30]           | BG-Sentinal | 0.62       | 0.09       | 24              | N                   | Author collection |
| Porto Alegre         | da Cruz Ferreira et al. (2017) [32] | MosquiTrap  | 0.66       | 0.02       | 712             | N                   | Dengue-MI [33,34] |
| Vitória              | Pepin et al. (2015) [31]            | MosquiTrap  | 0.25       | <0.001     | 1392            | Y                   | Dengue-MI [33,34] |
| Governador Valadares | Pepin et al. (2015) [31]            | MosquiTrap  | 0.20       | <0.001     | 373             | Y                   | Dengue-MI [33,34] |
| Sete Lagoas          | Pepin et al. (2015) [31]            | MosquiTrap  | 0.44       | <0.001     | 411             | Y                   | Dengue-MI [33,34] |



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# Appendix B

## Supplementary material for Chapter 3

|                                                                               |     |
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## **B.1. Pilot experiment to determine range of food treatments**

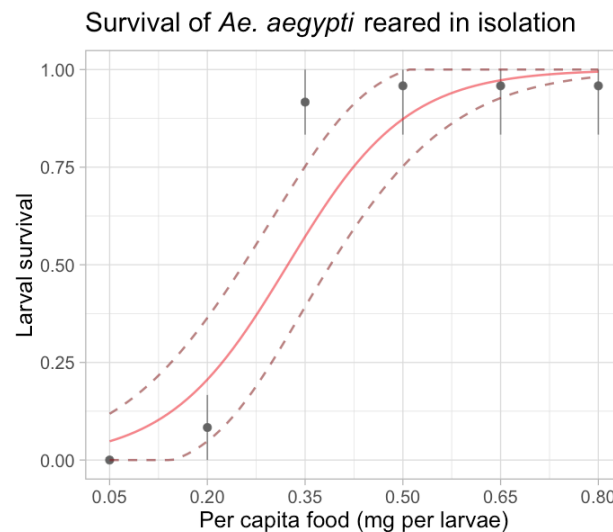


Figure B. 1. Survival probability of *Ae. aegypti* reared in isolation and fed per capita for pilot experiment. Points represent the mean proportion of surviving larvae per six-well plate across three plates and the error bars represent the range of plate-level survival proportions. This figure displays a Gamma-distributed log-link GLM fit (solid line) with 95% confidence intervals (dashed lines).

A pilot experiment was conducted to investigate an appropriate range of food treatments to capture the effects of food limitation on larval development. Results from the pilot study were used to inform the full study protocol. In the pilot study, *Aedes aegypti* larvae were reared in 10 mL of deionised water in six-well plates with one larva per well. Larvae were fed at six food conditions: 0.05, 0.20, 0.35, 0.50, 0.65 and 0.80 mg of liver powder per larva every two days for six days after hatching (three total feeds). 18 larvae were monitored across three plates for each food condition. The probability of survival per plate was analysed using logit-link binomial generalised linear models (GLMs) with food treatment as the explanatory variable. The GLM fit with 95% confidence intervals is shown in Figure B. 1. It was observed

in the pilot experiment that the gradient of the survival curve was largest between 0.30 mg and 0.50 mg per larva. Therefore, per-capita feeding experiments in the full study were designed to cross this range in order to capture a wide spectrum of survival probabilities.



## **B.2. Model predictions from posterior distributions of model parameters**

Posterior distributions were multiplied by a two-dimensional prediction matrix,  $\boldsymbol{\rho}_{D,F}$ , to obtain posterior distributions of larval survival, development time and wing length as estimated by relevant the model. The prediction matrix was as follows:

$$\boldsymbol{\rho}_{D,F} = \begin{bmatrix} \omega_{1,1} & \cdots & \omega_{1,h} \\ \vdots & \ddots & \vdots \\ \omega_{g,1} & \cdots & \omega_{g,h} \end{bmatrix} \quad (\text{B.1})$$

where  $\omega_{1,1}, \dots, \omega_{g,h}$  are posterior samples for model parameters  $\alpha_0, \dots, \alpha_3$  (beta-binomial survival model),  $\eta_0, \dots, \eta_3$  (Gamma development time model) or  $\delta_1, \dots, \delta_1$  (Gamma wing length model).  $g$  is the number of samples and  $h$  is the number of parameters estimated.

A one-dimensional matrix of values to be predicted for,  $\boldsymbol{P}$ , was defined depending on the results of model selection as follows

$$\boldsymbol{P} = \begin{cases} [1 & D] \\ [1 & D & F] \\ [1 & D & F & DF] \end{cases} \quad (\text{B.2})$$

where  $\boldsymbol{P}$  holds combinations and density,  $D$ , and food,  $F$ , values depending on the selected model.

Posterior distributions of model-predicted values were estimated by the matrix multiplication:  $\boldsymbol{\rho}_{D,F} \boldsymbol{P}$ . It should be noted that the first term of  $\boldsymbol{P}$  is 1 to preserve the predicted intercept values. Mean predicted survival proportions, development times and wing lengths as well as 95% credible intervals were calculated from the resulting posterior distributions.

### B.3. Parameter estimates

Table B. 1. Parameter estimates for beta-binomial inverse-logit link models of larval survival probability. Results are displayed for models of per capita and per pot feeding experiments with 95% credible intervals (CIs). Results are also displayed for the model of per pot feeding experiment data transformed to a per capita scale with 95% CIs.

|                                                                        | Parameter  |                        |                       |            |                        |                         |
|------------------------------------------------------------------------|------------|------------------------|-----------------------|------------|------------------------|-------------------------|
|                                                                        | $\alpha_0$ | $\alpha_1$             | $\alpha_2$            | $\gamma_0$ | $\gamma_1$             | $\gamma_2$              |
| <b>Per capita feeding experiment</b>                                   |            |                        |                       |            |                        |                         |
| <b>Value</b>                                                           | -4.30      | $1.90 \times 10^{-3}$  | 8.28                  | 2.75       | $-1.86 \times 10^{-3}$ | 0.71                    |
| <b>2.5% CI</b>                                                         | -4.89      | $1.27 \times 10^{-3}$  | 7.34                  | 1.68       | $-3.18 \times 10^{-3}$ | -0.87                   |
| <b>97.5% CI</b>                                                        | -3.73      | $2.59 \times 10^{-3}$  | 9.36                  | 3.76       | $-0.68 \times 10^{-3}$ | 2.24                    |
| <b>Per pot feeding experiment</b>                                      |            |                        |                       |            |                        |                         |
| <b>Value</b>                                                           | -2.11      | $-6.64 \times 10^{-3}$ | $3.70 \times 10^{-1}$ | 4.51       | $-0.86 \times 10^{-3}$ | $-7.87 \times 10^{-2}$  |
| <b>2.5% CI</b>                                                         | -2.56      | $-8.07 \times 10^{-3}$ | $3.22 \times 10^{-1}$ | 3.23       | $-2.27 \times 10^{-3}$ | $-11.31 \times 10^{-3}$ |
| <b>97.5% CI</b>                                                        | -1.68      | $-5.52 \times 10^{-3}$ | $4.23 \times 10^{-1}$ | 5.92       | $0.46 \times 10^{-3}$  | $-4.62 \times 10^{-2}$  |
| <b>Per pot feeding experiment data transformed to per capita scale</b> |            |                        |                       |            |                        |                         |
| <b>Value</b>                                                           | -4.01      | $1.71 \times 10^{-3}$  | 9.10                  | 2.06       | $-2.38 \times 10^{-4}$ | -0.18                   |
| <b>2.5% CI</b>                                                         | -4.44      | $1.08 \times 10^{-3}$  | 8.67                  | 1.14       | $-1.73 \times 10^{-3}$ | -0.50                   |
| <b>97.5% CI</b>                                                        | -3.58      | $2.39 \times 10^{-3}$  | 9.26                  | 3.02       | $1.11 \times 10^{-3}$  | 0.12                    |

Table B. 2. Parameter estimates for Gamma log-link models of larval development time (days from hatch to pupation). Results are displayed for models of per capita and per pot feeding experiments with 95% credible intervals (CIs).

|                                      | Parameter |                        |                        |                        |
|--------------------------------------|-----------|------------------------|------------------------|------------------------|
|                                      | $\eta_0$  | $\eta_1$               | $\eta_2$               | $\eta_3$               |
| <b>Per capita feeding experiment</b> |           |                        |                        |                        |
| <b>Value</b>                         | 2.49      | $-0.32 \times 10^{-3}$ | -0.65                  | $0.42 \times 10^{-3}$  |
| <b>2.5% CI</b>                       | 2.45      | $-0.38 \times 10^{-3}$ | -0.72                  | $0.33 \times 10^{-3}$  |
| <b>97.5% CI</b>                      | 2.53      | $-0.26 \times 10^{-3}$ | -0.59                  | $0.52 \times 10^{-3}$  |
| <b>Per pot feeding experiment</b>    |           |                        |                        |                        |
| <b>Value</b>                         | 2.02      | $0.30 \times 10^{-3}$  | $-0.25 \times 10^{-2}$ | $-0.49 \times 10^{-5}$ |
| <b>2.5% CI</b>                       | 1.99      | $0.24 \times 10^{-3}$  | $-0.33 \times 10^{-2}$ | $-0.65 \times 10^{-5}$ |
| <b>97.5% CI</b>                      | 2.05      | $0.35 \times 10^{-3}$  | $-0.17 \times 10^{-2}$ | $-0.34 \times 10^{-5}$ |

Table B. 3. Parameter estimates for Gamma log-link models of adult wing length (mm). Results are displayed for models of per capita and per pot feeding experiments with 95% credible intervals (CIs).

|                                      | Parameter  |                        |                       |
|--------------------------------------|------------|------------------------|-----------------------|
|                                      | $\delta_0$ | $\delta_1$             | $\delta_2$            |
| <b>Per capita feeding experiment</b> |            |                        |                       |
| <b>Value</b>                         | 0.86       | $5.66 \times 10^{-5}$  | 0.25                  |
| <b>2.5% CI</b>                       | 0.83       | $2.50 \times 10^{-5}$  | 0.20                  |
| <b>97.5% CI</b>                      | 0.90       | $8.87 \times 10^{-5}$  | 0.30                  |
| <b>Per pot feeding experiment</b>    |            |                        |                       |
| <b>Value</b>                         | 1.02       | $-2.67 \times 10^{-4}$ | $4.07 \times 10^{-3}$ |
| <b>2.5% CI</b>                       | 1.00       | $-3.67 \times 10^{-4}$ | $2.31 \times 10^{-3}$ |
| <b>97.5% CI</b>                      | 1.05       | $-1.67 \times 10^{-4}$ | $5.84 \times 10^{-3}$ |

## B.4. Predicted and observed larval survival probabilities

Table B. 4. Predicted *Ae. aegypti* survival probabilities and 95% credible intervals (CIs) from Bayesian beta-binomial inverse-logit link models across all empirically measured food and density conditions. Within the table, data are presented in the format: *mean (2.5% CI, 97.5% CI)*.

|                               |       | Density (larvae per litre) |                   |                   |                   |                   |
|-------------------------------|-------|----------------------------|-------------------|-------------------|-------------------|-------------------|
|                               |       | 100                        | 330               | 550               | 780               | 1000              |
| Per capita feeding experiment |       |                            |                   |                   |                   |                   |
| Food per capita (mg)          | 0.05  | 0.02 (0.01, 0.03)          | 0.03 (0.02, 0.04) | 0.04 (0.03, 0.06) | 0.06 (0.04, 0.08) | 0.09 (0.06, 0.14) |
|                               | 0.30  | 0.23 (0.19, 0.28)          | 0.32 (0.29, 0.35) | 0.42 (0.38, 0.47) | 0.53 (0.45, 0.61) | 0.63 (0.53, 0.74) |
|                               | 0.55  | 0.61 (0.57, 0.65)          | 0.71 (0.67, 0.75) | 0.79 (0.74, 0.84) | 0.85 (0.79, 0.90) | 0.90 (0.84, 0.94) |
|                               | 0.80  | 0.90 (0.88, 0.93)          | 0.93 (0.91, 0.96) | 0.96 (0.93, 0.97) | 0.97 (0.95, 0.98) | 0.98 (0.96, 0.99) |
| Per pot feeding experiment    |       |                            |                   |                   |                   |                   |
| Food per pot (mg)             | 2.75  | 0.15 (0.11, 0.19)          | 0.04 (0.02, 0.05) | 0.01 (0.00, 0.02) | 0.00 (0.00, 0.00) | 0.00 (0.00, 0.00) |
|                               | 16.50 | 0.96 (0.94, 0.98)          | 0.86 (0.81, 0.90) | 0.56 (0.49, 0.33) | 0.24 (0.16, 0.33) | 0.07 (0.03, 0.12) |
|                               | 30.25 | 1.00 (1.00, 1.00)          | 0.99 (0.99, 1.00) | 0.97 (0.95, 1.00) | 0.89 (0.81, 0.94) | 0.64 (0.46, 0.78) |
|                               | 44.00 | 1.00 (1.00, 1.00)          | 1.00 (1.00, 1.00) | 1.00 (1.00, 1.00) | 1.00 (1.00, 1.00) | 0.99 (0.98, 1.00) |

Table B. 5. Mean and standard deviation (SD) of the observed proportion of *Ae. aegypti* larvae surviving to pupation over all empirically measured food and density conditions. Within the table, data are presented in the format: *mean (SD)*.

|                               |       | Density (larvae per litre) |             |             |             |             |
|-------------------------------|-------|----------------------------|-------------|-------------|-------------|-------------|
|                               |       | 100                        | 330         | 550         | 780         | 1000        |
| Per capita feeding experiment |       |                            |             |             |             |             |
| Food per capita (mg)          | 0.05  | 0.00 (0.00)                | 0.00 (0.00) | 0.00 (0.01) | 0.00 (0.01) | 0.00 (0.00) |
|                               | 0.30  | 0.13 (0.13)                | 0.43 (0.12) | 0.50 (0.01) | 0.53 (0.07) | 0.67 (0.02) |
|                               | 0.55  | 0.65 (0.15)                | 0.80 (0.14) | 0.84 (0.10) | 0.77 (0.13) | 0.81 (0.11) |
|                               | 0.80  | 0.89 (0.10)                | 0.93 (0.08) | 0.91 (0.08) | 0.91 (0.06) | 0.92 (0.03) |
| Per pot feeding experiment    |       |                            |             |             |             |             |
| Food per pot (mg)             | 2.75  | 0.13 (0.08)                | 0.51 (0.06) | 0.00 (0.01) | 0.01 (0.00) | 0.02 (0.00) |
|                               | 16.50 | 0.96 (0.10)                | 0.93 (0.08) | 0.52 (0.07) | 0.27 (0.10) | 0.13 (0.02) |
|                               | 30.25 | 0.97 (0.07)                | 0.94 (0.06) | 0.96 (0.04) | 0.86 (0.05) | 0.59 (0.01) |
|                               | 44.00 | 0.94 (0.09)                | 0.94 (0.06) | 0.95 (0.06) | 0.96 (0.06) | 0.97 (0.01) |

## B.5. Predicted and observed larval development times

Table B. 6. Predicted *Ae. aegypti* development times (days from hatch to pupation) and 95% credible intervals (CIs) from Bayesian Gamma-distributed log link models across all empirically measured food and density conditions. Within the table, data are presented in the format: *mean (2.5% CI, 97.5% CI)*.

|                               |       | Density (larvae per litre) |                      |                    |                   |                     |
|-------------------------------|-------|----------------------------|----------------------|--------------------|-------------------|---------------------|
|                               |       | 100                        | 330                  | 550                | 780               | 1000                |
| Per capita feeding experiment |       |                            |                      |                    |                   |                     |
| Food per capita (mg)          | 0.05  | 11.31 (10.94, 11.71)       | 10.58 (10.34, 10.84) | 9.90 (9.74, 10.06) | 9.26 (9.09, 9.42) | 8.66 (8.43, 8.88)   |
|                               | 0.30  | 9.71 (9.51, 9.92)          | 9.30 (9.17, 9.44)    | 8.91 (8.82, 9.00)  | 8.53 (8.44, 8.62) | 8.17 (8.04, 8.30)   |
|                               | 0.55  | 8.34 (8.25, 8.43)          | 8.17 (8.11, 8.24)    | 8.01 (7.97, 8.06)  | 7.86 (7.81, 7.91) | 7.70 (7.64, 7.77)   |
|                               | 0.80  | 7.16 (7.06, 7.25)          | 7.18 (7.12, 7.25)    | 7.21 (7.16, 7.27)  | 7.24 (7.17, 7.31) | 7.27 (7.18, 7.36)   |
| Per pot feeding experiment    |       |                            |                      |                    |                   |                     |
| Food per pot (mg)             | 2.75  | 7.78 (7.61, 7.96)          | 8.32 (8.19, 8.45)    | 8.88 (8.74, 9.04)  | 9.26 (9.16, 9.73) | 10.14 (9.80, 10.50) |
|                               | 16.50 | 7.32 (7.24, 7.40)          | 7.64 (7.59, 7.70)    | 7.98 (7.92, 8.04)  | 8.33 (8.24, 8.43) | 8.70 (8.56, 8.84)   |
|                               | 30.25 | 7.13 (7.07, 7.19)          | 7.37 (7.33, 7.42)    | 7.62 (7.58, 7.66)  | 7.88 (7.82, 7.94) | 8.14 (8.06, 8.23)   |
|                               | 44.00 | 6.84 (6.75, 6.94)          | 6.97 (6.90, 7.03)    | 7.09 (7.04, 7.15)  | 7.22 (7.15, 7.29) | 7.35 (7.25, 7.45)   |

Table B. 7. Mean and standard deviation (SD) of the observed *Ae. aegypti* larval development time (days from hatch to pupation) for larvae surviving to pupation over all empirically measured food and density conditions. For observations where the observed proportion of larvae surviving to pupation was <2%, development times were not displayed due to highly variable data. Within the table, data are presented in the format: *mean (SD)*.

|                               |       | Density (larvae per litre) |              |             |             |             |
|-------------------------------|-------|----------------------------|--------------|-------------|-------------|-------------|
|                               |       | 100                        | 330          | 550         | 780         | 1000        |
| Per capita feeding experiment |       |                            |              |             |             |             |
| Food per capita (mg)          | 0.05  | NA                         | NA           | NA          | NA          | NA          |
|                               | 0.30  | 10.6 (2.02)                | 8.84 (1.14)  | 8.75 (1.35) | 8.53 (1.14) | 8.30 (1.92) |
|                               | 0.55  | 9.09 (2.23)                | 7.72 (1.20)  | 7.83 (2.27) | 7.94 (1.87) | 7.85 (1.77) |
|                               | 0.80  | 7.35 (1.18)                | 6.95 (1.75)  | 7.05 (1.43) | 7.26 (1.43) | 7.41 (1.86) |
| Per pot feeding experiment    |       |                            |              |             |             |             |
| Food per pot (mg)             | 2.75  | 9.62 (1.72)                | 12.00 (1.25) | NA          | NA          | NA          |
|                               | 16.50 | 7.10 (0.78)                | 7.59 (1.61)  | 7.83 (1.30) | 7.99 (0.92) | 8.04 (0.94) |
|                               | 30.25 | 7.04 (0.77)                | 7.19 (0.98)  | 7.84 (2.29) | 8.14 (1.99) | 7.96 (1.89) |
|                               | 44.00 | 6.94 (0.68)                | 7.15 (0.86)  | 7.06 (1.41) | 7.25 (1.11) | 7.27 (1.18) |

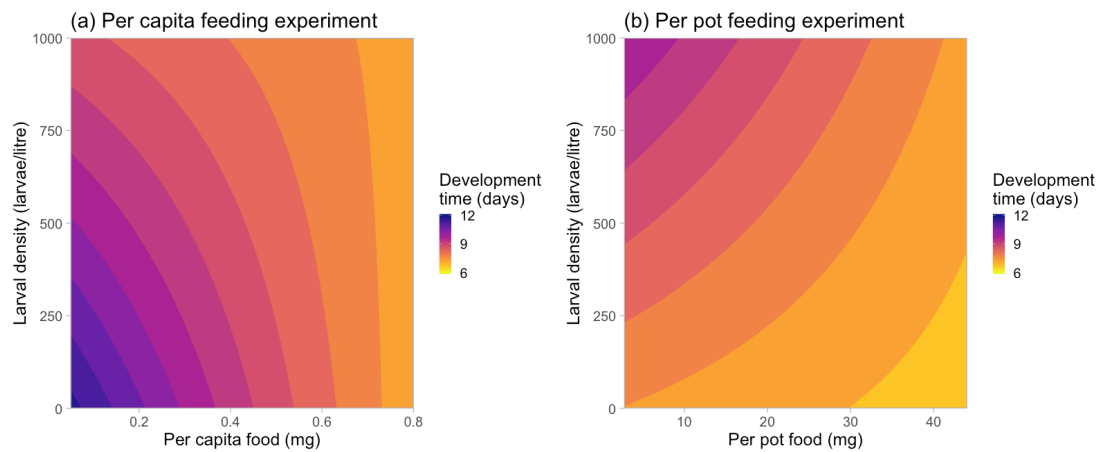


Figure B. 2. Predicted larval development times (days from hatch to pupation) under a (a) per capita feeding regime and (b) per pot feeding regime. Models were used to predict development times for unmeasured combinations of larval density and food availability using Equation (3.9) and Equation (3.16) in the main text. Colours represent the development time in days and contour lines delineate changes in development time. The inverse association between density and development time under per capita and per pot feeding regimes is evident by comparison of (a) and (b).

## **B.6. Predicted and observed emerged adult wing lengths**

Table B. 8. Predicted *Ae. aegypti* adult wing lengths (mm) and 95% credible intervals (CIs) from Bayesian Gamma-distributed log link models across all empirically measured food and density conditions. Within the table, data are presented in the format: *mean (2.5% CI, 97.5% CI)*.

|                               |       | Density (larvae per litre) |                   |                   |                   |                   |
|-------------------------------|-------|----------------------------|-------------------|-------------------|-------------------|-------------------|
|                               |       | 100                        | 330               | 550               | 780               | 1000              |
| Per capita feeding experiment |       |                            |                   |                   |                   |                   |
| Food per capita (mg)          | 0.05  | 2.45 (2.38, 2.52)          | 2.48 (2.42, 2.55) | 2.52 (2.46, 2.58) | 2.55 (2.49, 2.62) | 2.59 (2.53, 2.67) |
|                               | 0.30  | 2.55 (2.49, 2.61)          | 2.59 (2.54, 2.64) | 2.62 (2.58, 2.66) | 2.66 (2.61, 2.71) | 2.70 (2.64, 2.76) |
|                               | 0.55  | 2.73 (2.69, 2.78)          | 2.78 (2.74, 2.81) | 2.81 (2.78, 2.84) | 2.86 (2.82, 2.89) | 2.90 (2.85, 2.95) |
|                               | 0.80  | 2.91 (2.85, 2.96)          | 2.95 (2.90, 3.00) | 2.99 (2.94, 3.04) | 3.04 (2.98, 3.09) | 3.08 (3.02, 3.15) |
| Per pot feeding experiment    |       |                            |                   |                   |                   |                   |
| Food per pot (mg)             | 2.75  | 2.79 (2.74, 2.84)          | 2.63 (2.56, 2.71) | 2.49 (2.38, 2.61) | 2.32 (2.17, 2.49) | 2.19 (2.00, 2.40) |
|                               | 16.50 | 2.90 (2.83, 2.98)          | 2.74 (2.68, 2.80) | 2.59 (2.50, 2.68) | 2.42 (2.28, 2.56) | 2.28 (2.11, 2.47) |
|                               | 30.25 | 3.07 (2.94, 3.21)          | 2.90 (2.81, 2.99) | 2.74 (2.66, 2.82) | 2.74 (2.44, 2.68) | 2.41 (2.26, 2.57) |
|                               | 44.00 | 3.25 (3.04, 3.47)          | 3.07 (2.91, 3.23) | 2.90 (2.77, 3.02) | 2.90 (2.58, 2.83) | 2.55 (2.41, 2.70) |

Table B. 9. Mean and standard deviation (SD) of the observed *Ae. aegypti* adult wing lengths for over all empirically measured food and density conditions. For the lowest food treatments, no measurements were taken due to low survival probabilities yielding insufficient sample sizes. These conditions are denoted with NA within the table. Within the table, data are presented in the format: *mean (SD)*.

|                               |       | Density (larvae per litre) |             |             |             |             |
|-------------------------------|-------|----------------------------|-------------|-------------|-------------|-------------|
|                               |       | 100                        | 330         | 550         | 780         | 1000        |
| Per capita feeding experiment |       |                            |             |             |             |             |
| Food per capita (mg)          | 0.05  | NA                         | NA          | NA          | NA          | NA          |
|                               | 0.30  | 2.45 (0.20)                | 2.60 (0.20) | 2.66 (0.13) | 2.74 (0.11) | 2.64 (0.08) |
|                               | 0.55  | 2.59 (0.22)                | 2.85 (0.17) | 2.90 (0.16) | 2.95 (0.15) | 2.84 (0.24) |
|                               | 0.80  | 2.95 (0.12)                | 3.01 (0.12) | 2.97 (0.12) | 2.95 (0.10) | 3.00 (0.09) |
| Per pot feeding experiment    |       |                            |             |             |             |             |
| Food per pot (mg)             | 2.75  | NA                         | NA          | NA          | NA          | NA          |
|                               | 16.50 | 3.04 (0.19)                | 2.63 (0.22) | 2.43 (0.10) | 2.25 (0.03) | 2.18 (0.09) |
|                               | 30.25 | 3.11 (0.18)                | 2.94 (0.11) | 2.78 (0.08) | 2.57 (0.12) | 2.46 (0.12) |
|                               | 44.00 | 3.06 (0.13)                | 3.02 (0.09) | 2.87 (0.10) | 2.71 (0.10) | 2.62 (0.19) |

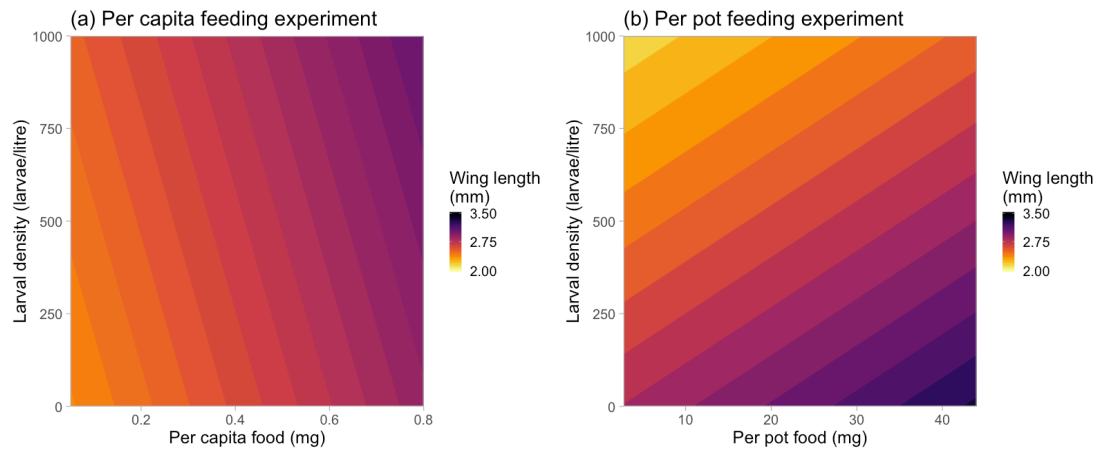


Figure B. 3. Predicted adult wing lengths (mm) under a (a) per capita feeding regime and (b) per pot feeding regime. Models were used to predict wing lengths for unmeasured combinations of larval density and food availability using Equation (3.12) and Equation (3.17) in the main text. Colours represent the adult wing length in mm and contour lines delineate changes in wing length. The inverse association between density and wing length under per capita and per pot feeding regimes is evident by comparison of (a) and (b).

## **B.7. Sampling points on per capita and per pot scales**

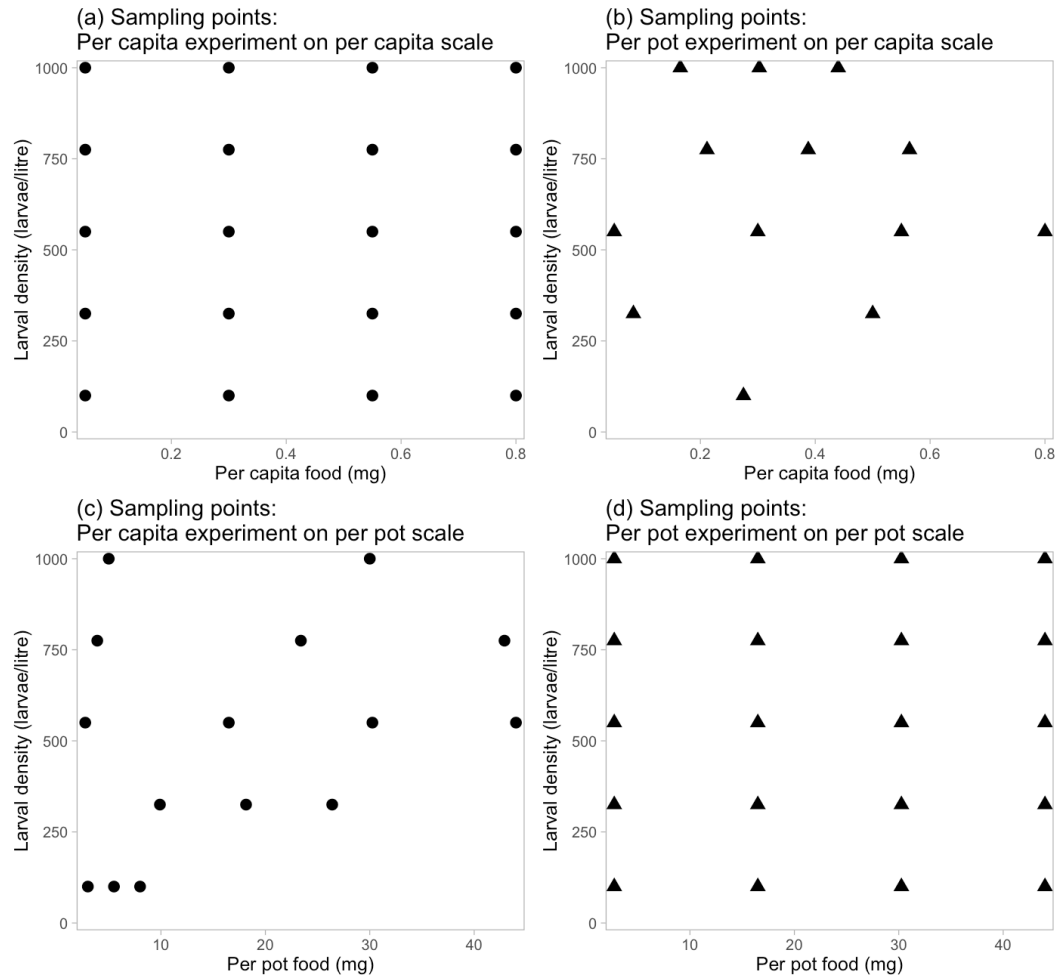


Figure B. 4. Distribution of sampling points across the density and food parameter space for the per capita and per pot feeding experiments. Subfigures (a) and (c) show the per capita feeding experiment sampling points on a per capita and per pot scale, respectively. Subfigures (b) and (d) show the per pot feeding experiment sampling points on a per capita and per pot scale, respectively. Both experiments shared a central axis on either scale at a density of 550 larvae/litre.

Converting data from the per pot feeding experiment to a per capita scale resulted in the survival data mirroring those of the true per capita feeding experiment as shown by comparison of Figure 3. 8(a) and Figure 3. 1(a) in the main text. Comparison of predicted survival probabilities for the true per capita data and the transformed per pot



data are shown in Figure 3. 8(b). The maximum difference in predicted survival probability was observed to be at low larval densities and between  $\sim 0.4$ - $0.8$  mg/larva. This occurred because the sampling points of the per pot data when converted to a per capita scale were not uniformly distributed across the parameter space as shown by comparison of Figure B. 4(a) and Figure B. 4(b). The biggest gap in sampling was between  $\sim 0.4$ - $0.8$  mg/larvae at low larval densities as shown in Figure B. 4(b). This corresponds with the largest difference in predicted survival probability for true per capita and transformed per pot data as shown in Figure 3. 8(b) in the main text. All experiments shared a central axis at 550 larvae/litre.



# Appendix C

## Supplementary material for Chapter 4

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## **C.1. Random forest hyper-parameters**

Individual regression trees within a single random forest model use  $m$  bootstrapped samples with replacement of the training data,  $D$ , and each split uses a subset of the predictor variables [1]. This framework facilitates assessment of ‘out-of-bag’ (OOB) samples. Each of the  $m$  trees are trained and tested using a subset,  $d$ , where  $d \subset D$ . OOB predictions are made by tree  $m$  on the complement with regard to  $d$ ,  $d^c = D \setminus d$ . As such, random forests internally cross-validate and reduce individual variable dominance and over-fitting. OOB errors indicate random forest model accuracy on novel data.

Random forests were used in a two-stage approach because random forests do not predict trends or relationships. There were numerous observations where *Cardisoma carnifex* burrow density was zero often due to habitat unsuitability such as concrete or soil, which prohibit *C. carnifex* burrowing. Random forests would have difficulty predicting values at distribution tail ends or values outside the range of training data. Therefore, *C. carnifex* presence/absence was estimated prior to burrow density to avoid inaccuracies at the low tail end of the distribution of burrow densities. This resulted in two random forest models:

- (1) Random forest classification with binary *C. carnifex* presence/absence as the response
- (2) Random forest regression with *C. carnifex* burrow density as the response.

Random forest ‘hyper-parameters’ can be adjusted within the randomForest package for R [2]. These hyper-parameters include the number of classification trees used and their depth (i.e. the number of splits). We used the default settings for the randomForest() function. The number of trees grown (ntrees) was 500 and the

number of variables randomly sampled as candidates at each split (`mtry`) was 3. A broad spectrum of `ntree` and `mtry` hyper-parameter values were explored with little meaningful improvement on model fit for both classification and regression trees using OOB testing as a performance metric.

## **C.2. Density-dependent larval mortality**

The density-dependent larval mortality constant,  $\kappa$ , was set to  $8.5 \times 10^{-4}$  on the basis of binomial-distributed Generalised Linear Models (GLMs) fitted to *Ae. polynesiensis* survival data from two French Polynesian islands (data not shown). However, the choice of value for  $\kappa$  is challenging, and somewhat arbitrary, because the degree of density-dependent mortality depends on many features such as resource availability and habitat volume. This has been comprehensively discussed in Chapter 3.

The purpose of this chapter has been to examine the capacity of the environment to support aquatic larval habitats. This is closely tied to the concept of density dependence because greater numbers of larval habitats increases the environmental carrying capacity for mosquito larvae; this has been discussed in the Introduction within the main text of this chapter. We concede that parameter  $\kappa$  may vary spatially and between *C. carnifex* burrows. However, the intensive empirical work required to establish values of  $\kappa$  across an environmental gradient is beyond the scope of this work. Therefore we limit our study to the number of *C. carnifex* burrows.

We used model equilibrium values (Equations (C.8) and (C.9)) to examine the interaction between density-dependent mortality,  $\kappa$ , and *C. carnifex* burrow density,  $\alpha_{i,j}$ , as shown in Figure C. 1. *C. carnifex* burrow density had a linear relationship with *Ae. polynesiensis* population size. Parameter  $\kappa$ , had an inverse exponential growth relationship with *Ae. polynesiensis* population size. Therefore, the value of  $\kappa$  affects the size of the estimated *Ae. polynesiensis* population but does not interfere with the effect of *C. carnifex* burrow density. High densities of burrows will affect mosquito population sizes additively and the effect will be equal across all grid cells with a constant value of  $\kappa$ .

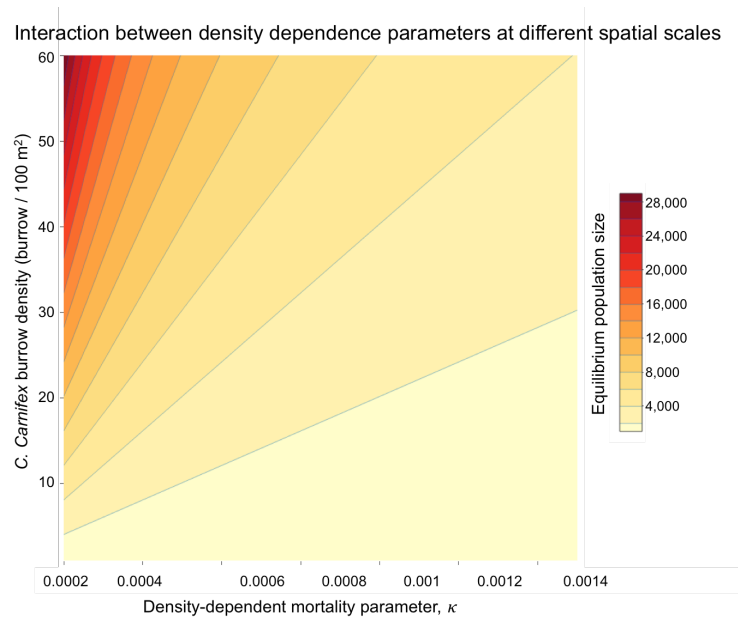


Figure C. 1. Interaction between density-dependent mortality constant,  $\kappa$  and *C. carnifex* burrow density,  $\alpha_{i,j}$ . The interaction is quantified using the equilibrium *Ae. polynesiensis* population size (male and female, without dispersal) from Equations (C.8) and (C.9).

Although the empirical work required to establish values of  $\kappa$  across an environmental gradient is beyond the scope of this thesis, a non-exhaustive list of potential hypotheses about important environmental variables in the context of the current work can be presented and briefly discussed.

- (1) Nutritional availability within *C. carnifex* burrows is likely to influence  $\kappa$ .

This could vary spatially due to changes in land cover. Burrows in forested areas may collect more detritus from trees and shrubs.

- (2) The size of *C. carnifex* burrows may affect  $\kappa$  because larger burrows hold more water, thereby facilitating higher larval densities. We found that burrow diameter was a significant predictor of burrow volume (see Results), however, random forest models were not able to spatially predict burrow diameter from



Landsat 8 reflectance values (data not shown), possibly due to the small dataset used for model training.

- (3) The presence of other aquatic organisms could influence  $\kappa$  through competition. We assumed in our model that copepod presence caused 100% mortality of *Ae. polynesiensis* larvae through predation. Other aquatic organisms, including other mosquito species, may compete for resources and induce larval stress.

### **C.3. Existence of equilibrium states and their stability**

The equilibrium states for the model without dispersal were used as initial conditions for the model with dispersal, which was subsequently run to equilibrium. When at equilibrium the model without dispersal fulfils the following:

$$0 = (1 - c) b \sigma_{i,j} F_{i,j}^* - \kappa \frac{J_{i,j}^*}{\alpha_{i,j} (1-c)} J_{i,j}^* - \rho J_{i,j}^* \quad (\text{C.1})$$

$$0 = g \rho J_{i,j}^* - \mu_F F_{i,j}^* \quad (\text{C.2})$$

$$0 = g \rho J_{i,j}^* - \mu_M M_{i,j}^* \quad (\text{C.3})$$

From Equation (C.2) and (C.3) we can derive

$$F_{i,j}^* = \frac{g \rho J_{i,j}^*}{\mu_F} \quad (\text{C.4})$$

$$M_{i,j}^* = \frac{g \rho J_{i,j}^*}{\mu_M} \quad (\text{C.5})$$

Substituting Equation (C.4) into Equation (C.1) we can derive

$$J_{i,j}^* \left[ \frac{(1-c) b \sigma_{i,j} g \rho}{\mu_F} - \frac{\kappa J_{i,j}^*}{(1-c) \alpha_{i,j}} - \rho \right] = 0 \quad (\text{C.6})$$

This gives us the trivial equilibrium solution of  $J^*(i, j) = 0$ . The non-trivial solution is therefore

$$J_{i,j}^* = \frac{[\alpha_{i,j} \rho (1-c)] [b \sigma_{i,j} g (1-c) - \mu_F]}{\mu_F \kappa} \quad (\text{C.7})$$

Substituting Equation (C.7) into Equations (C.4) and (C.5) we find that

$$F_{i,j}^* = \frac{[\alpha_{i,j} g \rho^2 (1-c)] [b \sigma_{i,j} g (1-c) - \mu_F]}{\mu_F^2 \kappa} \quad (\text{C.8})$$

$$M_{i,j}^* = \frac{[\alpha_{i,j} g \rho^2 (1-c)] [b \sigma_{i,j} g (1-c) - \mu_F]}{\mu_F \mu_M \kappa} \quad (\text{C.9})$$

giving us the three equilibrium states of the model without dispersal in Equations (C.7)-(C.9).

To establish the stability of the equilibrium states, the Jacobian

$$\mathbf{A} = \begin{bmatrix} \frac{-2\kappa J_{i,j}^*}{\alpha_{i,j}(1-c)} - \rho & (1-c) b \sigma_{i,j} & 0 \\ g \rho & -\mu_F & 0 \\ g \rho & 0 & -\mu_M \end{bmatrix} \quad (\text{C.10})$$

is used to fulfil

$$\det|\mathbf{A} - I\lambda| = 0 \quad (\text{C.11})$$

where  $I$  is an identity matrix and  $\lambda$  are possible eigenvalues. Substituting Equation (C.10) into (C.11) we can derive

$$\begin{aligned} & \left( \frac{-2\kappa J_{i,j}^*}{\alpha_{i,j}(1-c)} - \rho - \lambda \right) \begin{vmatrix} -\mu_F - \lambda & 0 \\ 0 & -\mu_M - \lambda \end{vmatrix} - \\ & \left( (1-c) b \sigma_{i,j} - \lambda \right) \begin{vmatrix} g \rho & 0 \\ g \rho & -\mu_M - \lambda \end{vmatrix} = 0 \end{aligned} \quad (\text{C.12})$$

which reduces to

$$\begin{aligned} & \left[ \left( \frac{-2\kappa J_{i,j}^*}{\alpha_{i,j}(1-c)} - \rho - \lambda \right) (-\mu_F - \lambda)(-\mu_M - \lambda) \right] - \\ & \left[ \left( (1-c) b \sigma_{i,j} - \lambda \right) (g \rho (-\mu_M - \lambda)) \right] = 0 \end{aligned} \quad (\text{C.13})$$

and subsequently a cubic of the form

$$a_0 \lambda^3 + a_1 \lambda^2 + a_2 \lambda + a_3 = 0 \quad (\text{C.14})$$

where

$$a_0 = -1 \quad (\text{C.15})$$

$$a_1 = \left( \frac{-2\kappa J_{i,j}^*}{\alpha_{i,j}(1-c)} - \rho \right) - \mu_F - \mu_M \quad (\text{C.16})$$

$$a_2 = (\mu_F + \mu_M) \left( \frac{-2\kappa J_{i,j}^*}{\alpha_{i,j}(1-c)} - \rho \right) - \mu_F \mu_M + (1-c) b \sigma_{i,j} g \rho \quad (\text{C.17})$$

$$a_3 = \mu_F \mu_M \left( \frac{-2\kappa J_{i,j}^*}{\alpha_{i,j}(1-c)} - \rho \right) + (1-c) b \sigma_{i,j} g \rho \mu_M \quad (\text{C.18})$$

Solving the cubic function, there are three possible solutions:

$$\lambda_1 = -\mu_M \quad (\text{C.19})$$

$$\lambda_2 = \frac{1}{2} \left( -\sqrt{\left( \frac{-2\kappa J_{i,j}^*}{\alpha_{i,j}(1-c)} - \rho \right)^2 + 2\mu_F \left( \frac{-2\kappa J_{i,j}^*}{\alpha_{i,j}(1-c)} - \rho \right) + 4\left( (1-c) b \sigma_{i,j} g \rho \right) + \mu_F^2} + \left( \frac{-2\kappa J_{i,j}^*}{\alpha_{i,j}(1-c)} - \rho \right) - \mu_F \right) \quad (\text{C.20})$$

$$\lambda_3 = \frac{1}{2} \left( \sqrt{\left( \frac{-2\kappa J_{i,j}^*}{\alpha_{i,j}(1-c)} - \rho \right)^2 + 2\mu_F \left( \frac{-2\kappa J_{i,j}^*}{\alpha_{i,j}(1-c)} - \rho \right) + 4\left( (1-c) b \sigma_{i,j} g \rho \right) + \mu_F^2} + \left( \frac{-2\kappa J_{i,j}^*}{\alpha_{i,j}(1-c)} - \rho \right) - \mu_F \right) \quad (\text{C.21})$$

Solutions  $\lambda_1, \lambda_2$  and  $\lambda_3$  are all negative for all values of  $\alpha_{i,j}$ . Therefore the model equilibrium is a stable, absorbing state.

## **C.4. Example coverage grids for larval source management**

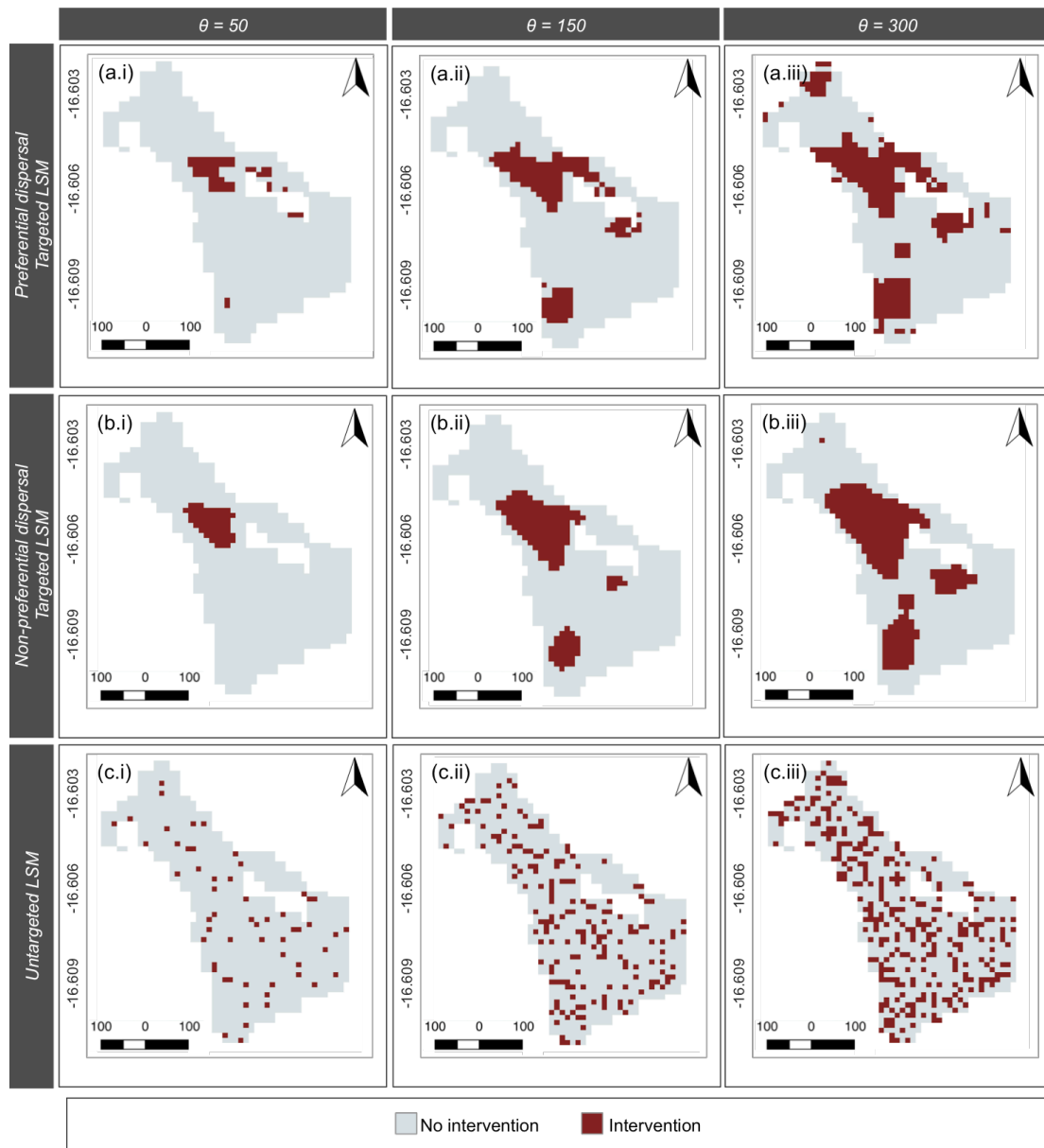


Figure C. 2. Examples of the intervention grids used for larval source management. Grids are displayed for three LSM coverage values (in terms of the number of cells where LSM is enacted),  $\theta=50$ ,  $\theta=150$  and  $\theta=300$ . Subfigures (a.i)-(a.iii) display intervention grids for preferential dispersal with targeted LSM; (b.i)-(b.iii) display grids for non-preferential dispersal with targeted LSM; (c.i)-(c.iii) display grids for untargeted LSM. Targeted LSM had different intervention grids for preferential and non-preferential dispersal models because the intervention cells were defined as the cells with the largest *Ae. polynesiensis* populations at equilibrium prior to LSM. This subset of cells differed between dispersal models.

## **C.5. Field sampling**

The associations between (a) *C. carnifex* burrow diameter and volume and (b) burrow volume and larval numbers are shown in Figure C. 3. Both associations were significant ( $p < 0.001$  for both) using linear regression. Parameter estimates and confidence intervals are shown in Table C. 1.

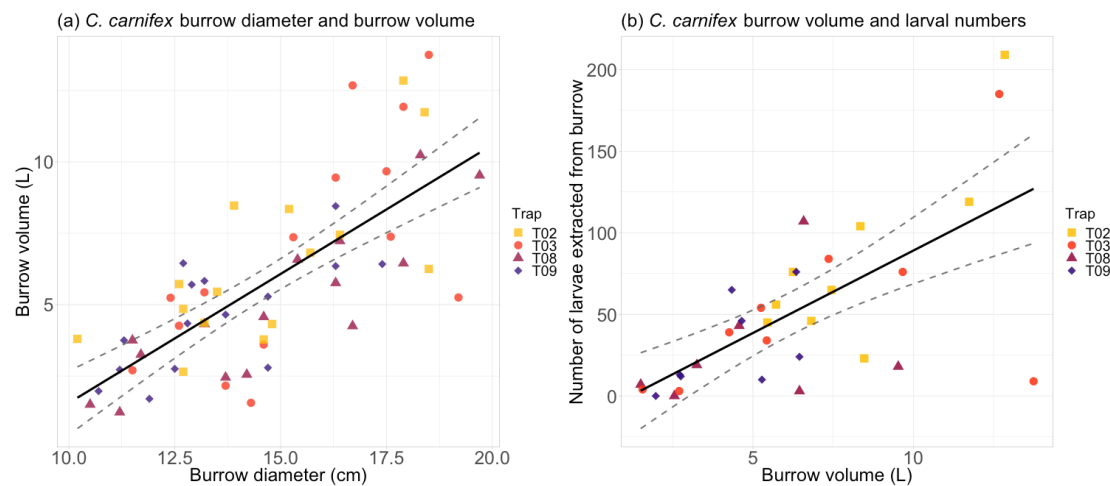


Figure C. 3. Associations between (a) *C. carnifex* burrow diameter and burrow volume and (b) *C. carnifex* burrow volume and the number of larvae extracted from a burrow at four trapping sites on motu Tautau. Both associations were significantly positive using linear regression. The regression lines and confidence intervals are shown.

Table C. 1. Parameter estimates and confidence intervals for linear regression models on field data.

| Model                     | Intercept |         |          | Gradient |         |          |
|---------------------------|-----------|---------|----------|----------|---------|----------|
|                           | Value     | 2.5% CI | 97.5% CI | Value    | 2.5% CI | 97.5% CI |
| volume ~ diameter         | -7.48     | -10.66  | -4.30    | 0.90     | 0.69    | 1.12     |
| larval numbers ~ volume   | -11.91    | -40.39  | 16.56    | 10.01    | 6.03    | 14.17    |
| larval numbers ~ diameter | -76.16    | -167.70 | 15.38    | 8.55     | 2.47    | 14.63    |

## **C.6. Accuracy of land cover classification**

The confusion matrix comparing observed and predicted land cover classes is shown in Table C. 2. The predicted land cover classes had a finer resolution (15×15 m) than the observed land cover classes (100×100 m). To compare observed and predicted classes, the most frequently occurring predicted class was taken around a central cell with the same coordinates as the observed sampling point.

Table C. 2. Confusion matrix for classification of land cover classes using Euclidian minimum distance classification algorithm. The sensitivity and specificity are displayed for each land cover class. Abbreviations for some land cover classes are used within the table headings. Exp. rock refers to Exposed rock; Indust./constr. refers to Industrial/construction; Resid./hotel refers to Residential/hotel; Shal. ocean refers to Shallow ocean.

|             |                  | Observed |            |           |        |             |                  |               |             |
|-------------|------------------|----------|------------|-----------|--------|-------------|------------------|---------------|-------------|
|             |                  | Beach    | Coral reef | Exp. rock | Forest | Fresh. lake | Indust./ constr. | Resid./ hotel | Shal. ocean |
| Predicted   | Beach            | 3        | 0          | 0         | 0      | 0           | 0                | 2             | 0           |
|             | Coral reef       | 3        | 0          | 0         | 1      | 0           | 0                | 0             | 0           |
|             | Exp. Rock        | 0        | 0          | 3         | 0      | 0           | 1                | 1             | 0           |
|             | Forest           | 5        | 0          | 5         | 15     | 0           | 2                | 14            | 0           |
|             | Fresh. Lake      | 1        | 0          | 0         | 0      | 2           | 0                | 1             | 0           |
|             | Indust./ constr. | 0        | 0          | 0         | 1      | 0           | 2                | 2             | 0           |
|             | Resid./ hotel    | 2        | 0          | 0         | 7      | 0           | 5                | 36            | 0           |
|             | Shal. ocean      | 2        | 0          | 0         | 0      | 0           | 0                | 0             | 0           |
| Sensitivity |                  | 0.19     | NA         | 0.38      | 0.63   | 1.00        | 0.20             | 0.64          | NA          |
| Specificity |                  | 0.98     | 0.97       | 0.98      | 0.72   | 0.98        | 0.97             | 0.77          | 0.98        |

## **C.7. Random forest predictions**

Cohen's  $\kappa$  [3] was used to assess random forest classification compared with the expected level of classification accuracy by random chance. Cohen's  $\kappa$ ,  $\left(\frac{\text{Accuracy}-\text{Expected accuracy}}{1-\text{Expected accuracy}}\right)$ , was calculated using the confusion matrix in Table C.

3.

Table C. 3. Confusion matrix used to calculate Cohen's  $\kappa$  to assess random forest classification accuracy.

|           |                               | Observed                     |                               |
|-----------|-------------------------------|------------------------------|-------------------------------|
|           |                               | <i>C. carnifex</i><br>absent | <i>C. carnifex</i><br>present |
| Predicted | <i>C. carnifex</i><br>absent  | 20                           | 21                            |
|           | <i>C. carnifex</i><br>present | 16                           | 59                            |

The importance of individual Landsat 8 bands is shown in Figure C. 4. The important bands for *C. carnifex* presence/absence classification were not the same as those for *C. carnifex* burrow density estimation.

The errors in predicted *C. carnifex* burrow density using random forest regression are shown in Figure C. 5. Random forest regression smoothed the data, overestimating at low burrow densities and underestimating at high burrow densities. The smallest prediction errors were observed for medial *C. carnifex* burrow densities of ~10-30 burrows/100 m<sup>2</sup>. The full random forest model predicting on all training data had consistently smaller prediction errors than OOB samples. This is intuitive because the



full random forest model used all available data to predict on data within the distribution of its training. The elevated OOB prediction errors demonstrate that the model may not be as accurate when applied to novel data. A larger training set may improve model accuracy on new data in future.

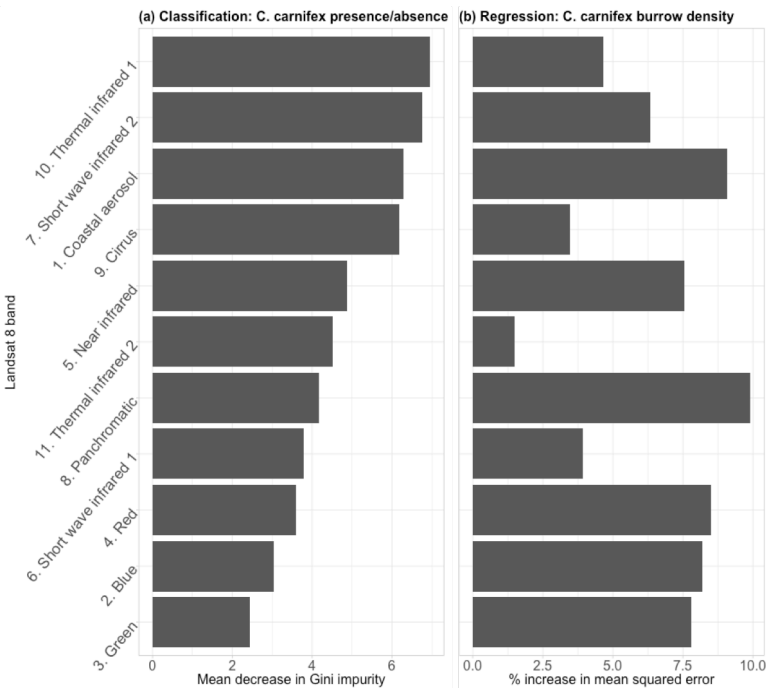


Figure C. 5. Importance of individual Landsat 8 bands for random forest (a) classification and (b) regression. Features are ordered by their importance for random forest classification.

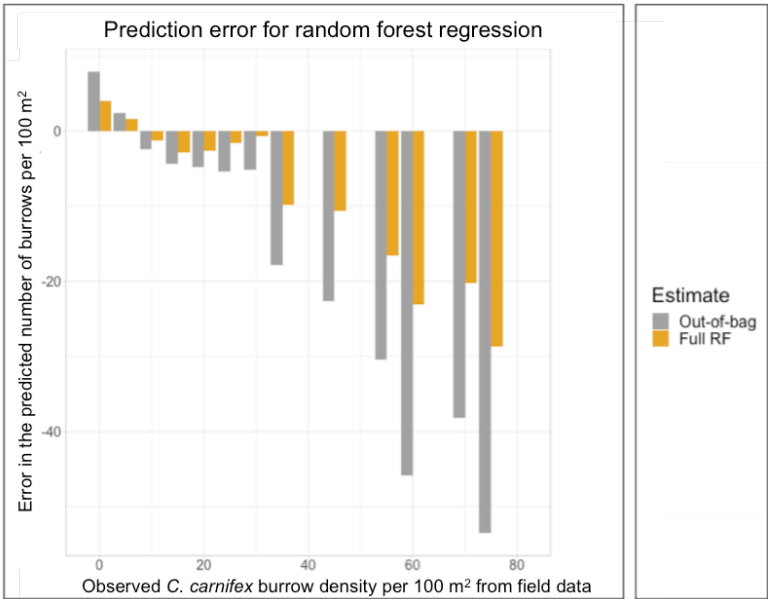


Figure C. 4. Prediction errors in *C. carnifex* burrow density for random forest (RF) regression modelling. Prediction errors are presented for out-of-bag (OOB) samples and the full random forest model on all training data.

## **C.8. Effects of larval source management**

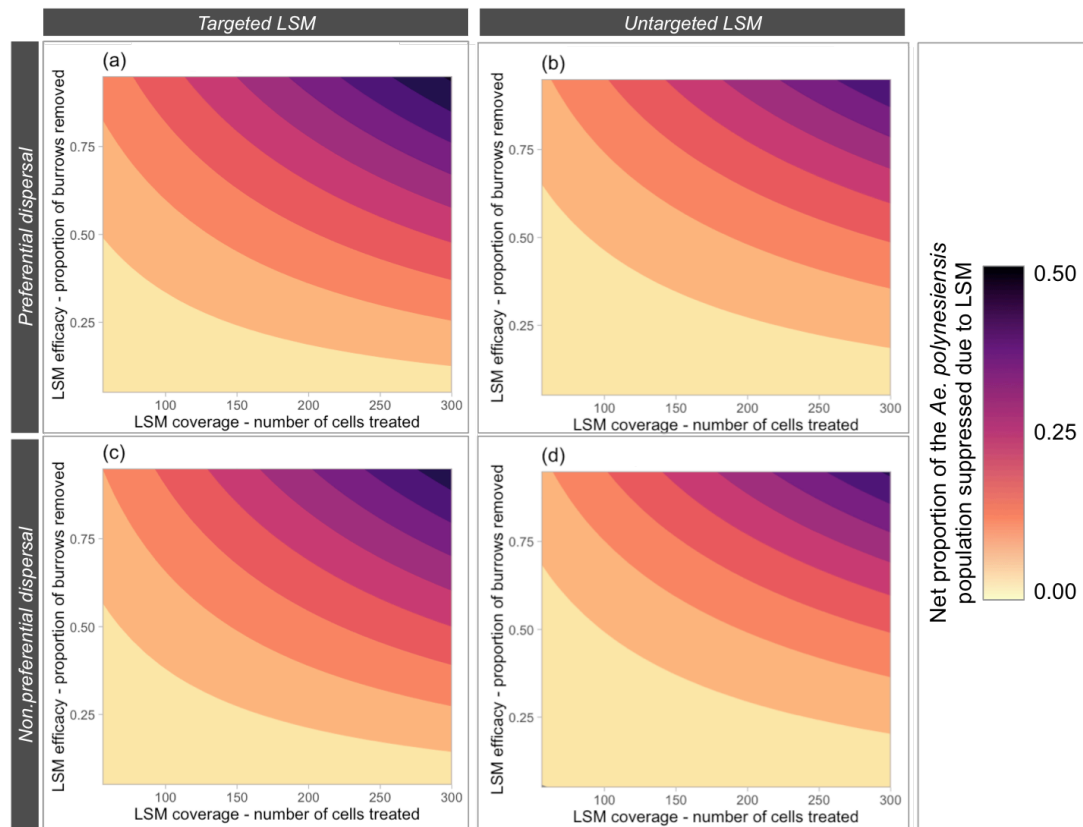


Figure C. 6. Net proportion of the *Ae. polynesiensis* mosquito population suppressed using targeted (a) & (c) and untargeted (b) & (d) larval source management (LSM) for the preferential (a)-(b) and non-preferential (c)-(d) dispersal models. Results are presented across a parameter space with  $\theta$ , the number of grid cells treated, on the x-axis and  $\epsilon$ , the efficacy of LSM treatment in terms of the proportion of burrows removed, on the y-axis. Targeted LSM was marginally more effective on average than untargeted LSM.

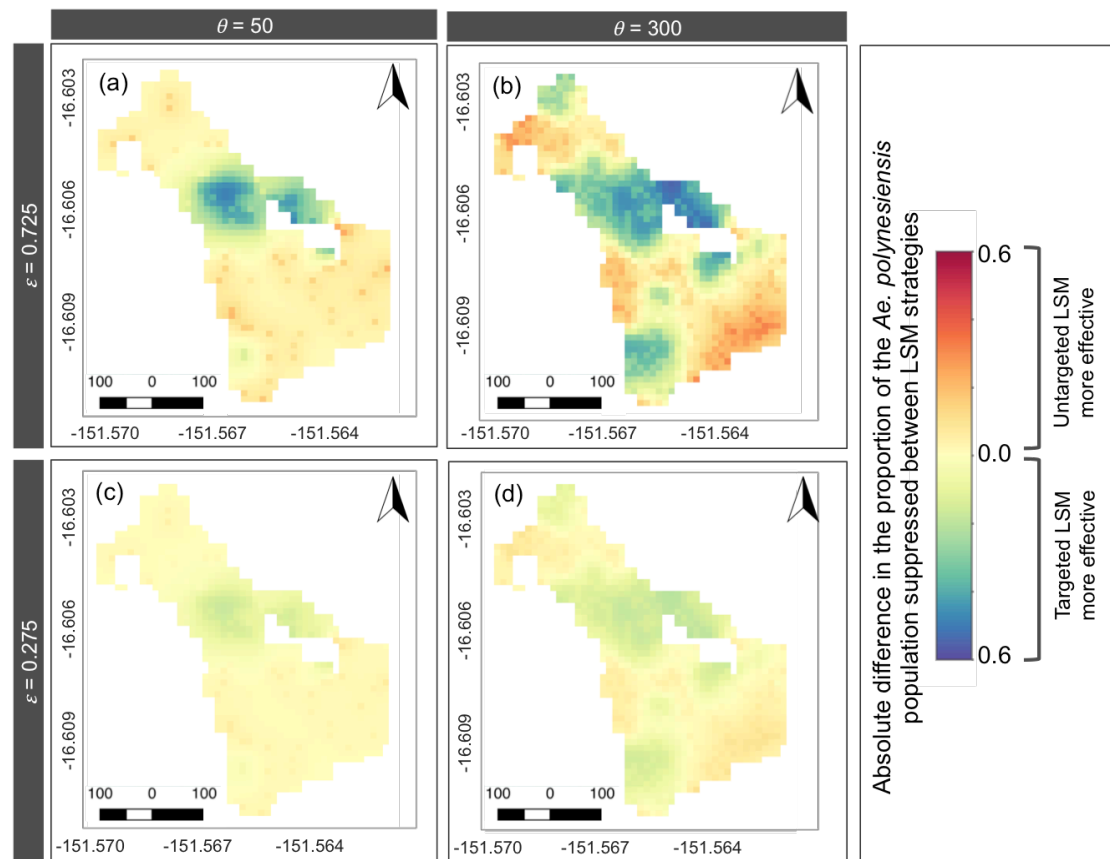


Figure C. 7. Using the preferential dispersal model, the absolute difference between larval source management (LSM) strategies in the proportion of the *Ae. polynesiensis* population suppressed. Results are displayed for a combination of LSM coverage values ( $\theta$ , the number of cells treated) and efficacies ( $\epsilon$ , the proportion of *C. carnifex* burrows removed at each treated cell). Orange/red colours indicate that untargeted LSM is more effective. Green/blue colours indicate that targeted LSM is more effective. Yellow indicates no substantial difference in the proportion of the population suppressed between LSM strategies.

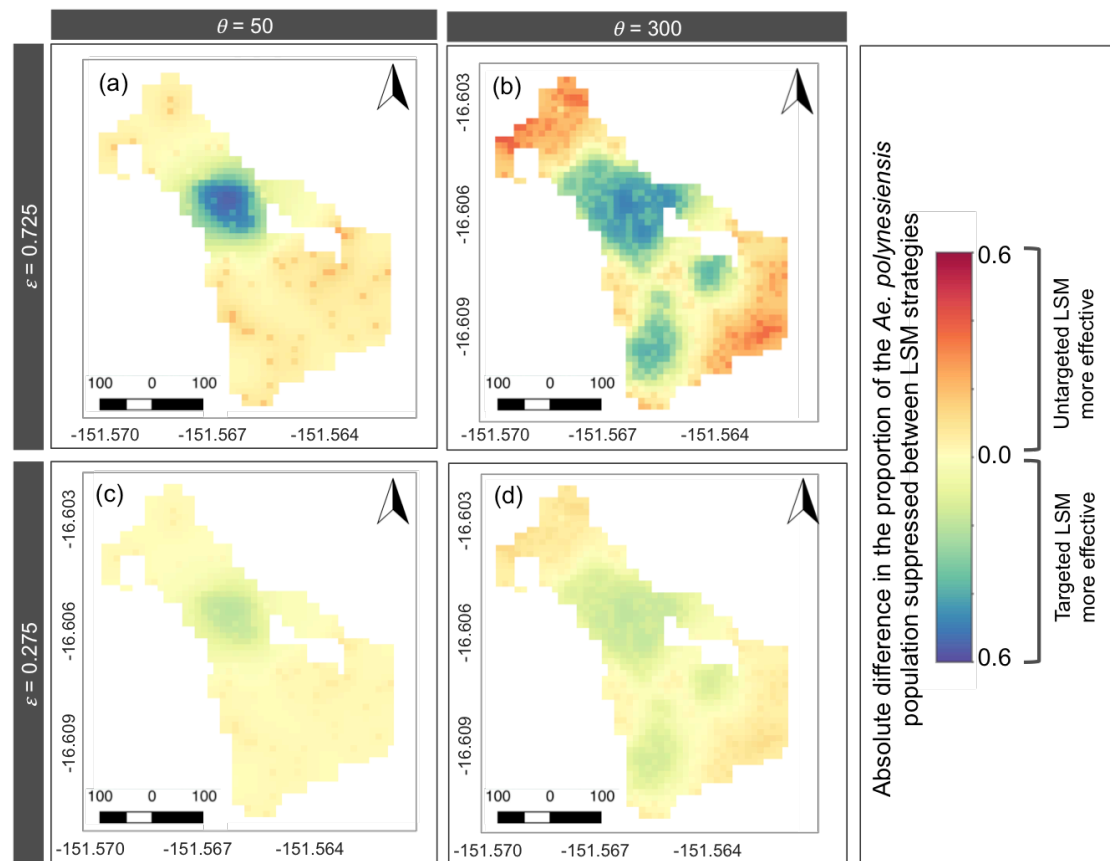


Figure C. 8. Using the non-preferential dispersal model, the absolute difference between larval source management (LSM) strategies in the proportion of the *Ae. polynesiensis* population suppressed. Results are displayed for a combination of LSM coverage values ( $\theta$ , the number of cells treated) and efficacies ( $\varepsilon$ , the proportion of *C. carnifex* burrows removed at each treated cell). Orange/red colours indicate that untargeted LSM is more effective. Green/blue colours indicate that targeted LSM is more effective. Yellow indicates no substantial difference in the proportion of the population suppressed between LSM strategies.

## **C.9. Spatial interpolation of field data**

Radial basis functions (RBFs) are an exact interpolation method. RBFs may therefore avoid smoothing of high and low *C. carnifex* burrow densities as incurred by random forest models. In addition, RBFs can predict outwith the range of training data unlike other spatial interpolators such as inverse distance weighting. We used RBFs to predict *C. carnifex* burrow density using the *geospt* package for R version 3.5.2 [4,5]. The optimal smoothing parameter,  $\eta$ , and the optimal parameter robustness,  $\rho$ , were selected by minimising the root-mean-square prediction error through cross-validation. Estimated *C. carnifex* burrow densities are shown in Figure C. 9. The maximum estimated *C. carnifex* burrow density was higher using RBFs than random forests due to the exact interpolation approach of RBFs.

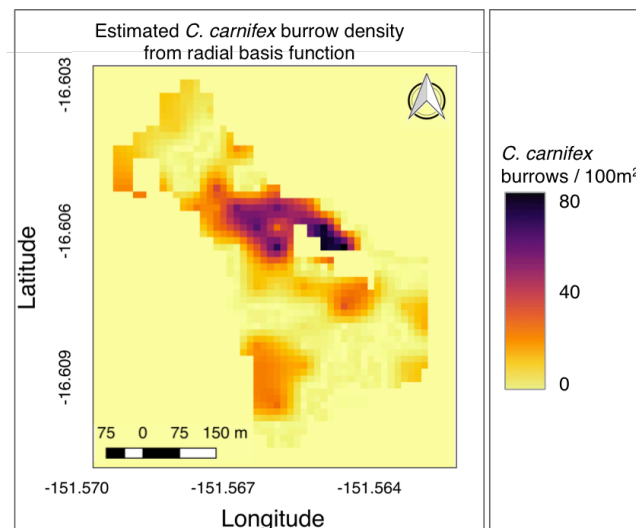


Figure C. 9. Estimated *C. carnifex* burrow density on motu Tautau using radial basis functions.

A comparison of preferential and non-preferential dispersal model results with BG-Sentinal (BGS) trap data using the RBF-estimated *C. carnifex* burrow density is shown Figure C. 10. The median preferential dispersal model predictions,

$med(\Psi \bar{A}_{i,j})$ , in the neighbourhood,  $n_{i,j}$ , of each trap were closer to the median observed mosquito numbers at each trap. The median difference between the number of trapped mosquitoes and model estimates was 102 for the preferential model and 309 for the non-preferential model. Therefore, estimation of *C. carnifex* burrow density using RBFs appears to result in slightly more accurate model results than using random forests for the preferential migration model, but notably less accurate results for the non-preferential migration model. The strengths and weaknesses of using interpolation methods such as RBFs compared to machine learning methods such as random forests are summarised in Table C. 4.

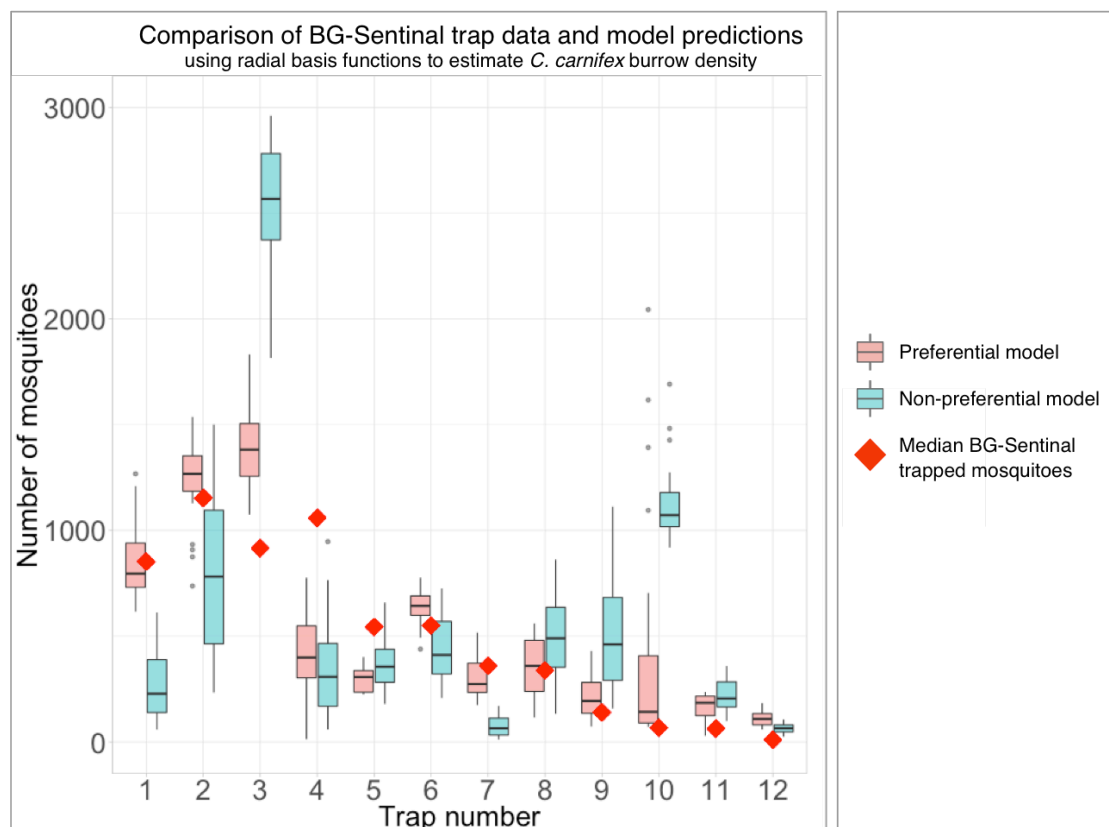


Figure C. 10. Comparison of preferential and non-preferential female dispersal models using *C. carnifex* burrow density predicted using radial basis functions with the median number of caught adult *Ae. polynesiensis* in BGS traps.

Table C. 4. Qualitative comparison of interpolation and machine learning methods for predicting environmental heterogeneity in the context of the current study. Interpolation methods could include radial basis functions (RBFs) or kriging. Machine learning methods could include random forests (RFs) or classification and regression trees (CART). The strengths and weaknesses of each approach are presented and the most appropriate scenarios to which they can be applied are highlighted.

| Method            |                                                                                                                                                                                                                      |                                                                                                                                                                                                                                            |
|-------------------|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
|                   | Interpolation                                                                                                                                                                                                        | Machine Learning                                                                                                                                                                                                                           |
| <b>Strengths</b>  | <ul style="list-style-type: none"> <li>• Retains observed data points</li> <li>• Able to predict trends</li> </ul>                                                                                                   | <ul style="list-style-type: none"> <li>• Captures non-linearity between sampling points</li> <li>• Can make use of other data (such as remote sensing data)</li> <li>• Can be applied to new areas outside sampling area</li> </ul>        |
| <b>Weaknesses</b> | <ul style="list-style-type: none"> <li>• Cannot predict non-linearity</li> <li>• Predictions are limited by the availability of sampling points</li> <li>• Cannot be applied outside of the sampling area</li> </ul> | <ul style="list-style-type: none"> <li>• Some over- and under- estimation (smoothing)</li> <li>• Not able to predict trends</li> <li>• Relies on external data holding meaningful information about environmental heterogeneity</li> </ul> |
| <b>Best for?</b>  | <ul style="list-style-type: none"> <li>• Small scale</li> <li>• Consistent sampling grid</li> <li>• Large number of sampling points</li> </ul>                                                                       | <ul style="list-style-type: none"> <li>• Large scale</li> <li>• Sparse sampling</li> <li>• Inconsistent sampling grid</li> </ul>                                                                                                           |

## **References for Appendix C**

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