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Title:
Decision Support Tools for Vector-borne Spread of Animal Disease

Date:
2020

Persistent Link:
https://hdl.handle.net/11343/280273

Decision Support Tools for Vector-borne Spread of Animal Disease

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A thesis submitted for the degree of Doctor of of Philosophy at

The University of Melbourne in 2020

Faculty of Veterinary and Agricultural Sciences

Abstract

Bluetongue is a vector-borne, viral disease of ruminants that can cause substantial losses in productivity in farmed livestock. It is transmitted by *Culicoides* midges (Diptera: Ceratopogonidae) which means that the geographic distribution of disease is restricted to those regions where these vectors are present. In 2006 a virulent serotype of bluetongue (BTV-8) was detected in Northern Europe causing losses of livestock with knock-on economic and welfare effects. Bluetongue virus is endemic in Northern Australia, but clinical signs of disease have not been reported in either cattle or sheep. The risk of incursion of a virulent strain of bluetongue into Australia represents a constant threat, particularly the risk imposed by infected *Culicoides* midges blown from Indonesia to the northern borders of the Northern Territory.

This thesis reports the results of a series of studies designed to enhance Australia's preparedness for an incursion of a virulent serotype of bluetongue. This objective was achieved by design and implementation of facilities to allow the Australian Animal Disease Simulation model (AADIS) to simulate the spread of vector-borne diseases. In Chapter 3 we developed a model to allow the spatial and temporal distribution of *Culicoides* spp. across Australia to be estimated as a function of ambient temperature, prevailing wind conditions and the presence of cattle. In Chapter 4 a model of bluetongue virus vector-host transmission was developed, using the simulated midge population from Chapter 3 for the source population of insect vectors and details from the National Livestock Identification Scheme for the cattle host population at risk. A novel approach in Chapter 4 was the separation of host and vector populations into two 'layers' of different spatial format: a raster layer for the insect vector population and a spatial vector layer (i.e. points) to represent the cattle herd population at risk. This allowed our model to be readily adapted for other insect vector-borne diseases where the precise geographic location of a disease reservoir cannot be defined at the point location level. This approach would also be suitable for diseases with a wildlife reservoir such as wild boar in the case of African swine fever.

In Chapter 5 we implemented the prototype models in Chapters 3 and 4 into the Australian Animal Disease Simulation (AADIS) model, taking advantage of AADIS's existing architecture to account for the geographic distribution of the herd population at risk and direct animal movements between herds. Simulations were carried out using AADIS, allowing the number and geographic of distribution of infected herds to be estimated following an incursion of virulent bluetongue virus into a single herd. Large outbreaks of bluetongue were predicted in Southern Queensland and Northern New South Wales with larger outbreaks occurring when incursions occurred during the summer. Outbreaks in Northern New South Wales were smaller compared with the other areas, with a similar seasonal effect.

In Chapter 6 the AADIS bluetongue model was re-parameterised using climate change temperature estimates provided by CSIRO (2020), providing an example of how the preparatory work presented in Chapters 3, 4 and 5 can be drawn together to support real-world animal health decision making. In Chapter 6 the geographic extent of bluetongue outbreaks in the area immediately surrounding the site of incursion were substantially different from those estimated under the non-climate change scenario. An important finding was that bluetongue was able to establish itself in previously non-endemic areas of the country after being seeded into those areas following incoming movement of infectious cattle. This has important implications for animal health policy: in the event of an incursion of bluetongue into Australia the single most important control measure is to limit the movement of cattle out of affected areas in order to prevent establishment of disease elsewhere. This recommendation becomes even more important under climate change scenarios because the extent of the country with suitable habitat for *Culicoides* spp. will be substantially greater than what it is today.

Author declaration

This thesis is composed of my original work, and contains no material previously published or written by another person except where due reference has been made in the text. I have clearly stated the contribution by others to jointly-authored works that I have included in my thesis.

I have clearly stated the contribution of others to my thesis as a whole, including computational assistance, data analysis, significant technical procedures, professional editorial advice, financial support and any other original research work used or reported in my thesis. The content of my thesis is the result of work I have carried out since the commencement of my higher degree by research candidature and does not include a substantial part of work that has been submitted to qualify for the award of any other degree or diploma in any university or other tertiary institution. I have clearly stated which parts of my thesis, if any, have been submitted to qualify for another award.

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Acknowledgements

First of all, I would like to thank my main supervisor Mark Stevenson for his tireless guidance, valued advice, constructive feedback and constant inspiration throughout the course of my PhD.

I also want to thank Simon Firestone for his tremendous help and advice in solving many obstacles I have faced through this research. In addition to this, Mark and Simon are each responsible for sparking my interest in this field (though I was a devoted parasitologist), and without their encouragement I would not have taken up the challenge and dipped into the unknown waters of epidemiology.

A special thank you goes to the Java wizard Richard Bradhurst for his support and for his collaboration to make this thesis successful by using the magic tool AADIS. I would also like to express my special thanks to Debbie Eagles for being an inspiring virological, epidemiological and entomological source of support and guidance. To Carol Hartley, I thank you for being a supportive, strong guiding force as Chair of my committee.

I would also like to thank Ian Langstaff and the NAMP Committee for providing access to the entomological data and inviting me to two of their annual meetings to give me the opportunity to present the results of my research and for providing valuable feedback and knowledge on the NAMP Program.

Rachel Iglesias from the Commonwealth Department of Agriculture and Water Resources and Jaimie Hunnam from the Victorian Department of Economic Development, Jobs, Transport and Resources are thanked for their epidemiological insights. I wish also to thank Kerryne Graham at the Australian Animal Health Laboratory for her assistance with HYSPLIT. Thanks also extended to Vanessa Round from the Australian Climate Science Centre, for providing future projection data and advising me on selecting the best model for my research.

I would love to thank Ling Zhu and Christina Marth for their long-lasting friendship and the inspiration and collegial advice that kept me going. And also big thanks go out to my epidemiology comrades, all the staff and friends for providing such an inspiring environment in which to work.

Last but most importantly, I want to thank my dear family and friends back in Oman for their ongoing support. To my dearest Shereen, Homoud and Aziza thank you for standing by my side when times got hard and for giving me a push when I needed it.

Nomenclature

ACF	: Australian Climate Futures
AADIS	: Australian Animal Disease model
ABM	: Agent based model
AGID	: Agar Gel Immunodiffusion
AHS	: African horse sickness
AKAV	: Akabane virus
AUSVETPLAN	: Australian Veterinary Emergency Plan
BT	: Bluetongue
BTV	: Bluetongue virus
BTV-	: Bluetongue serotype-
CMIP	: Coupled Model Inter Comparison Project
CSIRO	: Commonwealth Scientific and Industrial Research Organisation
DAWR	: Department of Agriculture and Water Resources
dsRNA	: Double-stranded RNA
EBM	: Equation-based model
EIP	: Extrinsic incubation period
ELISA	: Indirect enzyme-linked immunosorbent assay
FMD	: Foot and mouth disease
GCMs	: Global climate models
HYSPLIT	: Hybrid single-particle lagrangian integrated trajectory
NAMP	: The National Arbovirus Monitoring Program
NAQS	: Northern Australian Quarantine Strategy
NOAA	: National Oceanic and Atmospheric Administration
ODE	: Ordinary differential equation

OIE	: World Organisation for Animal Health
ppm	: Parts per million
RCP	: Representative concentration pathway
RT-PCR	: Reverse-transcription polymerase chain reaction
VBD	: Vector-borne diseases
VNT	: Virus neutralisation test
$W.m^{-1}$	: Watts per square metre
WHO	: World Health Organization

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Chapter 1

Introduction

Bluetongue is a vector-borne, viral disease of ruminants that can cause substantial losses in productivity in farmed livestock. It is transmitted by *Culicoides* midges (Diptera: Ceratopogonidae) which means that the geographic distribution of disease is restricted to those regions where these vectors are present. In 2006 a virulent serotype of bluetongue (BTV-8) was detected in Northern Europe causing losses of livestock with knock-on economic and welfare effects. Bluetongue virus is endemic in Northern Australia, but clinical signs of disease have not been reported in either cattle or sheep. There are five different *Culicoides* species reported in Australia, but *C. brevitarsis* is the most important because it is the most widely distributed and numerous of the five, although it is not an efficient competent vector. The previous outbreak of BTV in Northern Europe and the unexpected ability of bluetongue to become endemic in cooler climates has resulted in more research activities, particularly modelling studies, to provide a better understanding of factors influencing disease transmission. Bluetongue transmission models are used to simulate the spread of disease within a population following virus incursion. They can also be used to determine appropriate decisions for control measures, such as vaccination, culling and/or animal movement bans.

The Australian Animal Disease model (AADIS) is a newly developed model designed to provide decision support for outbreaks of foot and mouth disease. The design of AADIS has been such that it can be readily extended to simulate the spread of other diseases of livestock, including those that are vector-borne. Hence, the overarching aim of the series of studies presented in this thesis is to provide the necessary preparatory work to implement a capacity for ADDIS to simulate vector borne disease spread. This work is accomplished by a review of the relevant literature related to bluetongue and methods used to model its spread (Chapter 2), adaptation of an existing model to estimate the geographic distribution of *Culicoides* midges across Australia over time (Chapter 3) and design of a prototype model to simulate the spread of bluetongue from vector to susceptible hosts and *vice versa* within AADIS (Chapter 4). With this work completed the prototype vector-borne disease spread model was then implemented within AADIS. Chapter 5 describes the use of AADIS to simulate the spread of bluetongue under current Australian conditions. Chapter 6 describes how climate change projection data can be used to estimate changes in the likely spread of bluetongue as a result of global warming.

This dissertation concludes with a general discussion (Chapter 7) providing a summary of the key findings and recommendations for policy and further research.

Chapter 2

Literature review

2.1 Vector-borne diseases of domestic livestock

According to the World Health Organization (WHO) vector-borne diseases (VBD) comprise 17% of the incident infectious diseases of humans in any given year. In addition, the number of arthropod-borne infections occurring each year and the geographical extent of affected areas is increasing due to climatic change, urbanisation and changing patterns of travel and trade (Jones et al. 2008). A notable example of VBD emergence was the outbreak of BTV-8 that occurred in Europe in 2008 (Saegerman et al. 2008, Conraths et al. 2009, Agren et al. 2010, Kampen & Werner 2010). Arthropod vectors and the diseases they transmit negatively impact on the health and productivity of humans, domestic livestock and wildlife. The most common disease vectors are arthropods which include flies (mosquitoes, midges, black flies, sand flies and tsetse flies), ticks, fleas, and lice. Many of the important pathogens carried by arthropod vectors are viruses (arboviruses) and these are responsible for the main categories of emerging diseases that affect human and domestic animals worldwide (Contigiani et al. 2017).

2.2 Bluetongue virus

Bluetongue is caused by bluetongue virus (BTV), a member of the genus *Orbivirus*, family *Reoviridae* (Borden et al. 1971). Bluetongue plays an important role in the trade of animals and animal product both domestically and internationally (Dungu et al. 2004). Prior to 1998 bluetongue was an exotic disease in Europe small numbers of incursions occurring each year (as in Spain and Portugal from 1956 through 1960) (Silva 1956). Between 1998 and 2005 the virus expanded in a northerly direction in continental Europe following a series of incursions, leading to severe outbreaks including one in which resulted in the death of over 1.5 million sheep (Mellor & Wittmann 2002, Purse et al. 2005).

The infection is usually subclinical in cattle, which then act as a reservoir for the virus. However, some serotypes, such as BTV-8, which caused outbreaks in northern Europe in 2006, has a greater virulence in cattle than other serotypes (Thiry et al. 2006). Sheep are the main host of BTV but infections are usually subclinical. Local breeds of sheep have a lower probability of showing clinical

signs of bluetongue when infection occurs (Thiry et al. 2006).

Although strains of BTV are already present in Australia, there is a risk that exotic strains could enter the domestic ruminant population either from movement of viraemic animals or inoculation of contaminated biological products into ruminants. Wind dispersal of BTV-positive insect vectors from areas where disease is endemic is another mechanism by which an exotic virus strain might enter the domestic ruminant population. While there has been no evidence of clinical disease in Australia (unlike Europe, Asia and Africa where bluetongue has killed large numbers of animals) evidence of exposure to BTV in export cattle is sufficient to halt trade with some countries (Animal Health Australia 2015).

2.2.1 Historical perspectives

Bluetongue was first described in the late 19th century as 'Tong-sikte' by the French zoologist Francois de Vaillant when he travelled to the Cape of Good Hope in 1781 and 1784 (Gutsche 1979). Spreull (1905) was the first to provide a comprehensive description of the disease which he called 'malarial catarrhal fever'. The description of clinical signs in infected sheep included high fever lasting 5 to 7 days, where after 7 days distinctive lesions appeared in the mouth and the tongue (Spreull 1905). Spreull suggested to name the disease 'bluetongue' on the basis of these characteristic lesions. The first reported cases of bluetongue in cattle were in 1933 in South Africa (Bekker et al. 1934). In 1944 du Toit identified *Culicoides* as the vector of bluetongue and African horse sickness (Du Toit 1944). Up until the start of World War II bluetongue was generally thought of as a disease mainly affecting cattle in Africa until there was an outbreak responsible for the death of 2500 sheep in Cyprus (Gambles 1949, Gibbs & Greiner 1994). In 1952, BTV was isolated from sheep with signs consistent with 'sore muzzle' in California, USA (McKercher et al. 1953). Later the disease caused a major outbreak in Portugal which then spread to Spain in 1956 (Manso-Ribeiro et al. 1957). As a result of this outbreak there were over 179,000 deaths over a period of 4 months. This outbreak of BTV aroused major concerns internationally, mainly in the sheep rearing areas of Europe and Australia. The first evidence of BTV in Australia came in March 1975 with the isolation of serotype 20 from *Culicoides* collected at Beatrice Hill (Northern Territory) (St. George 1996, Ward 1994). Bluetongue is a listed disease of OIE because of its transboundary nature and major economic impact (Rushton & Lyons 2015).

2.2.2 Global distribution

Except for Antarctica, BTV, has been diagnosed on all continents (Gibbs & Greiner 1994, Tabachnick 2003, Maclachlan & Osburn 2006, Mellor et al. 2008, Maclachlan 2010). The distribution of BTV is consistent with the geographic distribution of haematophagous *Culicoides* spp. where climatic conditions are appropriate (Maclachlan 2011). In brief, BTV occurs in a geographic band that includes tropical, subtropical and temperate regions between the latitudes of 40° North and 35° South (Maclachlan & Osburn 2006). An exception is Asia and the western areas of North America where the disease occurs as far north as latitude 50° North (Clavijo et al. 2000, Lundervold et al. 2003,

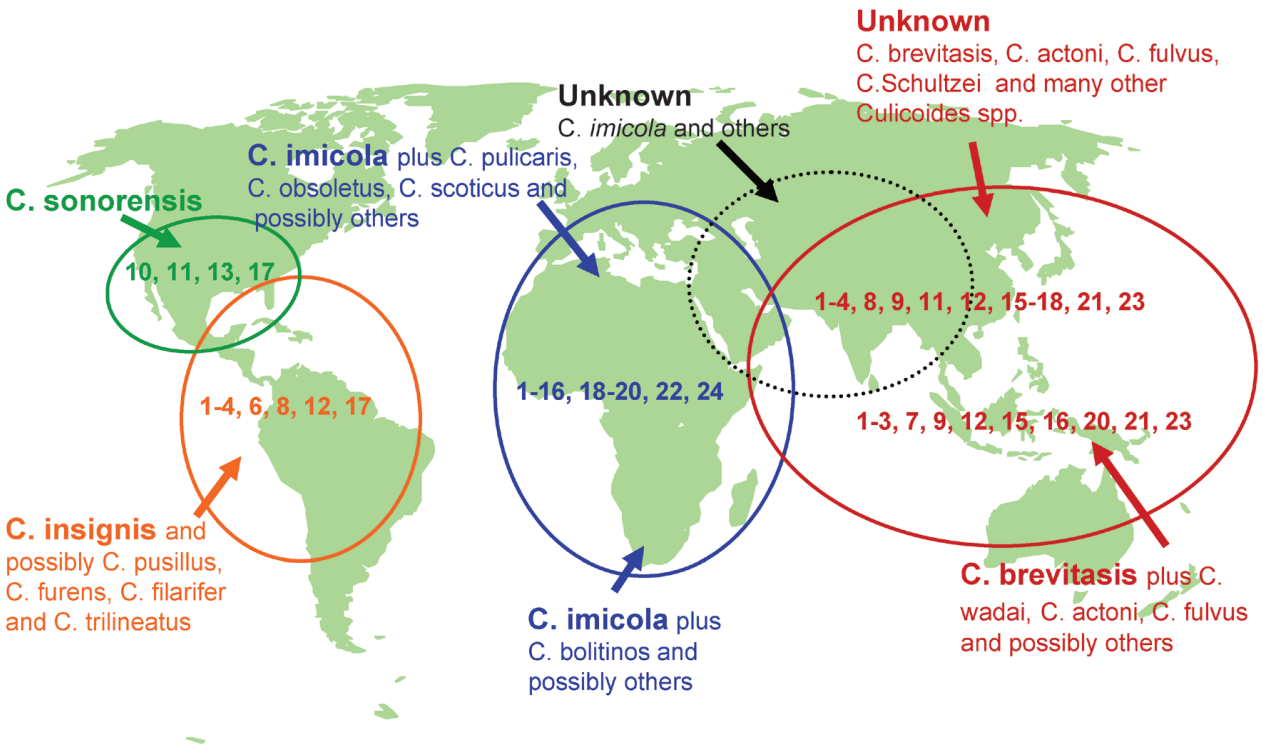


Figure 2.1: Map showing the global distribution of bluetongue virus serotypes and (known) *Culicoides* vector species. Adapted from Tabachnick (2003).

Tabachnick 2003, Shoorijeh et al. 2010) and recently northern Europe and the Mediterranean Basin to a latitude of at least 45° North, including portions of Italy, Greece, Spain, France and the Balkans (Giovannini et al. 2004, Purse et al. 2005). BTV is endemic in sub-Saharan Africa, large portions of Asia and much of the Middle East (Maclachlan 2010). However, the distribution of different BTV serotypes and their insect vectors differ throughout the world as shown in Figure 2.1 (Gibbs & Greiner 1994, Tabachnick 2003, Maclachlan & Osburn 2006, Balasuriya et al. 2008).

In 2006 BTV-8 was first detected in northern Europe and from the site of first detection BTV-8 in Europe has spread widely, from the Mediterranean Basin to north Europe (Saegerman et al. 2008, Conraths et al. 2009, Agren et al. 2010, Kampen & Werner 2010). BTV serotypes that entered the Mediterranean after 1998 (with the exception of BTV-8) are known to have originated in either northern Africa or Asia (Purse et al. 2005). These incursions are believed to have initially reached Europe by wind-borne spread of virus-infected vectors which then infected ruminants in destination areas (Maclachlan 2010). Thus, these animals were the source of infection to vectors already present. Also, BTV serotypes 2, 10, 11, 13 and 17 have long been present in extensive portions of North America, but after 1998 some 10 additional BTV serotypes (1, 3, 5, 6, 9, 12, 14, 19, 22 and 24) have been identified in the south east of the USA 1998 (Maclachlan 2010, Ostlund 2010). It is assumed that these serotypes entered North America from the Caribbean where they are endemic. In Australia, most serotypes of BTV are closely grouped together and are distinct from those from Africa or the Americas and are more related to those from Asia (St George et al. 2001). In March 1975 BTV-20 was first identified in

Australia following isolation of the virus from *Culicoides* midges trapped near Darwin (Ward 1994). Later, evidence of exposure to a further eleven serotypes (1-3, 5, 7, 9, 12, 15, 16, 21 and 23) has been identified in healthy sentinel cattle, mainly in the Northern Territory (Animal Health Australia 2015).

2.2.3 Aetiology

Bluetongue is a double-stranded RNA (dsRNA) virus of the *Reoviridae* family within the genus *Orbivirus* (Borden et al. 1971, Mertens et al. 2004). The family *Reoviridae* is comprised of 15 genera of multi-segmented dsRNA viruses, of which some are pathogens of mammals, fish, reptiles, insects, plants and humans.

The genome of *Orbivirus* genus is comprised of 10 segments of dsRNA (Verwoerd et al. 1970, Mertens et al. 2004). BTV is icosahedralin shape and comprised of a segmented dsRNA genome encapsidated in a double-layered protein coat (Mertens et al. 2004). In addition to BTV, viruses of the genus *Orbivirus* cause African horse sickness, epizootic haemorrhagic disease and equine encephalitis (Mertens et al. 2004, Pfeffer & Dobler 2010).

At the time of writing a total of 27 BTV serotypes have been recognised worldwide (Schulz et al. 2016, Zientara et al. 2014). Serotype 27 was recently identified in goats showing no clinical signs during a monitoring programme in Corsica, France, in 2014 (Zientara et al. 2014).

BTV-27 is closely related to serotypes BTV-25 and BTV-26 (Jenckel et al. 2015). BTV-25 and 26 were recently detected in goats without clinical signs in Switzerland (Chaignat et al. 2009) and in sheep in Kuwait (Maan et al. 2011), respectively. In addition, the detection of two putative novel serotypes in a Capripox vaccine in the Middle East (BTV-28) and in an alpaca in South Africa (BTV-29) has recently been identified, but the criteria that determine a novel serotype by percentage divergence in sequence identity in comparison with other BTV serotypes need to be clarified (Wright 2014, Zientara et al. 2014, Maan et al. 2015). BTV-2 was isolated in California in the USA indicating trans-continental spread of the virus serotype first described in the United States in Florida in 1982 and originally believed to be limited to the southeastern United States (Maclachlan et al. 2013). The BTV-2 is a reassortant of BTV-2 and BTV-6, the latter of which was previously unknown in North America (Gaudreault et al. 2014). Similarly, the BTV-3 strain that have recently expanded their distribution beyond the southeastern United States are able to readily reassort with BTV strains that are historically enzootic in the USA (Schirtzinger et al. 2018). Mayo et al. (2020) provides a review of BTV serotypes recently identified in the USA.

Bluetongue strains vary considerably in their virulence with some the cause of subclinical disease while others can lead to severe clinical signs with high rates of mortality (Maclachlan 2011). BTV-8, when it emerged in the north of Europe in 2008 (Thiry et al. 2006) caused deaths and production losses in affected stock. Additional losses occurred due to bans on the trade of livestock between BTV-infected and non-infected areas (Zientara & Sanchez-Vizcaino 2013). BTV-20 was the first detected bluetongue serotype in Australia (Boyle et al. 2012) and was among the first eight serotypes detected between 1975 and 1986 (BTV-1, 3, 9, 15, 16, 20, 21 and 23) (St George et al. 2001). Since 2007

Australia has detected additional BTV serotypes, BTV-7 (2007), BTV-2 (2008) and, more recently, BTV-12 (2015) (Eagles et al. 2014, Maan et al. 2015, National Arbovirus Monitoring Program 2015). Even though BTV has been present in Australia for a long period of time there have been no reports of clinical disease due to the virus in either cattle or sheep.

2.2.4 Bluetongue transmission cycle

BTV is spread between by specific species of *Culicoides* biting midges (Diptera: Ceratopogonidae). For this reason the geographic distribution of bluetongue is limited to those areas where midges occur. Within midge-positive areas BTV transmission is restricted to those times of the year when vectors are most abundant.

Adult *Culicoides* are crepuscular which means that their peak period of feeding activity is at sunset and sunrise and, to a lesser extent, through the night (Martínez-de la Puente et al. 2009). Peaks in biting activity occur just before and after sunset and just before dawn (Bellis et al. 2004). Adult female midges feed on the blood of ruminants during these times, spreading the virus if they are BTV positive. Once an insect vector is infected, it remains infectious for its lifetime and is able to transmit the virus with every blood meal.

Clinical signs of bluetongue last 7 to 28 days in cattle and 7 to 14 days in sheep (Ward 1994, St George et al. 2001). During this period, BTV might be transferred to *Culicoides* that take a blood from the infectious host. The probability of virus transfer from a blood meal is thought to be in the order of 1% (Gerry & Mullens 2000, O'Connell 2002). The probability that an insect vector becomes infectious varies according to its species competence and the concentration of virus in the blood of the infectious host. Competence refers to the ability of *Culicoides* to support BTV replication within the insect vector and to transmit virus to a susceptible host. Increases in environmental temperatures results in elevated rates of BTV replication within *Culicoides* vectors and a shorter latent period. Working in the other way, increases in environmental temperatures lead to higher vector mortality rates (Gerry & Mullens 2000). Recovery in the infected host is dependent on the length of time virus containing red blood cells circulate in the blood (Bonneau et al. 2002). Figure 2.2 provides a diagrammatic summary of the stages of the bluetongue transmission cycle.

2.2.5 Pathogenesis and clinical signs

Once a host becomes infected, BTV multiplies in the lymph nodes with subsequent spread to the vascular endothelium and dendritic cells in many organs (DeMaula et al. 2002a). Infected hosts becomes viraemic for 2 to 6 days (Mellor 2001, Purse et al. 2005); some can remain infectious for a period of up to 60 days (OIE 2016). In most cases clinical signs last for 7 to 28 days in cattle and 7 to 14 days in sheep (Ward 1994, Animal Health Australia 2015).

After receiving a bite from an infected midge, BTV is carried by the host's dendritic cells from the skin to the local lymph nodes (Hemati et al. 2009) which become the first sites of viral replication (Maclachlan 2004). A viraemia then occurs which then spreads the virus to secondary organs including

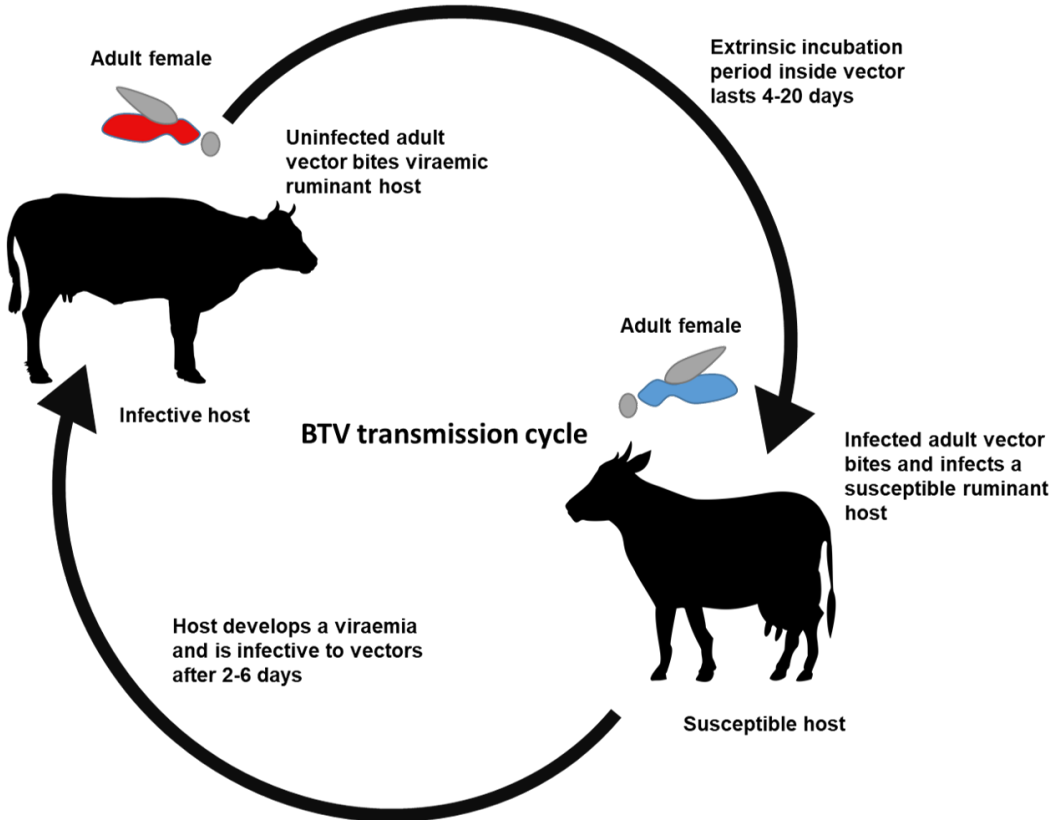


Figure 2.2: Transmission cycle of bluetongue virus.

the lymph nodes, spleen and lungs (Barratt-Boyes & Maclachlan 1994). The virus replicates in the vascular endothelium, macrophages and lymphocytes (Barratt-Boyes & Maclachlan 1994, Maclachlan 2004). In the early stages of the disease the virus is associated with both red and white blood cells, while at later stages it is primarily associated with just the red blood cells (Maclachlan 2004). Prolonged viraemia is caused when virus particles become sequestered in invaginations of the red blood cell membrane (Maclachlan 2004). Cell necrosis and apoptosis is the initial result of infection with BTV (Barratt-Boyes & Maclachlan 1995, DeMaula et al. 2001) and, by activating the p38MAP kinase, vascular permeability is increased (Chiang et al. 2006).

Bluetongue induces the production of TNFα, IL-1, IL-8, IL-6, IFN-I and cyclooxygenase-2 and increases concentrations of prostacyclin and thromboxane in the plasma. These two effects lead to an inflammatory response by the host (DeMaula et al. 2001). Bluetongue causes injury to the small blood vessels, giving rise to vascular occlusion and tissue infarction. This leads to clinical signs related to the development of oedema and effusions (Drew et al. 2010).

Outbreaks of bluetongue mainly occur when it is introduced into disease free areas where there are large numbers of susceptible naïve hosts, particularly sheep (Maclachlan 2010). Clinical signs of bluetongue include the presence of necrosis, erosions and ulceration in the mouth, nose and conjunctiva, facial oedema, lameness and coronitis, and general debility (Spreull 1905, Maclachlan et al. 2008). In acute cases there is swelling and oedema of the lips and tongue. Hyperaemia is intense leading to small red or purple haemorrhagic patches in the mouth, nose and conjunctival linings (Animal Health Australia 2015). The mortality rate varies reaching up to 70% with deaths occurring around five weeks

after the onset of clinical signs (Animal Health Australia 2015).

When cattle are exposed to BTV they can, in some cases, develop mild clinical signs, but in most cases the disease is subclinical (Luedke et al. 1970). Differences in clinical signs between cattle and sheep have been linked to species variation in the susceptibility of endothelial cells to BTV infection (DeMaula et al. 2001, 2002a,b).

2.2.6 Diagnosis

Whereas many strains of BTV cause subclinical disease in susceptible animals, reliable and fast confirmation of the presence of BTV infection and the ability to differentiate which serotype is involved is important at the start of an outbreak, allowing appropriate vaccines to be selected. Laboratory confirmation of the serotype involved in a bluetongue outbreak is based on the isolation and amplification of virus following inoculation of washed and lysed sheep red blood cells into embryonated chicken eggs and/or cell cultures. Subsequently the virus is serotyped using the virus neutralisation test (VNT) (Bréard et al. 2004).

A serological response to BTV develops 7 to 14 days after infection in which neutralising and non-neutralising anti-BTV antibodies are generated (Stott et al. 1985). Because anit-BTV antibodies are long lasting diagnostic tests for BTV infection can be based around detection of theire presence. Serological techniques for BTV detection can be organised into two main categories: those that detect the VP7 protein and those that detect the VP2 protein (Rojas et al. 2019).

Agar gel immunodiffusion (AGID) and indirect enzyme-linked immunosorbent assay (ELISA) are the most used techniques for serogroup determination. Serum neutralisation is the most often used assay for BTV serotype identification. Despite developments in the field of molecular biology, conventional diagnostic methods for detecting and distinguishing BTV remain. One of the major challenges in BTV diagnosis is not just the detection of virus but also differentiation of virus serotype. Viral purification, adaptation and amplification in embryonic chicken eggs, tissue culture, cells derived from *Culicoides* or inoculation of susceptible animals are important tools for identifying BTV. In the early 1990s diagnostic tests were developed based on the reverse-transcription polymerase chain reaction (RT-PCR) allowing a limited number of serotypes to be detected (Rojas et al. 2019). A part of the viral genome was amplified providing more reliable information on serogroup and serotype. A disadvantage was that these procedures required running the samples on agarose gels, making it impossible to implement them in developing countries. Since the 1990s there have been numerous improvements to these procedures and many RT-PCR protocols have now been validated and made accessible for use in resource-poor settings. The next stage is to use second- and third-generation sequencing (Wright et al. 2011) but at the time of writing these techniques are difficult and expensive to implement. Table 2.1 provides a summary of the main diagnostic tests for bluetongue recommended by the OIE.

Table 2.1: Characteristics of diagnostic tests for bluetongue.

Test type	Population freedom	Individual freedom	Eradication policy	Case confirmation	Surveillance	Post-vaccination
Real-time PCR	-	+++	-	+++	++	-
RT-PCR	-	+++	-	+++	++	-
Virus isolation	-	+++	-	+++	-	-
C-ELISA	++	+++	++	-	++	++
VN	++	+++	++	-	++	++
AGID	+	-	+	-	+	+
CFT	+	-	+	-	+	+

Key: +++ recommended method; ++ suitable method; + may be used in some situations, but cost, reliability, or other factors severely limits its application; - not appropriate for this purpose. RT-PCR: reverse-transcription polymerase chain reaction; C-ELISA: competitive enzyme-linked immunosorbent assay; VN: virus neutralisation; AGID: agar gel immunodiffusion; CFT: complement fixation test. Although not all of the tests listed as category +++ or ++ have undergone formal validation, their routine nature and the fact that they have been used widely without dubious results, makes them acceptable.

2.2.7 Treatment and control

Apart from supportive therapy there is no specific treatment for bluetongue. Once the causative serotype has been identified serotype-specific vaccines can developed to prevent further disease spread. The role of bluetongue vaccination is to protect susceptible hosts against infection and to induce a barrier to transmission through herd immunity. Approaches for BTV vaccination include vaccination of sheep only, cattle only or both cattle and sheep. Vaccination of cattle is likely to be a more effective control measure than vaccination of sheep because cattle are likely to be viraemic for longer periods of time compared with sheep (Animal Health Australia 2015). In some Europe cattle are vaccinated to permit their transport from infected to non-infected areas. Two types of bluetongue vaccines are in use: inactivated (killed) and attenuated (live). Recombinant bluetongue vaccines are under development based on different methods but, at the time of writing, none have been approved (OIE 2016).

Bluetongue outbreak control measures include placement of restrictions on the movement of susceptible hosts out of infected areas, the slaughter of identified infected hosts to prevent them acting as a source of virus to others and housing of susceptible hosts during times of high insect activity (Spreull 1905, Bréard et al. 2004). Of these methods the use of protective housing is of little practical use for extensive livestock production systems and the utility of housing is dependent on the degree of endophilic or exophilic activity exhibited by the vector species present in each area (Cheah & Rajamanickam 1991, Doherty et al. 2004, Napp et al. 2011). Restrictions on the movement of animals are important for the control of bluetongue outbreaks, but movement restrictions are often associated with negative economic effects (Mellor et al. 2009). For example, during a recent outbreak of bluetongue in Italy, cessation of the movement of livestock from Sardinia to Tuscany led to substantial negative economic impacts on livestock producers which in turn led to social unrest (Giovannini et al. 2004). Culling strategies for bluetongue are not generally regarded as effective due to the relatively high rate of subclinical infections (Maclachlan & Mayo 2013).

Vaccination is widely used for the control of bluetongue and is the most efficient way of controlling disease outbreaks. However, due to the presence of different BTV serotypes it is important that vaccines used match the serotype of BTV responsible for a given outbreak situation (Mellor et al. 2009, Zientara et al. 2010) with the ideal situation being a vaccine that induces immunity to all 26 serotypes. Currently, only attenuated (modified live virus) vaccines are commercially available.

Vector-based control strategies can be used to either reduce the number of adult or immature *Culicoides* or to eradicate them entirely. Methods for vector control can be divided into four broad categories: mechanical, chemical, biological and genetic. Mechanical control methods involve removal of vector habitat areas (e.g. dung and wastewater ponds) in an attempt to reduce or eradicate larval populations (Harrup et al. 2016). Chemical control methods involve a range of techniques which include the use of topical repellents, topical adulticides, the use of insecticide impregnated ear tags, insecticide treated mesh, larvicides, host systemic treatments and semiochemical-based systems (Harrup et al. 2016). Biological control refers to strategies in which entomophagous and entomogenous organisms are used to eradicate a pest species (Van den Bosch & Stern 1962). Over the last 10 years, research on *Culicoides* in this field has been limited to a small number of laboratory-studies showing the larvicidal effects of insect pathogenic fungi (Ansari et al. 2010, 2011). Regulators of insect growth (for example, mermithid parasites, iridescent viruses and pansporoblastic microsporidia) have been investigated as biological control agents (Carpenter et al. 2008, Mullens & Przhiboro 2008).

Since 2010 there have been substantial developments in the application of genetics and genomics to *Culicoides* research. Vector control strategies using genetic modification are showing promise as methods to either reduce vector population abundance or promote a refractory phenotype within vector populations (Alphey 2014).

2.3 *Culicoides* biting midges

Culicoides biting midges (Diptera: Ceratopogonidae) include Culicidae (mosquitoes), Tipulidae (crane flies), Chironomidae (non-biting midges) and Bibionidae (march flies). The suborder includes disease vectors such as black flies, biting midges and sand flies and agricultural pests such as gall midges. *Culicoides* are among the world's smallest haematophagous flies at 1 to 3 mm in length. So far greater than 1400 *Culicoides* species have been described and they are found in most parts of the world with the exception of Antarctica, New Zealand, Patagonia and the Hawaiian Islands (Mellor et al. 2000). Although they are of small size, *Culicoides* can cause substantial economic damage by being a biting nuisance to livestock and being vectors of disease. For example, the presence of *Culicoides* have a negative impact on tourism and outdoor activities in many parts of the world (Kettle 1995). *Culicoides* carry a range of pathogens including 53 viruses (Coetzer et al. 1994), 12 species of protozoa and 18 species of filarial nematodes (Linley 1985).

2.3.1 Life cycle

The life cycle of *Culicoides* includes four larval stages, a pupa stage and an adult stage (Figure 2.3). The duration of the *Culicoides* life cycle varies between species and the location of breeding sites (Uslu & Dik 2007). The complete life cycle can occur in two to six weeks, dependent on the species involved as well as the environmental conditions such as ambient temperature.

It is essential for the adult female to take a blood meal for her eggs to develop. Some *Culicoides* species mature a first batch of eggs without a blood meal but then need to take a blood meal for subsequent egg batches (Boorman & Goddard 1970). Male *Culicoides* midges do not feed on blood. Autogeny (where an adult female must take a blood meal before laying eggs) is not a trait of *C. imicola*, *C. brevitarsis*, *C. variipennis* or *C. obsoletus* but is a trait of *C. reithi*, *C. circumscriptus* (Becker 1960) and *C. impunctatus* (Boorman & Goddard 1970).

Female *Culicoides* lay eggs either singly or in batches of anywhere between 25 and 300 eggs. Each of the immature stages of the *Culicoides* life cycle require free water or moisture and *Culicoides* can be found in various habitats including pools, streams, animal dung, saturated soil and rotting fruit (Blanton & Wirth 1979, Wirth & Hubert 1989, Coetzer et al. 1994). Eggs hatch within 2 to 7 days (Coetzer et al. 1994). In some situations the egg stage of *C. vexans* may last over four months, while the larval stage may last for up to six months (Jobling 1953).

After larvae have passed through their three stages of development, they pupate and emerge as adults in 7 to 10 days (Campbell & Kettle 1976). The fourth instar larvae enter a period of suspended development over the winter which prolongs this phase to many months (Kettle 1995). Adult *Culicoides* have a short life span in the order of 20 to 30 days. In exceptional circumstances adult *Culicoides* may survive for up to 90 days (Mellor et al. 2000).

2.3.2 Feeding and flying activity

Adult females are obligate blood suckers (males are not) and are crepuscular with their main period of activity occurring before sunrise and sunset when conditions are often warm and without wind (Boorman 1993, Mellor et al. 2000). In general, female flight activity is to mate, find a blood meal or find an oviposition site. Because males do not feed on blood they tend to remain closer to breeding sites compared with females (Lillie et al. 1981, Kettle 1995, Mellor et al. 2000). The flight range of adult *Culicoides* is short and with a range from a several hundred metres to up to 3 kilometres (Lillie et al. 1981, Kettle 1995). Some studies have identified an average travel distance of between 2.0 and 2.2 kilometres over 4 days and a range of 1.2 kilometres within 12 hours (Lillie et al. 1985). Temperature is undoubtedly a major factor influencing the behaviour of *Culicoides* spp. Their activities are highest between 13 and 35 °C and insignificant at temperatures below 10 to 12.5 °C depending on species (Bishop et al. 1996, Saegerman et al. 2008).

Some studies have found that the wind influences flight distance and the direction of flight. This is because, by being small, midges are are dispersed by the wind which allows them to traverse long distances, even across bodies of water such as the sea (Hayashi et al. 1979, Sellers & Walton 1992).

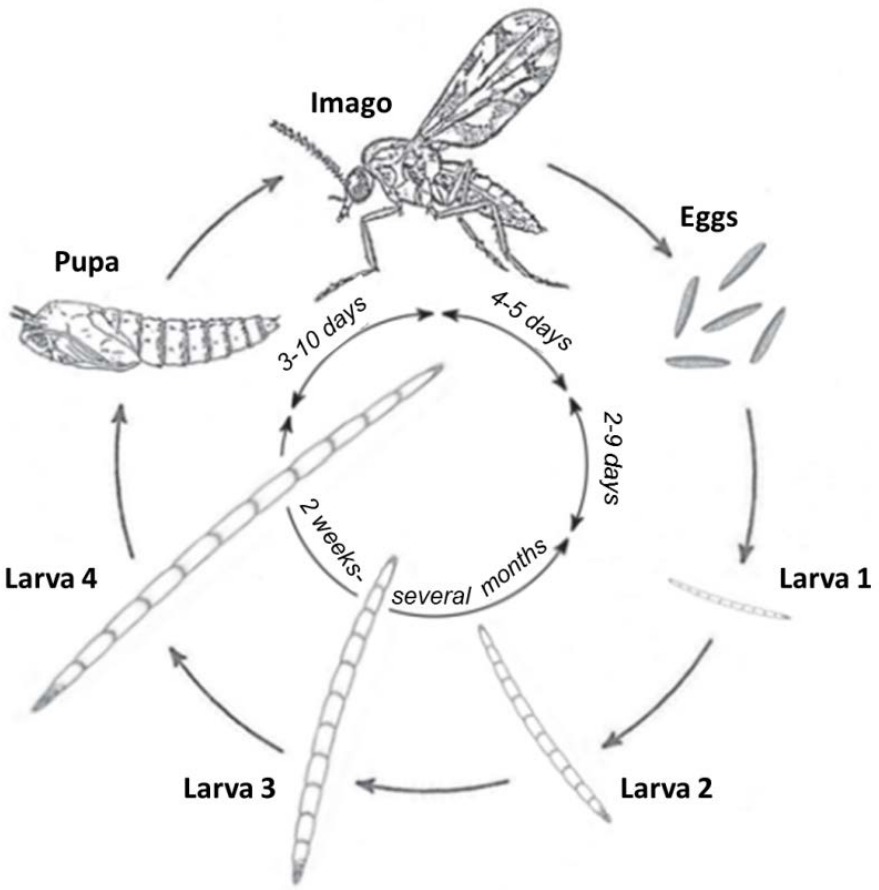


Figure 2.3: Life cycle of *Culicoides* spp. Adapted from Schulz et al. (2016) and Benelli et al. (2017).

Studies report varying effects of wind speed and direction on *Culicoides* dispersal. Some report high rates of recapture in the direction of prevailing winds (Beeeland & Smith Jr 1962, Williams 1962, Bréard et al. 2003) while others conclude that dispersal was not assisted by the wind (Lillie et al. 1985). Regardless of whether *Culicoides* will fly upwind following attractive host odours, as proposed by Kirkeby et al. (2013), or omnidirectionally, as proposed by others (Brenner et al. 1984, Sedda et al. 2012), the effect of the wind on *Culicoides* dispersal remains unclear and is likely to depend on midge species, presence of hosts and environmental characteristics. In summary, the wind is a possible route by which vectors can be introduced into non-endemic areas, in addition to animal movement events.

Rainfall is a determinant of adult *Culicoides* activity and survival but not *Culicoides* presence or absence. *Culicoides* are not active during periods of moderate to heavy rainfall and so are less likely to ascend vertically when these conditions are present (Murray 1987, Agren et al. 2010). While rainfall has been listed as an activity inhibitor, high humidity levels (promoted by rainfall) increase rates of *Culicoides* activity (Murray 1986). This is likely to be through the provision and improvement of breeding sites.

Most *Culicoides* feed on a range of hosts including cattle, sheep, horses, birds and humans. Specfic species have host preferences and aversions, for example, *C. brevitarsis* has a strong host preference for cattle and horses (Animal Health Australia 2015) whereas *C.imicola* does not feed on humans (Kettle 1995). In general *Culicoides* are attracted towards the strongest smell and visual stimulus. For

example, if a mixed herd of cattle and sheep is present, midges tend to feed on cattle, which have skin that is more accessible for biting (Animal Health Australia 2015).

2.3.3 Overwintering

The activity of midges is reduced during the winter months when temperatures are low which means that BTV transmission during the colder months of the year is interrupted. Some vectors can survive extended periods of low temperatures (in a process known as overwintering) allowing disease transmission to resume when temperatures start to rise again during the spring (Wilson et al. 2008). Most *Culicoides* survive the winter as larvae and hence BTV virus is theoretically able to be transmitted from infected adults to their offspring through transovarial transmission (Wilson et al. 2008). White et al. (2005) found that BTV could not be isolated from PCR detection of viral RNA in larvae providing no evidence to support this as a transmission mechanism. In Northern Europe, entomological surveillance systems have shown that a small proportion of the biting midge population remain active during the winter months (Wittmann et al. 2002, Losson et al. 2007) and the year-round presence of infectious *Culicoides* was thought to be the most likely reason for the persistence of BTV in ruminant populations (Algers et al. 2007). Another possible explanation for the persistence of BTV in ruminant populations is that transmission may occur between ruminants during coitus, since it has been reported that infected bulls shed BTV in their semen (Vanbinst et al. 2010).

In Europe it has been shown that BTV can may be transmitted vertically in cattle (Menzies et al. 2008, Santman-Berends et al. 2010). In the studies of Menzies et al. (2008) and Santman-Berends et al. (2010) newborn dairy calves from BTV-8 positive dams were BTV-8 positive, presumably as a result of transplacental transmission. The transplacental route is probably a transmission mechanism of relatively low importance when vectors are abundant. No instances of vertical transmission of BTV have been detected in Australia.

2.4 The bluetongue situation in Australia

In Australia, 12 of the 26 BTV serotypes have been isolated: BTV-1, 2, 3, 5, 7, 9, 12, 15, 16, 20, 21 and 23 (Animal Health Australia 2015). Testing of archived serum samples from sentinel cattle herds show the presence of bluetongue group-specific antibodies dating back to 1957 (St George et al. 1982). In 1968, the Commonwealth Scientific and Industrial Research Organisation (CSIRO) established the first sentinel cattle herds for monitoring arboviruses and by 1977 these were supplemented with a series of co-located vector traps (St. George 1996). After 1993 the program was maintained by the Northern Australian Quarantine Strategy (NAQS). Subsequently the program was expanded from Northern Australia to the Eastern States to become the National Arbovirus Monitoring Program (NAMP) in 1993. The NAMP monitors the geographic distribution of arboviruses of ruminants and their insect vectors throughout Australia. The diseases monitored by the NAMP include bluetongue, Akabane and bovine ephemeral fever. The locations of sentinel NAMP herds are limited to areas where commercial

cattle are kept (Melville 2004). Sentinel herds are selected to allow the geographic distribution of infection to be mapped. For this reason most of NAMP's sentinel herds and vector collection sites are strategically placed along the border areas of virus presence and absence, and in far northern sites in an effort to detect incursions of exotic serotypes. Additional areas, which are expected to be BTV-free are also monitored to provide on-going evidence of their BTV-free status (St George et al. 2001).

At NAMP traps and sites (Figure 2.4) counts of *Culicoides* vectors are recorded at the species level which are reported annually.[1] The NAMP allows changes in the distribution of arboviruses and their vectors to be monitored within years and between years and provide a means by which incursions of exotic BTVs and *Culicoides* may be promptly detected. In addition, this information provides a means by which exporters can meet certification requirements and provide confidence to trading partners that Australian cattle are bluetongue free. Approximately 250 *Culicoides* species have been reported in Australia (Animal Health Australia 2015) with only a small number capable of transmitting BTV and Akabane virus. Out of the 16 species of *Culicoides* tested, a total of seven were able to support virus growth, but only *C. fulvus*, *C. wadai*, *C. actoni* and *C. brevitarsis* were competent vectors (Standfast et al. 1985). While *C. fulvus* has the highest bluetongue competency, *C. brevitarsis* is the most widespread species throughout Australia (Kirkland et al. 2004).

[1] `https://www.animalhealthaustralia.com.au/what-we-do/disease-surveillance/national-arbovirus-monitoring-program/`

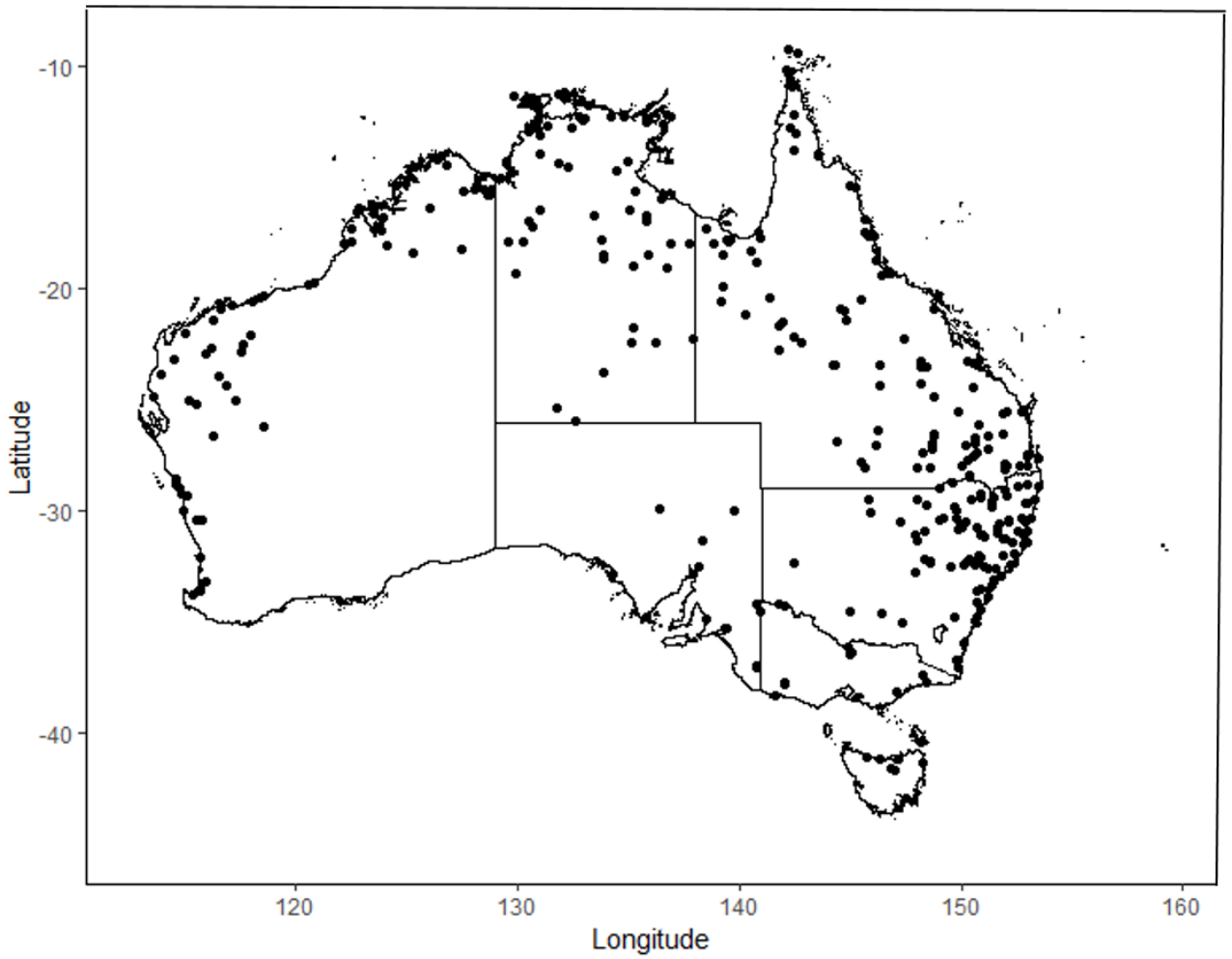


Figure 2.4: Map of Australia showing the location of National Arbovirus Monitoring Program sentinel herds and *Culicoides* trap sites, 1994 – 2018.

2.5 Disease models

Many challenges face disease control managers when it comes responding to outbreaks of emerging or exotic infectious diseases. For outbreaks of exotic, infectious disease it is important that appropriate control measures are applied quickly and efficiently. For outbreaks of emerging diseases it is important that control measures are consistent with the short-term and long-term risks involved. In this context, short term risks include loss of animal life or productivity as a result of disease whereas longer term risks include spillover of infection into human populations (in the case of zoonotic conditions) and loss of the ability to trade animals and animal product internationally (OIE 2016).

For an incursion of a virulent serotype of bluetongue into Australia it is important to decide on exactly which control measures will be implemented and exactly how they these measures will be implemented (for example, restriction of the movement of livestock initially followed by implementation of a vaccination program, assuming a suitable vaccine is available). Epidemiological modelling is particularly useful in this regard by providing a means by which the effect of alternative control strategies can be compared. While disease models of foot and mouth disease (FMD) have been developed and used extensively for outbreak response planning by a number of countries (Bates et al. 2003, Garner & Beckett 2005, Harvey et al. 2007, Stevenson et al. 2013) the same cannot be said about bluetongue and the bulk of modelling work related to bluetongue has arisen following the 2008 incursion of BTV-8 into Europe (Saegerman et al. 2008, Conraths et al. 2009, Agren et al. 2010, Kampen & Werner 2010).

Different models have been developed relating to animal health and examples cover the areas of risk analysis, epidemiology, analytical models and economics (Taylor 2003). Risk models identify and clearly define a hazard of interest and assess, either qualitatively or quantitatively, the likelihood of the hazard being released into an animal population and the probability of animals in the population of interest being exposed (Murray 2002). Epidemiological models can be defined as a mathematical and/or simulation-based representations of the epidemiology of disease transmission within a population (Garner & Hamilton 2011). Analytical models (also called empirical models) are those that use statistical analyses (typically multivariable regression techniques) to identify factors that either increase or decrease the risk of disease (Thrusfield 2013). Economic models, as the name suggests, model the production and use of resources in economic terms. Other models used in veterinary science include air flow models which have been used to estimate windborne spread of foot and mouth disease virus (Taylor 2003).

Epidemiological models of disease spread can be differentiated in terms of how they deal with time (discrete or continuous), space (spatially-explicit or non-spatial), variability (deterministic or stochastic) and the structure of the animal population at risk (homogenous or heterogenous) (Taylor 2003, Garner & Hamilton 2011). Deterministic models use fixed values for parameters and generate a single expected outcome, unlike stochastic models which account for natural variability in event outcomes plus the effect of chance to generate a range of possible outcomes (Garner & Hamilton 2011). Continuous time models may not realistically represent events that occur irregularly although

they are computationally efficient. Discrete models break time into equal units, continuously updating population disease status for each time period (Garner & Hamilton 2011).

2.5.1 Bluetongue transmission models

With compartmental, mathematical models of disease transmission the population is divided into compartments, with the assumption that every individual in the same compartment has the same characteristics. Transmission of bluetongue in a host population can involve development one of two types of compartmental models: (1) a herd-centred model, attributing one health state for each of the herds that might exist in a defined study area; and (2) animal-centred models, attributing a time-changing health state to each animal within a herd. The model of Gubbins et al. (2007) is generally cited as the original work from which most animal-centred bluetongue models are based. The bluetongue models cited in the literature (Saegerman et al. 2008, Conraths et al. 2009, Agren et al. 2010, Kampen & Werner 2010) all have a structure similar to that of the model of Gubbins et al. (2007), but vary in the way they incorporate additional factors influencing disease transmission or the ability to handle different control measures. Szmaragd et al. (2009) extended the non-spatial, deterministic Gubbins model to account for stochastic variability and geographic spread, focusing on BTV-8 spread in Great Britain in 2006 to 2007. Other models which share characteristics of the Gubbins et al. (2007) model include those of Græsbøll et al. (2012) and Bessell et al. (2016). These differ from the Gubbins et al. (2007) model through inclusion of an exposed state in susceptible hosts (in effect, an SEIR model) to accommodate the interval from onset of infection to onset of infectiousness.

Bluetongue models vary depending on host species with some considering only cattle and others considering both cattle and sheep (Table 2.2). None of the models reviewed accounted for the role that wild ruminants might play in disease transmission. BTV transmission from wild animals (e.g. deer) to insect vectors remains to be demonstrated and vector competency may differ between *Culicoides* species found in forests and open areas. The role wild ruminants play in the epidemiology of BTV in Australia need to be investigated in more detail but given the density of wild ruminants is low in areas in which domestic livestock are kept a plausible initial assumption is that the role of wild ruminants in BTV transmission is relatively small.

Susceptible herds are those where there are no BTV exposed or infected animals. Infectious herds those with at least one animal BTV exposed and in the infectious state. In all of the models listed in Table 2.2 an infectious herd is assumed to remain in that state until the end of the model simulation period. Three of the studies listed in Table 2.2 used susceptible-infectious (SI) models whereas Ducheyne et al. (2011) included a compartment to account for vaccinated herds. The model developed by Turner et al. (2012) included a total of seven compartments to account for herds where BTV was present but hosts within those herds had not yet become infectious and herds where hosts were infectious with or without showing clinical signs (Table 2.2).

A similar compartmental representation was applied to the insect vectors of bluetongue in all of the animal-centred models listed in Table 2.2 apart from the model of (Santman-Berends et al. 2013).

For the vector population model blood-feeding adult female *Culicoides* are designated to be in the susceptible, latent or infectious states. Once midges become infected following a blood meal from infectious hosts, they enter the extrinsic incubation period defined as the interval from virus ingestion (via a blood meal) to the point they become infectious. Midges are then assumed to remain infectious for the remainder of their lifetime. Most bluetongue transmission models are comprised of a single vector population, representing all species of *Culicoides* as a single group. However, the model of Guis et al. (2012) differs from the others in that it uses seperate parameters for *C. imicola* and *C. obsoletus* to account for the different geographical distribution of these midges. The model of Santman-Berends et al. (2013) focused on within-herd transmission of BTV-8 during the warmer months of 2007 and did not account for BTV transmission within insect vectors.

In the herd centred models, herds (i.e. groups of animals managed as a single group at a single location) are the epidemiological unit of interest and transmission of virus between individual animals within herds is not accounted-for. However, this could be less realistic since *Culicoides* play a major role in determining the dynamics (i.e. how quickly) BTV transmission occurs within a herd and therefore the length of time taken for a herd to become infectious following entry of BTV into the herd.

Between herd transmission within each of the published bluetongue disease models occurs by movement of animals from one location to another and vector dispersal. These mechanisms are either represented separately (Græsbøll et al. 2012, Turner et al. 2012, Ensoy et al. 2013, Græsbøll et al. 2014, Sumner et al. 2017), or jointly (Szmaragd et al. 2009, Gubbins et al. 2010, Szmaragd et al. 2010a,b, de Koeijer et al. 2011, Gubbins et al. 2012, Sumner et al. 2013, Boender et al. 2014) by combining transmission routes of transmission into a single probabilistic description. Most of the models use one or more transmission kernels that are dependent on the straight line distance between farm locations. Various distributional forms have been assumed for these kernels including the Gaussian, exponential and fat-tailed distributions. The distributional form of the kernel and the user-defined kernel bandwidth plays a key role in determining the distance over which one herd poses a risk to others in terms of disease transmission risk (de Koeijer et al. 2011, Boender et al. 2014).

Some models separately compared the contribution of BTV transmission via animal movement with that of vector dispersal (Table 2.2). Although systems are in place in most countries to record details of individual animal movement events, each of the models listed in Table 2.2 account for the dispersal of infection by animal movement using distance-based kernel functions (Turner et al. 2012, Sumner et al. 2017).

The models of Ducheyne et al. (2011), Græsbøll et al. (2012) and Græsbøll et al. (2014) were the only three that differentiated between active *Culicoides* flight and passive, wind-borne vector dispersal. Græsbøll et al. (2012, 2014) used Gaussian kernels to account for wind direction. In addition, Græsbøll et al. (2012, 2014) accounted for cattle movement between both farms and pasture areas, whereas Ducheyne et al. did not account for cattle movement in their model at all.

The speed of bluetongue spread depends on the size of the host population at risk, the number of infectious female midges present and the frequency of contact between host and vector populations.

Differences in the geographic distribution of host and vector densities was accounted-for in all models. In addition, all models used a metric referred to as the vector-to-host ratio to estimate the force of infection (with the force of infection greater when vector-to-host ratios were higher). Most simulations were carried out over relatively short time frames (typically less than 12 months, Table 2.2) so variation in the number of susceptible hosts arising from population turnover (i.e. births, purchases, sales, deaths and culls) was not accounted-for. Host populations were assumed to be constant except in those models where disease associated mortality was accounted-for (Gubbins et al. 2007, Szmaragd et al. 2009, Gubbins et al. 2010, Szmaragd et al. 2010a,b, Gubbins et al. 2012, Sumner et al. 2013, 2017). In contrast, vector population renewal was accounted-for in all models because it occurs at a much faster rate compared with host populations Midge mortality was typically set to vary with temperature. To ensure vector population sizes remained constant for the duration of a simulation period all models assumed that vector mortality was equal to vector recruitment rate.

Modelling contact between hosts and vectors is problematic due to (often) insufficient empirical data on the geographic and seasonal fluctuations in vector abundance and behaviour. The animal-centered models models typically used an explicit representation of vector populations. The effect of temperature on vector activity was accounted-for by inclusion of three vector-associated parameters: vector biting rates, vector mortality rates and the duration of the extrinsic incubation period. Other models did not account for the effect of temperature on vector abundance but instead allowed the extrinsic incubation period to vary with temprature (Bessell et al. 2016). Of the temperature-dependent parameters the extrinsic incubation period was the most important determinant of vector to host transmission with the gamma distribution used to capture its distributional form (Szmaragd et al. 2009, Bessell et al. 2016).

Some models used high-resolution climatic data to provide a more realistic estimate of the effect of climate on BTV transmission (Brugger & Rubel 2013, Guis et al. 2012, Hartemink et al. 2009, Racloz et al. 2007).

In summary, the geographical distribution of *Culicoides* in a defined study area was carried out using a three-step process: (1) specification of the environmental determinants of *Culicoides* presence and abundance; (2) assignment of these environmental predictors to geographical locations; and (3) overlay of these distributions to map the location of endemic vector species. This allowed predictions of vector abundance to be made which could then be used to estimate vector-to-host ratio. In the case of the Hartemink et al. (2009) study temperature, moisture and vegetation indices were combined to develop vector abundance maps for *C. obsoletus*, *C. chiopterus*, *C. dewulfi* and *C. pulicaris*. Guis et al. (2012) developed estimates of vector-to-host ratios for *C. imicola* and *C. obsoletus* using temperature, precipitation and sun index which then allowed prediction of bluetongue risk in Europe from 1960 to 2050.

Most models were used to assess the effect of various control measures on BTV transmission. Different control strategies were assessed with vaccination reducing within herd and between herd transmission and animal movement restrictions reducing between herd transmission only. In the model of Szmaragd et al. (2010b) a reference model of between herd BTV spread in Great Britain was

adapted to incorporate BTV-8 vaccination. Vaccination was used to minimise the risk of BTV infection in hosts and to decrease the risk that a vector acquires infection from an infected host. Some models focused on between herd transmission as opposed to within herd transmission (Græsbøll et al. 2012, 2014) whereas in other models herds within vaccinated areas were assumed to contribute differently to disease spread. A typical example would be the model of Ducheyne et al. (2011): these authors allowed vaccinated herds to remain susceptible to BTV infection but eliminated their ability to transmit virus to other herds.

The effect of movement restrictions on between herd BTV transmission was assessed in most of the models listed in Table 2.2. Animal movement restrictions were modelled by allowing transmission to occur from infected herds to those located nearby (i.e. vector-borne spread) but not to herds located further away (i.e. where BTV transmission would occur as a result of transport of an infectious animal from a source herd to a destination herd located some distance away). Some studies compared the effect of movement restrictions by using kernels to represent transmission at different scales (de Koeijer et al. 2011, Boender et al. 2014). The effect of the size of restriction zones around infected farms was assessed by Ensoy et al. (2013) and Turner et al. (2012) where they imposed new restriction zones as new BTV-positive herds were detected.

2.5.2 *Culicoides* dispersion models

In contrast to the models described above, other approaches have focused on simulating the temporal and spatial distribution of different vectors in relation to satellite-derived climatic variables (Ward & Carpenter 1996, Purse et al. 2004). Kelso & Milne (2014) described and applied a spatially-explicit model that combines insect vector dispersal with climate dependent insect vector population dynamics. Most models use weather data at a relatively low spatial and temporal resolutions and used only a single trajectory to represent the potential flight paths taken by *Culicoides* vectors (Ducheyne et al. 2007, Hendrickx et al. 2008). This is likely to underestimate the complex, stochastic nature of the atmosphere and dispersal of wind-borne *Culicoides* within it.

Few studies have used model-based approaches to simulate BTV spread and dispersal in Australia (Ward & Carpenter 1996, Eagles et al. 2013, Kelso & Milne 2014, Eagles et al. 2014). Kelso & Milne (2014) coupled *Culicoides brevitarsis* dispersal with climate dependent population dynamics. In this model disease transmission between or within herds was not accounted-for. Thus, it is logical to extend the capability of the Kelso & Milne (2014) model by including the disease transmission pathways.

Table 2.2: A summary of studies that have modelled BTV transmission.

Type	Spatial	Compartments	Time-step	Climatic factors	Study area	Temporal scale	Serotype	Host	Reference
Deterministic	No	SIR SLI [e]	Daily	Temperature	Great Britain	Time of incursion	NS	CS	Gubbins et al. (2007)
Stochastic	Yes	SIR SLI [e]	Daily	Temp	Great Britain	Year	BTV-8	CS	Szmaragd et al. (2009)
Stochastic	Yes	SIR SLI [e]	Daily	Temp	Scotland	Year	BTV-8	CS	Gubbins et al. (2010)
Stochastic	Yes	SIR SLI [e]	Daily	Temp	Scotland	Year	BTV-8	CS	Szmaragd et al. (2010a)
Stochastic	Yes	SIR SLI [e]	Daily	Temp	Great Britain	Year	BTV-8	CS	Szmaragd et al. (2010b)
Stochastic	Yes	SIR SLI [e]	Daily	Temp	Great Britain	Month	BTV-8	CS	Gubbins et al. (2012)
Stochastic	Yes	SEIR SLI [e]	Daily	Temp	Great Britain	Year	BTV-1	CS	Sumner et al. (2013)
Stochastic	Yes	SEIR SLI [e]	Daily	Temp	Great Britain	Year	BTV-8	CS	Sumner et al. (2017)
Stochastic	Yes	SEIR SLI [e]	Daily	Temp, wind	Denmark	Year	BTV-8	C	Græsbøll et al. (2012)
Stochastic	Yes	SEIR SLI [e]	Daily	Temp, wind	Denmark	Year	NS	C	Græsbøll et al. (2014)
Stochastic	Yes	SEIR SLI	Daily	Temp	Scotland	Year	BTV-8	CS	Bessell et al. (2016)
Deterministic	Yes	SEIR	Daily	-	The Netherlands	Year	BTV-8	C	Santman-Berends et al. (2013)
Stochastic	Yes	SI	Weekly	Temp, rainfall	Belgium	Year	BTV-8	C	Ensoy et al. (2013)
Stochastic	Yes	SEIDW	Daily	Temp	Eastern England	Year	NS	CS	Turner et al. (2012)
Stochastic	Yes	SIV	Weekly	Wind	South-France	Year	BTV-8	CS	Ducheyne et al. (2011)
Deterministic	Yes	SI	Daily	Temp	Western Europe	Year	BTV-8	CS	de Koeijer et al. (2011)
Deterministic	Yes	SI	Daily	Temp	NW Europe	Year	BTV-8	CSG	Boender et al. (2014)

Abbreviations: S, susceptible; E, exposed; L, latent; I, infectious; R, recovered; V, vaccinated; D, detected; $SEIDW_{SE}W_{SI}W_{EI}$, waiting from S to E / S to I / E to I (farm will become exposed/infectious when mandatory 6-day movement standstill expires); NS, not specific e, extended models; C, cattle; CS, cattle & sheep; CSG, cattle, sheep & goats.

2.5.3 The Australian Animal Disease Model

The Australian Commonwealth Department of Agriculture and Water Resources (DAWR) has developed animal disease modelling capability — the Australian Animal Disease Model (AADIS) to support FMD preparedness and response (Bradhurst 2015). AADIS was developed after recognising the threat of FMD to Australia's livestock industries (Buetre et al. 2013, Bradhurst et al. 2015). AADIS uses a deterministic equation-based approach to model within-herd spread of FMD and a stochastic, spatially-spatially-explicit agent-based approach to model between-herd spread and control (Bradhurst et al. 2015). The architecture of AADIS was developed to allow efficient handling of Australia's national, multijurisdictional, livestock population. Moreover, the model has efficiency for large-scale stochastic models and can run scenario hundreds of times to determine if patterns in disease spread are evident after accounting for the underlying stochastic processes.

AADIS uses five discrete pathways of infection spread: local spread, direct contact, indirect contact, spread through markets/saleyards and airborne spread. This approach is sufficiently granular to support the evaluation of targeted control measures such as livestock movement standstills, movement restrictions of animals and increases in farm biosecurity.

In AADIS an equation based model (EBM) is implemented within each FMD infected herd and this model deterministically predicts within-herd prevalence of infection and within-herd prevalence of clinical signs over time. EBM outputs feed into a stochastic agent based model (ABM) to allow spread between herds. The agent based model also uses equation based model outputs to estimate the probability that herds will be detected with disease and then queued for sanitary measures. AADIS provides a highly configurable suite of control measures based on the AUSVETPLAN national guidelines (Animal Health Australia 2006). In brief, in the event of an FMD incursion the current Australian policy is to eradicate the disease as quickly as possible using a policy known as stamping out, which involves culling and disposal of infected and exposed animals. Australian policy for the control and eradication of BTV is outlined in AUSVETPLAN (Animal Health Australia 2015). The strategy for a clinical disease outbreak caused by BTV is to reduce the economic impact and, where circumstances permit, eradicate clinical disease. The combination of strategies applied during a response to a clinical disease outbreak include: assessment of the epidemiological situation, imposition of quarantine and movement restrictions, treatment and husbandry procedures to control vectors, tracing and surveillance to determine the source and extent of infection, zoning to define infected and disease-free areas and vaccination to protect non-infected susceptible animals. Eradication may be feasible if the disease is detected early and there are no infected vectors if the outbreak is detected in a vector-free area or if frost is imminent in vector active areas.

The AADIS event-driven hybrid equation based model and agent based model architecture is flexible and efficient and provides an extensible design for modeling the spread and control of other diseases of livestock on a national scale. Since bluetongue is considered a threat to Australian livestock industries, the series of studies documented in this thesis aims to extend the modelling capability of AADIS to handle bluetongue.

Chapter 3

A model of the spatial distribution of a *C. brevitarsis* like midge in Australia

3.1 Abstract

Introduction: Effective emergency animal disease management is dependent on a detailed understanding of factors influencing disease spread. Disease models are tools used to prepare for emergency animal disease outbreaks. Bluetongue is a disease of livestock caused by a the bluetongue virus (genus *Orbivirus*, family *Reoviridae*) which is spread by *Culicoides* midges. The aim of this study was to estimate the spatial and temporal distribution of *Culicoides* spp. midges throughout Australia. A knowledge of the geographic distribution of insect vectors provides a necessary first step towards the development of a fit-for-purpose model to estimate the spread of bluetongue under Australian conditions.

Methods: We used a spatial raster-based approach to adapt a previously published model of *Culicoides* spp. growth to provide estimates of the distribution of *Culicoides* spp. across Australia and how that distribution changes on a seasonal basis. A raster-based approach was used in which the growth of *Culicoides* spp. within each raster cell varied according to average daily temperature. Dispersal of *Culicoides* from raster cells was set to depend on short-range diffusion and long-range (windborne) spread. The direction and distance of long-range spread was estimated using the Hybrid Single Particle Lagrangian Integrated Trajectory Model, HYSPLIT. Partial validation of our model was achieved by comparing *Culicoides brevitarsis* counts at four locations throughout Australia, as recorded by the National Arbovirus Monitoring Program, with *Culicoides* spp. count predictions.

Results: Our model provided biologically plausible estimates of the spatial distribution of *Culicoides* spp. across Australia as a function of time. While *Culicoides* spp. were not present further south than the north coast of New South Wales during the cooler months of the year, as temperatures increased they recovered to extend to the more southerly coastal regions of New South Wales.

Conclusion: Our model provides estimates of the distribution of *Culicoides* spp. across Australia in response to temperature and wind. This model provides a basis for simulating the dispersal and control of bluetongue virus in Australia.

3.2 Introduction

Among the haematophagous insects, *Culicoides* biting midges (Diptera: Cerato-pognidae) are the most abundant and occur throughout most of the inhabited world with the exception of Antarctica,

New Zealand, Patagonia and the Hawaiian Islands (Mellor 2000). Although they are relatively small, measuring from 1 to 3 mm in length, *Culicoides* biting midges have the ability to transmit several diseases of livestock of economic importance such as African horse sickness (AHS), epizootic haemorrhagic disease (EHD) and bluetongue (Mellor 2000). Recently, it was found that *Culicoides* midges are the vector of Schmallenberg virus (SBV) (De Regge et al. 2012), a cause of arthrogryposis and deformities in newborn calves. Prior to 1998 the geographic distribution of bluetongue was limited to tropical and subtropical areas of the world (Mellor et al. 2008). After 1998 incursions and outbreaks of bluetongue occurred in northern Europe and the Mediterranean Basin (Giovannini et al. 2004, Purse et al. 2005). Bluetongue is an internationally important emerging disease and 27 serotypes have been notified to the World Organisation for Animal Health (Maan et al. 2012). Transmission of BTV to ruminants occurs following the bite of an adult female *Culicoides* midge. As a result, the disease is restricted to those areas where biting midges are present which largely depends on environmental conditions (Mellor 2000). BTV can infect all species of ruminants and even though the disease is often subclinical, some serotypes can cause severe clinical signs with high rates of mortality, particularly in sheep (Maclachlan 2011).

Concerns were raised in the international animal health community when serotype 8 (BTV-8) was first detected in northern Europe between 2006 and 2008, causing moderate to severe clinical signs in infected cattle (Backx et al. 2009, Wilson & Mellor 2009*a*). These incursions caused considerable losses including mortality, morbidity, reduced production, abortions and foetal malformations (Vercauteren et al. 2008, Zanella et al. 2012). In addition, losses arising from the imposition of trade restrictions of ruminants between BTV infected and BTV non-infected areas have been substantial, prompting affected countries to establish control programs using inactivated vaccines (Sailleau et al. 2017). The introduction of BTV-8 into northern Europe has led to increased interest in understanding the drivers of arboviral diseases in domestic ruminant populations. It is believed that BTV entered Europe via wind-borne infected midges arriving from north Africa (see Wilson & Mellor 2009*b* for a comprehensive review).

Understanding the relationship between climatic and environmental factors helps to predict the behaviour of *Culicoides* midges and facilitates the development of models which can be used as decision support tools to determine appropriate measures to limit disease spread (Baylis & Rawlings 1998, Bishop et al. 2000, Kelso & Milne 2014, Leta et al. 2019). The influence of climatic conditions, particularly temperature, rainfall and wind speed on the activity and abundance of midges is well established (Kettle 1962). Temperature plays a major role in allowing *Culicoides* to complete their life cycle, flight activity, disease transmission and their ability to survive outside of endemic areas (Bishop et al. 1996). *Culicoides* midges have a short distance flying ability which is typically restricted to one to two hundred metres (Kettle 1995). On some occasions, with the assistance of the wind, flight can occur over 2 to 3 km (Lillie et al. 1981) and can sometimes reach several hundreds of kilometres (Sellers et al. 1977).

In Australia, the National Arbovirus Monitoring Program (NAMP) monitors the distribution of insect-borne diseases of ruminant livestock and their insect vectors. Arboviruses monitored by

NAMP include bluetongue, Akabane and bovine ephemeral fever (BEF) viruses. NAMP data are gathered throughout Australia by the serological monitoring of cattle in sentinel herds and strategic serological surveys of other cattle herds (serosurveys) and trapping of insect vectors. Approximately 250 *Culicoides* species have been reported in Australia (Animal Health Australia 2015), though only a small number have been shown to be capable of transmitting BTV and Akabane virus. *C. brevitarsis* are widespread throughout Australia and can transmit both BTV and Akabane virus. Other *Culicoides* species that can transmit BTV (with different competencies) include *C. fulvus*, *C. actoni* and *C. wadai* (Bishop et al. 1995, Eagles et al. 2013).

Several studies have addressed the biogeography of *C. brevitarsis* from an epidemiological perspective in Australia. The Hybrid Single-Particle Lagrangian Integrated Trajectory (HYSPLIT) model (for computing simple air parcel trajectories, as well as complex transport, dispersionand deposition simulations, Draxler & Hess 1998) was used by Eagles et al. (2013) to simulate the spatio-temporal spread of *Culicoides* dispersal into northern Australia from Indonesia, Timor-Leste and Papua New Guinea. Kelso & Milne (2014) developed a spatially-explicit model that combines insect vector dispersal with an insect vector population growth model dependent on temperature. In each of these models a limited number of trajectory sites was used to disperse *Culicoides*. In the model developed by Kelso & Milne (2014), populations of *Culicoides* were simulated without midge dispersal between cells. As a result, it is likely that the stochastic nature of atmospheric and long-dispersal range of *Culicoides* spp. were underestimated.

With this background, the aim of this study was to estimate the spatial and temporal distribution of *Culicoides* spp. across Australia using an approach based, in part, on the Kelso & Milne (2014) model. A secondary objective was to validate our model by comparing predictions with empirical data collected by NAMP.

3.3 Materials and methods

We developed a spatial simulation model of the growth and spread of *Culicoides* spp. on a national scale. This was achieved by adapting the *Culicoides* model of Kelso & Milne (2014) to estimate the spread of *C. brevitarsis* across Australia as a function of calendar time accounting for short-range diffusion (flying activity) and long-range dispersal. The relationship between these processes is shown in Figure 3.1. Later, a partial validation of the model was carried out by comparing our model predictions with *Culicoides brevitarsis* trap counts recorded by NAMP (Bishop et al. 2015). In the sections that follow we provide a description of our approach, focusing on modifications made to the Kelso and Milne model.

3.3.1 Modelling methodology

Our *Culicoides* spread model is a spatially-explicit simulation model which captures *Culicoides* population dynamics and movement of midges over time. The spatial unit of interest for our work is

a regular grid cell size of 10 km $\times$ 10 km cells covering the land mass of Australia. This grid size results in herd densities ranging from 0 to 264 with a median of four herds per cell. Furthermore, of the 167,028 grid cells, approximately 86% of them were devoid of herds. A smaller grid cell size would be considered if the study was at a small regional scale, however, because the continent of Australia comprised the area of interest grid cells of less than 10 $\times$ 10 km in size would have been computationally infeasible. Raster grid cells, as well as time, were treated discretely, which means that the count of *Culicoides* in each cell has been estimated for each day of a simulation period with the count of adult and juvenile *Culicoides* generated on day i passed to the next simulation day, day $i + 1$. Each grid cell's state is influenced by the state of other grid cells, for example, an infested cell spreads *Culicoides* to nearby grid cells by short-range movement or to distant cells by wind-borne dispersal.

3.3.2 *Culicoides* population dynamics

For each grid cell comprising the regular lattice, two populations were generated to represent the immature and adult stages of the *Culicoides* spp. life cycle. Temperature dependent midge population dynamics (that is, estimation of the density of immature *Culicoides* spp. entering the population each day and estimation of the number of immature *Culicoides* spp. transitioning from the immature state to the mature state) were estimated using the approach described by Kelso & Milne (2014). In each grid cell: (1) oviposition of eggs by adult females produce immature *Culicoides* spp.; (2) immature *Culicoides* spp. mature to adult *Culicoides* spp.; and (3) for each time period death of both immature and adult *Culicoides* spp. occurs subject to a defined mortality rate. We assumed that movement of *Culicoides* spp. occurs by a combination of two mechanisms: (1) short- range movement arising from active flight; and (2) long-range (wind-borne) dispersal.

3.3.3 Short-range dispersal

In this paper the term 'short-range dispersal' is used to refer to the movement of *Culicoides* spp., in the absence of wind. We assumed short-range dispersal of *Culicoides* occurred according to a cellular automata process with average movement distances of up to 100 m per day (Lillie et al. 1981, Kirkeby et al. 2013). Kelso & Milne (2014) proposed that a small fraction of midges will move up to 5 km per day with the amount of diffusive spread dependent on midge population density and a species-dependent diffusion coefficient. Two studies have reported diffusion coefficients of 60 $m^2.s^{-1}$ for *C. impunctatus* (Kettle 1995, Rudd & Gandour 1985) and 13 $m^2.s^{-1}$ for *C. variipennis* (Lillie et al. 1981, Backer & Nodelijk 2011). In the absence of reported diffusion coefficients for *C. brevitarsis* we assumed the same values as those reported for *C. variipennis*. The *C. variipennis* value was used, because the methodology by which it was derived is described in much greater detail compared to the *C. impunctatus* value. Following Kelso and Milne, lofting (i.e. short-range dispersal) was assumed to occur only when mean daily temperature was $\geqslant 18^{\circ}$C. Given the dimensions of each cell of our raster surface were 10 km $\times$ 10 km the proportion of adult *Culicoides* spp. in each cell that undertook short-range spread was set to a fixed value of 1%.

3.3.4 Long-range dispersal

Long-range dispersal of *Culicoides* spp. can occur over several hundred kilometres when winds are no greater than 8 km.h^{-1}. If wind speeds are more than 8 km.h^{-1} midges tend to stay on the ground attached to vegetation (Murray 1987). Once airborne, *Culicoides* spp. may loft above their usual 3 to 4 m flying height by thermals (upward currents of warm air) or topography-induced wind turbulence, which allows them to reach relatively high altitudes (Burgin et al. 2013, Eagles et al. 2013). In this situation midges can travel several hundreds of kilometres. We used the HYSPLIT model (Draxler & Hess 1998) to estimate the atmospheric dispersal of *Culicoides* spp. from each grid cell. HYSPLIT was developed for general applications in atmospheric science and has been adapted for specific applications including atmospheric chemical transport and deposition, dispersion of smoke from forest fires and volcanoes and dispersion of radioactive material from accidental releases. In animal health HYSPLIT has been used to model long-distance dispersal of *Culicoides* spp. (Kedmi et al. 2010, García-Lastra et al. 2012) and other insects (Zhu et al. 2006) as well as airborne dispersal of foot-and-mouth disease virus (Garner et al. 2006). HYSPLIT allows for assessment of both trajectories and concentration of a particle or pollutants using Eulerian and Lagrangian methods. For our model calculation of *Culicoides* spp. trajectories were based on time integration of an air parcel's position as it is transported by wind speed estimates that vary at specified heights above the ground (Maclachlan et al. 2008). For the analyses reported in this paper the source parameters were assigned to a concentration model using an emission approach. This was used because, for each day of a simulation period, each grid cell has different *Culicoides* spp. adult and juvenile counts, making it difficult to simulate dispersion from every grid cell. The HYSPLIT concentration model simulated daily emigration flights of adult midges. This approach allows for the transport of particles dependent on wind speed and a random component to account for wind turbulence (Garner et al. 2006). In Hayama et al. (2016), HYSPLIT was used to assess the possibility of between-island transmission by windborne infected vectors by using back-trajectory analysis to estimate the potential source sites of infected vectors.

Following estimation of immature and adult *Culicoides* spp. counts in each raster cell and adjustment of adult counts to account for midge dispersal by diffusive spread, adult midges in each grid cell were dispersed using HYSPLIT, as shown in Figure 3.1. The HYSPLIT model requires three dimensional gridded meteorology data to drive dispersion simulations, downloaded from the USDC-NOAA Air Resources Laboratory.[1] *Culicoides* spp. were allowed to travel for 24 h from the time of release. The following criteria were used to determine if lofting occurred from a given grid cell on a given day: (1) adult *Culicoides* spp. were present; (2) average wind speed was $\leqslant$ 8 km.h^{-1}; (3) average temperature was $\geqslant$ 18 °C; and (4) cattle herds were present. Wind data were obtained from the daily near-surface wind speeds provided by the CSIRO (McVicar 2011). These daily near-surface wind speed grids have been developed over all of Australia at 5 km spatial resolution by interpolating terrestrial regions.[2] Diffusive spread was simulated by the release of the calculated number of adult *Culicoides* midges present in a grid cell on a given day.

[1] `http://www.ready.noaa.gov/archives.php`

[2] `https://data.csiro.au/`

3.3.5 Inputs

Each grid cell has its own state with several variables that influence *Culicoides* spp. counts (e.g. temperature, wind and the presence or absence of cattle). Meteorological data enters the model as a daily input time series. The number of cattle herds and their locations were obtained from the Australian Bureau of Statistics 2010 - 2011 Agricultural Census (Australian Bureau of Agricultural and Resource Economics and Sciences 2014). Daily minimum and maximum temperature data for the period 1 January 2014 to 31 December 2015 at a resolution of 5 km $\times$ 5 km were obtained by the Australian Bureau of Meteorology (Australian Government Bureau of Meteorology 2014). By determining the (maximum) carrying capacity of the immature *Culicoides* spp. population the model was initialised with an arbitrary number of 100 adult and 200 juvenile *Culicoides* midges in each grid cell.

Simulations were run for two years, from 1 January 2014 to 31 December 2015, with the first 12 months of the simulation used as a 'burn-in' period. A burn-in period was important because it allowed *Culicoides* populations to reach an endemic level following the contrived initialising conditions. In the model all three processes were run simultaneously: for each day, adult and juvenile population counts were processed for each cell, adult *Culicoides* spp. from each grid cell were transferred to other grid cells using the stochastic local diffusion and long-range dispersal mechanisms (using HYSPLIT), as described above. Simulation outputs comprised a series of raster maps (two maps for each simulation day) providing estimates of adult and juvenile *Culicoides* spp. counts in each raster cell.

For a relative scale to be used for the vector density model adult outputs were multiplied by the grid cell values of normalised cattle density of the cell which act as the population-limiting resources. The normalised cattle density is calculated from the raw cattle density by multiplying by 100 to (to ensure that there are no negative values in the transformed data), taking a log base 10 transformation, and then dividing all values by the maximum (transformed) value, producing a final range between zero and one.

3.3.6 Model validation

Light traps have been routinely used for insect sampling as part of the NAMP. These traps are placed near or where cattle herds are present (Bishop et al. 2015). Identification and counts of midges trapped were processed in the laboratories of each of the cooperating states and territories and each record of *Culicoides* spp. counts was accompanied by their respective site identifier. Our approach for validation was to compare, for a series of locations throughout Australia, the number of adult *Culicoides* spp. predicted by our model as a function of calendar month with counts of *C. brevitarsis* caught each month at NAMP trap sites at the same location. Figure 3.2 is a map of Australia showing the point location all NAMP trap sites for the period 1994 to 2018. For the period 1 January 1994 to 31 May 2018 the number of NAMP trap sites and the frequency of sampling at each site was highly variable (Bishop et al. 2000). For the most part, particularly in the north of Australia, *Culicoides* counts at each trap site were recorded monthly. Below the tropic of Capricorn (latitude 23.5°S) counts of *Culicoides*

were infrequently recorded during the southern hemisphere winter months (May to September in a given year).

Since some NAMP trap sites had low numbers of observations we constructed a circular area of radius 50 km around a given NAMP trap site and used *Culicoides* counts recorded for NAMP trap sites within this area to compare with model outputs. This increased our ability to more clearly define temporal trends in *Culicoides* spp. counts for the location of interest, assuming spatial autocorrelation existed in NAMP trap site *Culicoides* spp. counts. In this study, we selected different trap locations from different states to cover the different climatic zones of Australia. These sites were selected based on their consistency of their records among the test trapping sites to identify with greater certainty the seasonal patterns of *C. brevitarsis* activity. The NAMP data have been aggregated over the entire time frame of data collection. This provided a greater number of observations, allowing seasonal trends in *Culicoides* spp. counts to be more clearly defined.

3.4 Results

3.4.1 Adult population dynamics and seasonal effects

Figure 3.3 is a series of raster maps showing our normalised *Culicoides* spp. densities across Australia for summer, autumn, winter and spring. In summer (December to February) *Culicoides* spp. are highly abundant and active throughout Australia; over the winter (June to August) *Culicoides* spp. remain active only in the northern tropics. In areas of the country where the temperature is increasing in summer, *Culicoides* spp. remain present even in the southern regions of Australia.

The model predictions showed the presence and activity of *Culicoides* spp. starts to decline in the south of the country when the temperature decreases in autumn and midges start to disappear from Victoria, the southern parts of South Australia and the south east of West Australia (Figure 3.3b). Moving to winter, the activity pattern for *Culicoides* spp. disappears from Victoria and Tasmania, where some small activity remains in parts of South Australia and New South Wales (above 30°S). However, the species activity remains similar in the northern tropics and eastern Australia to that in summer (Figure 3.3c). *Culicoides* spp. activity increases continuously from the north to the south and spreads more to southern Queensland and New South Wales when moving from winter to spring (Figure 3.3d). This rise in temperature allow the modelled extent of *Culicoides* spp. to move down again from the north to the south and become active.

3.4.2 Model validation

Figure 3.4 provides a comparison of our model predictions and NAMP records at four locations, Kempsey (152.83°E, -31.08°S), Casino (152.96°E, -28.80°S), Biggenden (152.06°E, -25.52°S) and Daly River (131.05°E, -13.91°S). The east coast of Australia has a predominantly sub-tropical climate, with tropical influences in the north and temperate influences in the south. In these areas, in the case of Kempsey and Casino, the number of adult *Culicoides* spp. decline markedly during the winter in

which populations disappear, but numbers quickly re-establish and surviving immature *Culicoides* spp. emerge and re-start their breeding cycle once temperatures increase. Our model predictions show a similar seasonal pattern to that of the NAMP observations, however, in Kempsey (Figure 3.4a) the NAMP *Culicoides* counts were slightly higher than the model predictions and re-emerge of *Culicoides* spp. after winter occurred later. For Casino (Figure 3.4b) and Biggenden (Figure 3.4c) there was generally good agreement between the NAMP data and the model predictions.

Adults are present year-around in the endemic areas in northern Australia. For Daly River in the Northern Territory (Figure 3.4d) NAMP *Culicoides* spp. counts were markedly less than the *Culicoides* spp. counts predicted by the model.

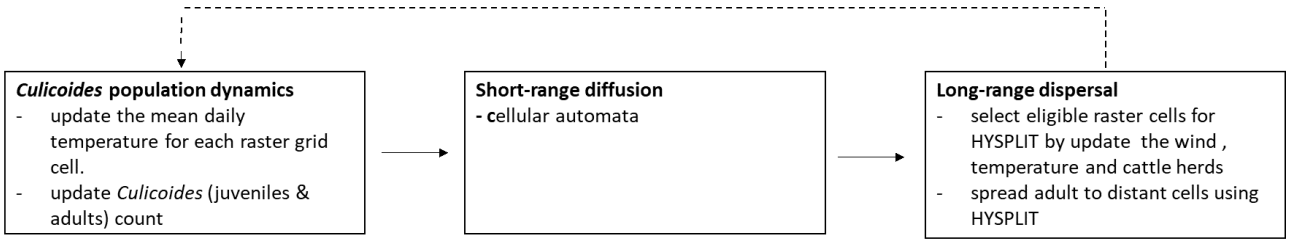


Figure 3.1: A model of the spatial distribution of *Culicoides* spp. in Australia. Diagrammatic representation of the three processes of simulating the distribution of *Culicoides* spp. conducted in this study.

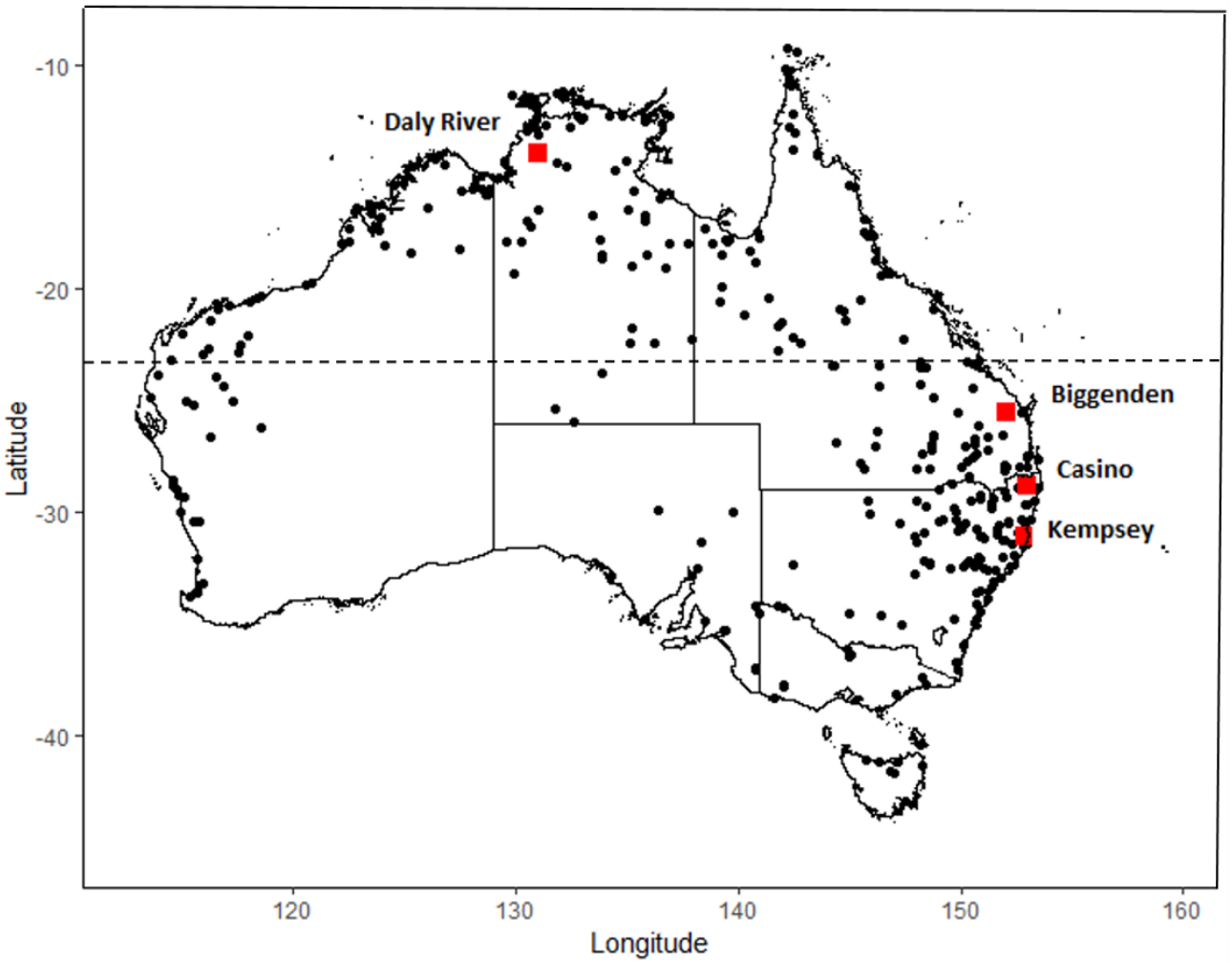
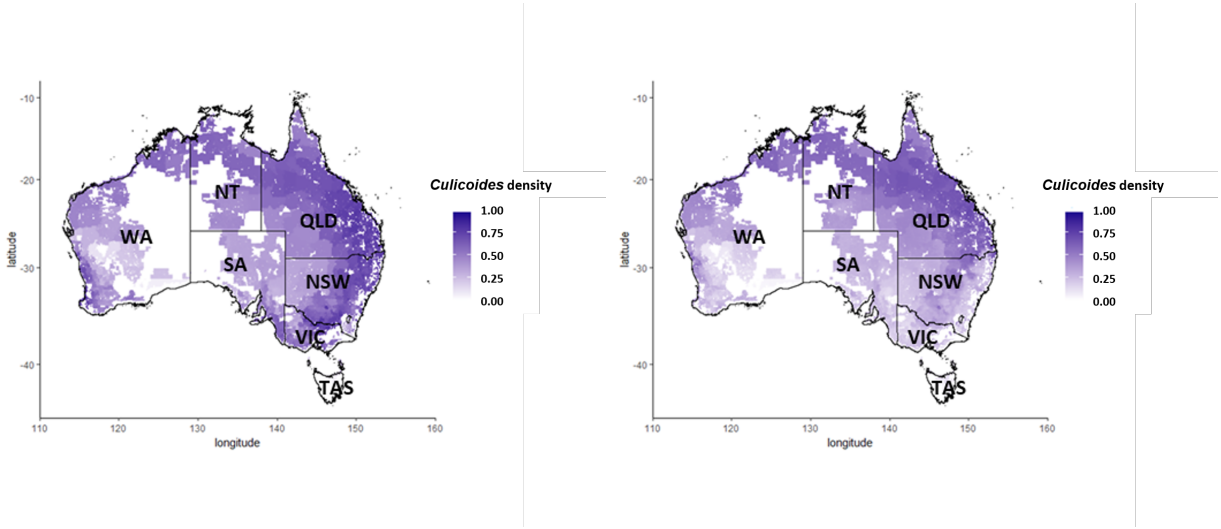
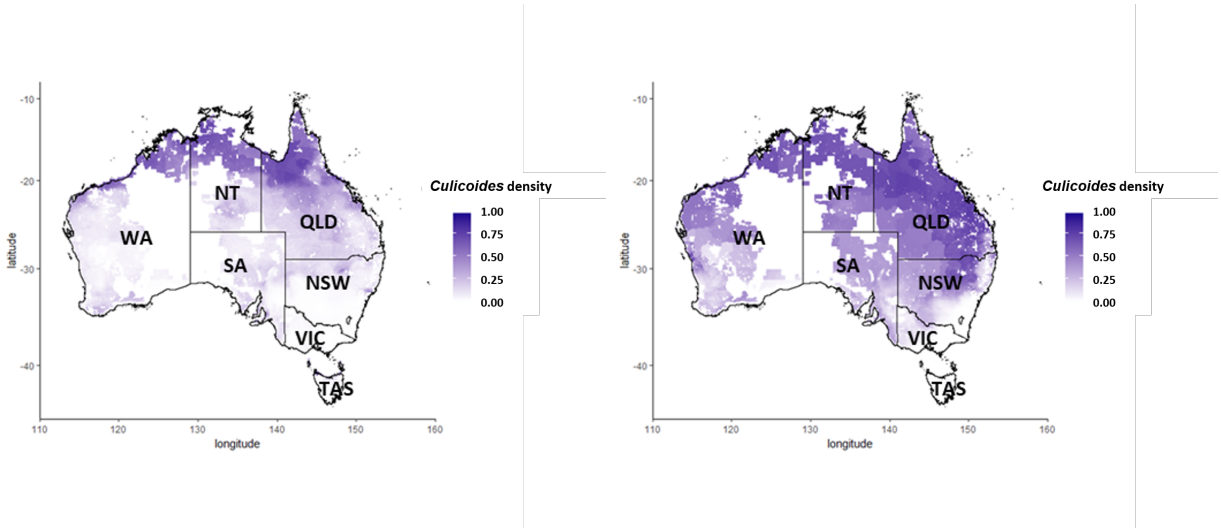


Figure 3.2: A model of the spatial distribution of *Culicoides* spp. in Australia. Map of Australia showing the location of National Arbovirus Monitoring Program (NAMP) sites, 1994 to 2018 and the selected sites for our model validation (in red) and the Tropic of Capricorn (dashed line).



(a) (b)



(c) (d)

Figure 3.3: A model of the spatial distribution of *Culicoides* spp. in Australia. Raster maps showing the spatial distribution of the normalised *Culicoides* spp. densities across Australia based on the simulation model described in this paper: (a) summer; (b) autumn; (c) winter; and (d) spring. Key: NSW New South Wales, NT Northern Territory, QLD Queensland, SA South Australia , TAS Tasmania, VIC Victoria, WA Western Australia.

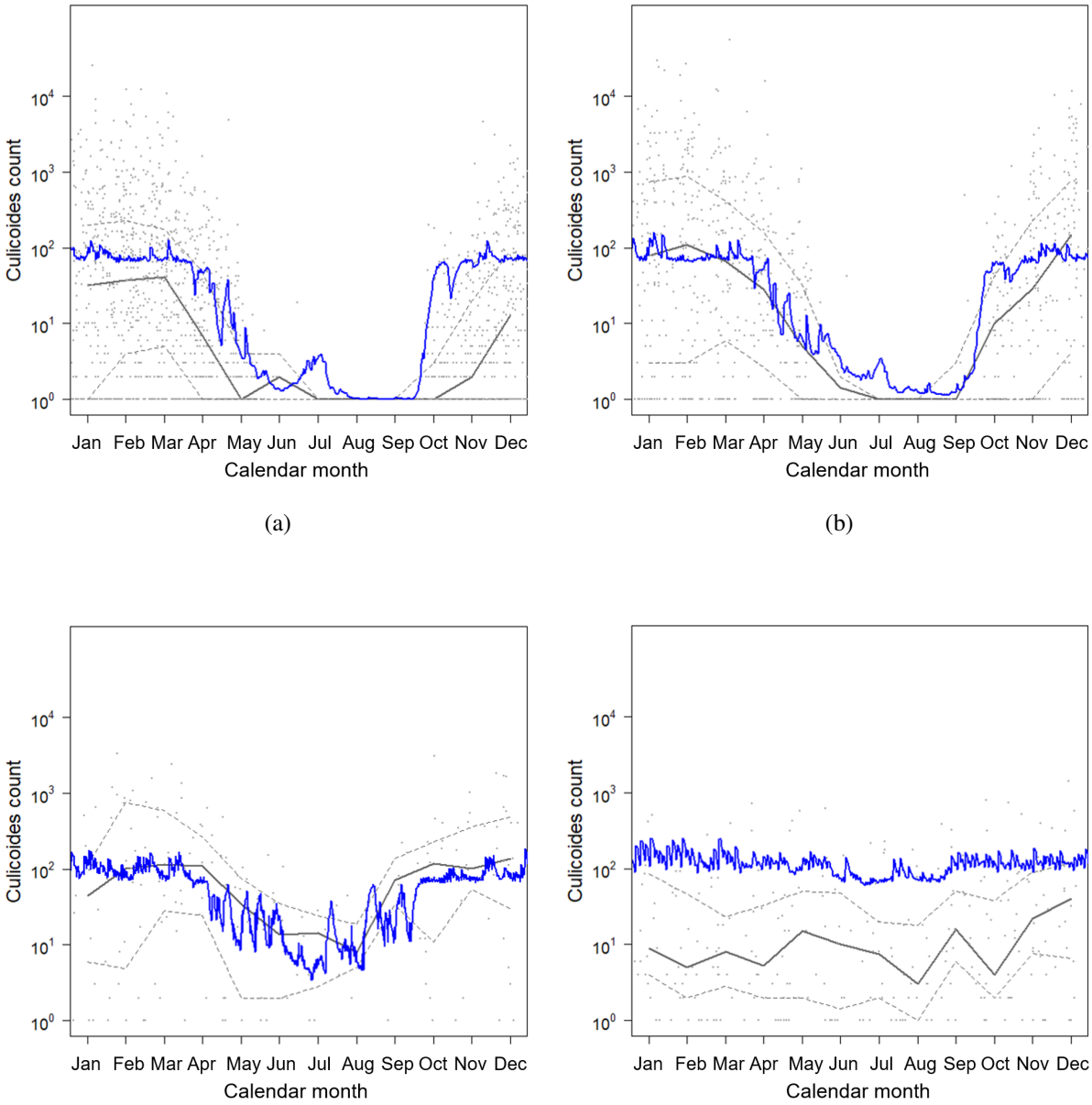


Figure 3.4: A model of the spatial distribution of *Culicoides* spp. in Australia. Scatter plots showing the log10 (n + 1) *Culicoides brevitarsis* spp. counts as a function of calendar month for the period 1994 to 2018, recorded by the NAMP (as points). Superimposed on each plot as: (a) Kempsey; (b) Casino; (c) Biggenden; and (d) Daly River. The grey lines represent the median (solid) and quartiles (dashed) for *C. brevitarsis* observations recorded by the NAMP. The blue lines show predictions by the model.

3.5 Discussion

The approach described in this paper extends the *Culicoides brevitarsis* model described by (Kelso & Milne 2014) in the following ways. Firstly, we developed a model to allow the spatial and temporal distribution of *Culicoides* spp. to be estimated across the entirety of Australia (as opposed to a focussed study area). Secondly, we compared the spatial and temporal distribution of our *Culicoides* spp. predictions with data collected over 24 years by the National Arbovirus Monitoring Program providing a necessary starting point for model validation. While the issue of airborne spread was discussed in their paper, the (Kelso & Milne 2014) model did not explicitly disperse *Culicoides* spp. from all eligible locations on a daily basis.

This study has used the wind-borne spread model HYSPLIT to simulate *Culicoides* spp. dispersion from multiple source locations using forward trajectories with different emission rates dependent on simulations of the underlying midge population dynamics. This approach has been used and developed to model the dispersal of other animal diseases such as FMD (Garner et al. 2006, Lambkin et al. 2019). HYSPLIT has been used to simulate *Culicoides* spp. dispersal from single source locations (Eagles et al. 2013, 2014). In other studies HYSPLIT has been used to disperse *Culicoides* spp. without accounting for temperature dependent population dynamics (Kelso & Milne 2014, Hayama et al. 2016).

Defining a means for modelling insect population dynamics and their movement are important preliminary steps for development of tools to simulate the spread and transmission of vector-borne pathogens such as bluetongue. In the coming years these tools will be useful for animal health decision makers, given climate change will inevitably change the geographic distribution of insect vector habitat sites. The issue of over-wintering, where, in areas of the country where temperatures do not fall below a certain level during the colder months of the year, the ability of *Culidoides* spp. to survive and transmit BTV is of particular importance. In the epidemic of BTV-8 in Europe in 2006, outbreaks occurred in BTV free areas after winter, thought to be due to over-wintering of BTV positive *Culicoides* spp. (Mintiens et al. 2008).

In contrast to predictions provided by Kelso & Milne (2014) where there was extinction of adult and mature *Culicoides brevitarsis* following the winter months of the year, our model showed persistence of *Culicoides* spp. most likely due to re-emergence of over-wintered adults and/or wind-borne dispersal. Other explanations for these differences include the use of different temperature data sets (Australian Bureau of Meteorology data for 1980 to 2000 in the case of Kelso & Milne (2014) versus Australian Bureau of Meteorology data for 2015 in this study). Our comparisons of predictions of *Culicoides* spp. with empirical data collected by NAMP showed good agreement in endemic areas but poorer agreement at southern latitudes (Figure 3.4).

It was interesting that our model predicted the presence of *Culicoides* spp. in more southern temperate regions (e.g. Victoria), which agree with current surveillance data.

We note that over time there were large variations in the number of *Culicoides brevitarsis* caught at each NAMP sampling site (Figure 3.4) which is no doubt due to a range of factors including the type of trap used, the phase of the moon at the time of sampling and ambient temperature and wind

conditions (Bishop et al. 2000). Our model estimated the relative number of midges over a 10 km $\times$ 10 km grid cell area. To make valid comparisons with the NAMP *Culicoides brevitarsis* trap data we included data from NAMP trap sites with an area of 50 km radius of the point location of each selected validation site (Figure 3.2). This approach returned a greater number of trap night records, providing a more precise estimation of seasonal changes in *Culicoides brevitarsis* counts.

The model presented in this paper provides a necessary first step towards development of modelling capacity for vector-borne diseases of livestock. The approach described in this paper could be easily adapted for use for other vector-borne or reservoir-borne diseases,[3] for example mosquitoes *Culex mirificens* and *Aedes natrionus*, biting flies *Stomoxys calcitrans* and *Biomyia fasciata* and male ticks *Riphicephalus appendiculatus* and *Amblyomma hebraeum* in the case of lumpy skin disease and wildlife vectors of disease such as wild boar (*Sus scrofa*) in the case of African swine fever.

[3]Throughout this thesis term 'vector-borne' is used to describe diseases transmitted by invertebrates. The term 'reservoir-borne' is used to describe diseases transmitted by terrestrial animals, for example wild boar in the case of African swine fever.

Chapter 4

A model of bluetongue transmission within and between livestock herds

Introduction: Bluetongue virus (BTV) occurs worldwide causing disease in ruminants in the Americas, Africa and southern Asia. Bluetongue is a non-contagious, vector-borne disease of ruminants. *Culicoides* spp. are the insect vector responsible for the transmission of BTV. Several studies have focused on development of models of BTV transmission that can be used to predict the spread of bluetongue and evaluate the impact of control measures. In this paper we describe a stochastic, spatially-explicit model to simulate the transfer of BTV from infected *Culicoides* midges to domestic ruminants and *vice versa* in an Australian context.

Methods: A model of BTV transmission was developed using the point location of cattle herds, estimates of *Culicoides* spp. abundance in raster format and environmental temperature. Parameter estimates for the model were derived from the peer reviewed literature. Transmission of BTV between susceptible herds was modeled assuming transmission risk from a source herd followed a Gaussian kernel distribution.

Results: Biologically plausible estimates of BTV spread between susceptible herds were developed using the model. One-at-a-time sensitivity analyses showed that changes in the size of the bandwidth radius of the kernel used to define the distance over which an infected herd posed a risk to others had the greatest impact on predicted outbreak size.

Conclusion: The model framework presented in this study is flexible and can be adapted to other vector-borne diseases of livestock. Estimation of an appropriate bandwidth radius for the transmission kernel suitable for Australian conditions needs further investigation.

4.1 Introduction

Bluetongue is a vector-borne viral disease of ruminants which, up until the mid 2000s, was restricted to tropical and subtropical areas of the world (Mellor et al. 2008). Bluetongue virus (BTV) is a double-stranded RNA virus (Reoviridae: Orbivirus) of which 27 serotypes have been identified (Maan et al. 2012). The virus is transmitted by midges of the genus *Culicoides* spp. (Mellor et al. 2000).

Bluetongue has been designated as a notifiable disease by the World Organisation for Animal Health due to its ability to spread rapidly within ruminant populations, often without warning (Gubbins et al. 2007). The largest recent epidemic of bluetongue (caused by serotype BTV-8) began in northern

Europe in 2006 (Elbers et al. 2007, 2008). Several studies have proposed that environmental and/or human factors may have been responsible for the dramatic expansion of bluetongue serotype 8 within Europe. Purse et al. (2008) discussed the European outbreak concluding that *Culicoides* biting midges were dispersed over long distances by prevailing winds (Sellers 1992, Sellers & Maarouf 1989) leading to rapid spread of the diseases that they carry. Hendrickx et al. (2008) supported the conclusions of previous studies by finding a positive association between wind trajectories and the geographic distribution of disease occurrence. Another study showed that the frequency and direction of animal movement events enhanced the spread of bluetongue during the initial phase of the outbreak (Mintiens et al. 2008). In Europe there is consensus of opinion that climate change has influenced the movement of *Culicoides imicola* into the more northerly regions of the continent (Mellor & Leake 2000, Purse et al. 2005). Based on the literature published to date it is clear that there is not one single factor that determined farm-level bluetongue risk in Europe, but rather a complex interplay of factors.

Understanding mechanisms of disease transmission is a central issue in epidemiology. Following the 2006 outbreak of bluetongue in northern Europe, disease transmission models have been developed to provide supporting evidence that current knowledge of disease transmission are consistent with empirical outbreak data and to assess the relative impact of alternative proposed control measures (Gubbins et al. 2007, Guis et al. 2007, Hartemink et al. 2009, Szmaragd et al. 2009, Sedda et al. 2012, Turner et al. 2012) with many models providing estimations of the likely geographic spread of disease following virus incursion (Szmaragd et al. 2009, de Koeijer et al. 2011, Græsbøll et al. 2012). While a good deal of work has been carried out to firstly describe the recent European outbreaks and then model the geographic distribution of disease, to the best of our knowledge relatively little work has been done in this area in Australia, with the notable exceptions of Eagles et al. (2012), Eagles et al. (2013), Eagles et al. (2014) and Kelso & Milne (2014).

The aim of this paper is to describe a modelling approach that can be used to simulate the transfer of bluetongue virus from infected *Culicoides* midges to domestic ruminants and *vice versa* in an Australian context. The model we present is a process-based stochastic simulation approach which extends previous modelling work described by Szmaragd et al. (2009). An end goal is to define a model of pathogen transmission that can be implemented within the hybrid, equation-based and agent-based modelling framework, the Australian Animal Disease Spread model AADIS (Bradhurst et al. 2015). While the focus of this study is on bluetongue our intent is to provide a design that is sufficiently flexible to allow the model (and its implementation within AADIS) to be adapted for other vector-borne diseases of livestock if (and when) the need arises.

4.2 Materials and methods

We define a herd as a single-species (e.g. cattle, sheep, pigs, goats) group of animals under a common system of management at a single geographical location. Using this approach a 'farm' is defined as a collection of one or more herds, which may or may not be at the same physical location. Within the model herds are represented spatially as point locations defined by longitude and latitude coordinates.

Attribute data associated with each herd include the type of production system (e.g. dairy, beef) and the number of animals present.

Culicoides spp., the insect vector population of interest for this study are represented spatially in raster format using a regular grid of 10 km $\times$ 10 km cells superimposed over the geographic extent of the herd population of interest (Figure 4.1). Attribute data for the vector population layer includes approximate counts of the insect vectors within each raster cell. Within the model the counts of insect vectors (and the corresponding normalised vector densities) within each raster cell change over time in response to temperature and wind speed (as described in Chapter 3).

4.2.1 Within-herd spread

The infection process within herds is represented by an equation-based compartmental model where members of a herd are in any one of four states at a given point in time: susceptible (S), exposed (E), infectious (I) and recovered (R). Similarly, insect vectors exist in one of three states at any point in time: susceptible (S), exposed (E) and infectious (I), Figure 4.2. The susceptible-exposed-infectious-recovered (SEIR) model for herds and susceptible-exposed-infectious (SEI) model for insect vectors use coefficients to define the probability of movement of a host or vector from one state to the next within a single time step. The dynamics of bluetongue virus infection within each herd as a function of time are described by the following set of differential equations:

$$\frac{dS_h}{dt} = -\beta_{vh} S_h \tag{4.1}$$

$$\frac{dE_h}{dt} = \beta_{vh} S_h - \psi_h E_h \tag{4.2}$$

$$\frac{dI_h}{dt} = \psi_h E_h - \gamma_h I_h \tag{4.3}$$

$$\frac{dR_h}{dt} = \gamma_h I_h \tag{4.4}$$

In Equations 4.1 and 4.2 β_{vh} provides a measure of the infection pressure exerted by the insect vector layer on the population of livestock hosts within a herd and h equals the probability that virus will be transferred from the insect vector layer to the herd population per unit time. ψ_h equals the inverse of the assumed latent period for bluetongue (in days) and γ_h is the recovery rate from infection.

The transmission rate β_{vh} is calculated as:

$$\beta_{vh} = d_v \times P_v \times f_v(temp) \times e_{vh} \tag{4.5}$$

where d_v equals the density of insect vectors in each 10 km $\times$ 10 km raster cell. P_v is the prevalence of infectious vectors in each raster cell, $f_v(temp)$ equals the temperature dependant vector biting rate and e_{vh} equals the probability of transmission from an infectious vector to a susceptible host, given contact.

The dynamics of bluetongue virus infection in the insect vector population is parameterised using a similar approach. Because there is no direct vector-to-vector transmission of bluetongue virus, the dynamics of infection in the insect vector population were represented as follows:

$$\frac{dS_v}{dt} = -\beta_{hv} S_v - \mu_v S_v \tag{4.6}$$

$$\frac{dE_v}{dt} = \beta_{hv} S_v - (\psi_v + \mu_v) E_v \tag{4.7}$$

$$\frac{dI_v}{dt} = \psi_v E_v - \mu_v I_v \tag{4.8}$$

In Equations 4.6 and 4.7 β_{hv} represents the infection pressure exerted by the animal host layer on the insect vector layer. ψ_v is the extrinsic incubation period for bluetongue (in days) and μ_v the daily vector mortality rate. The susceptible vector population become exposed at a rate determined by β_{hv}:

$$\beta_{vh} = d_h \times P_h \times f_v(temp) \times e_{hv} \tag{4.9}$$

where d_h is the density of hosts in each raster cell, P_h is the prevalence of infectious hosts in each raster cell, f_v equals the temperature dependent vector biting rate and e_{hv} the probability of transmission from host to vector, given contact. An infectious host remains infectious until it recovers whereas an infectious insect vector is assumed to remain infectious until it dies.

The biting rate f_v, the extrinsic incubation period ψ_v and the insect vector mortality rate μ_v all temperature dependent. In the warmer months of the year insect vectors will become infectious sooner after exposure but their rate of mortality rate will be higher.

Values for each of the parameters listed in Equations 4.1 to 4.9, with supporting references are provided in Table 4.1.

4.2.2 Between-herd spread

When bluetongue is present in a given herd, herds that are geographically close are at risk of becoming infected. This occurs when *Culicoides* spp. feed on an infectious host and travel to a neighbouring herd, resulting in transfer of BTV when they feed on susceptible hosts in the destination herd. To develop disease control measures designed to protect neighbouring herds it is important to know the geographic extent of enhanced disease risk around a given (infected) herd location.

A standard way to model the geographic spread of disease from a known point source is to use a kernel-based approach which allows the probability of disease transmission to decrease as a function of distance from an identified source (Skarpaas et al. 2005). Kernel density estimation is a statistical method used to estimate the density of point data (Cromley & McLafferty 2011) and has been extensively used to describe the spatial epidemiology of both animal (Stevenson et al. 2000, Wilesmith et al. 2003) and human (Kelsall & Diggle 1995) diseases. In our model local spread of

bluetongue from an infected (point) source herd location was defined using a Gaussian smoothing kernel function (k_v) as follows:

$$k_v = \frac{1}{(r\sqrt{2\pi})} e^{-}(\frac{x^2}{2r^2}) \tag{4.10}$$

In Equation 4.10, r represents the radius of the kernel (the bandwidth), which determines the distance over which an infected herd poses to others in terms of bluetongue transmission risk and x represents the average distance between herds. In our model we used a fixed bandwidth of 8.8 km (based on de Koeijer et al. 2011) and x was calculated using the location of herds used to populate our model. We acknowledge that the 8.8 km bandwidth calculated for the European outbreaks did no take into account a lack of animal movement restrictions or wind borne dispersal of midges so for these reasons the bandwidth used should not be assumed to be a proxy for *Culicoides* flight distance.

Given the presence of infectious midges within an insect vector raster cell, transfer of BTV to a recipient herd on a simulation day was set to depend on risk of transmission based on kernel density. This ensured that herds which were located a long distance from the centroid of the infectious insect vector raster cell had a lower probability of infection transfer compared with those herds that were close.

In the model described in this paper between-herd transmission of bluetongue occurs only via 'local' (i.e. short distance, kernel dependent) spread, as described above. Following implementation of our model into AADIS, between-herd transmission of bluetongue occurred using a combination of local and long-distance (i.e. animal movement) spread, using the existing short and long-distance disease spread functionality implemented within AADIS, developed for foot and mouth disease.

Our model was developed and prototyped in R (R Core Team 2020) using the contributed `spatstat` package (Baddeley & Turner 2005). Pseudo code and the corresponding R code for the model are provided in Appendix B.

The model was tested using data from 686 cattle herds located within a 245 square km area on the north coast of New South Wales. Point locations of herds and counts of animals present within each herd were derived from existing ruminant population data sets used to parameterise the existing AADIS foot and mouth disease model (Bradhurst et al. 2015).

One-at-a-time sensitivity analyses were carried out to determine which of the model input variables had the greatest influence on: (1) the geographic spread of disease over a fixed time period; and (2) the incidence rate of bluetongue, defined as the number of newly infected herds per 100 herds at risk per week. We allowed the radius r of the transmission kernel k_v (based on European data, de Koeijer et al. 2011) to vary from 4 km to 9 km. The initial proportion of insect vectors exposed in a raster cell was varied from 1% to 10% and the initial number of exposed hosts in the first infected herd was varied from 1 to 20 animals. In addition, the scaling value for insect vector abundance in each raster cell was set to 10 and 100,000. The model input variables were systematically varied to assess changes in simulation outputs.

4.3 Results

We evaluated model outputs arising from the parameter settings presented in Table 4.1. A bluetongue outbreak was initiated on 1 January 2015 in a herd in the north east of the study area (Figure 4.3).

Our simulations show that in a single herd, four animals (from a herd comprised of 194 cattle) exposed to BTV were sufficient to trigger a bluetongue outbreak. A total of 471 of the 686 herds had been infected with bluetongue by the end of the 12-month simulation period (Figure 4.4). The density of BTV positive herds was higher in the area adjacent to the first infected herd. The within-herd prevalence of BTV infection varied across herds, with the prevalence of infection at the end of the simulation period greater in herds that were larger.

The number of newly infected herds reached a maximum of $n = 62$ per week soon after incursion then declined into a propagating epidemic pattern over the remaining simulation time period (Figure 4.4). This is expected behaviour for the model as vector activity was dependent on temperature and the model was initiated in the summer. The study area was in northern New South Wales so temperatures would have been sufficient to allow *Culicoides* spp. to survive throughout the year.

We ran the model using the same input parameters 100 times to assess the variability in model outputs. A line plot showing the cumulative number of BTV-positive herds as a function of calendar date for each of the 100 simulations is shown in Figure 4.5. Figure 4.5 shows that, due to the stochastic nature of the model, the cumulative number of BTV-positive herds after 12 months was greater for some iterations compared with others.

The results for each of the sensitivity analyses are based on 100 iterations of the model. Each scenario begins with different inputs at the start of the simulation as shown in Figure 4.6. The initial percentage of exposed vectors, the initial percentage of exposed hosts in the first infected herd and vector population size had little effect on the number of infected cattle at the end of the simulation period (Figures 4.6a, 4.6b and 4.6c). The kernel radius had a marked effect on the predicted size of the outbreak with larger bandwidths associated with larger outbreaks due to its effect on increasing the range of between-herd transmission.

Table 4.1: A model of the transmission of bluetongue between livestock and insect vector hosts. Variables and parameters used in the model.

Symbol	Description	Estimate or range	Reference
d_h	Herd density per grid cell		
P_h	The prevalence of bluetongue in the cattle population		
$f_{v(temp)}$	Vector biting rate, dependent on temperature	$0.0002T(T-3.7)(41.9-T)^{1/2.7}[0-0.5]$	Birley & Boorman (1982), Braverman et al. (1985)
e_{hv}	Effectiveness of contact between infectious cattle and susceptible insect vectors	0.01	Nevill (1978), Braverman et al. (2003)
$1/\psi_h$	Average latent period of bluetongue in cattle (days)	7	Gubbins et al. (2014)
$1/\gamma_h$	Average infectious period of bluetongue in cattle (days)	20.6	Melville et al. (1996)
$1/\psi_v$	The extrinsic incubation period for bluetongue (in days)	$(0.0003(T-10.4))[4-26]$	Gerry & Mullens (2000), Wittmann & Baylis (2000)
μ_v	Vector mortality rate	$(0.009exp(0.16T))[0.1-0.5]$	Birley & Boorman (1982)
d_v	Density of the insect vector in each raster cell		
P_v	Prevalence of bluetongue in insect vectors in each raster cell		
e_{vh}	Effectiveness of contact between infectious insect vectors and cattle	0.9	O'Connell (2002)
r	Kernel bandwidth (in kilometres)	8.8	de Koeijer et al. (2011)

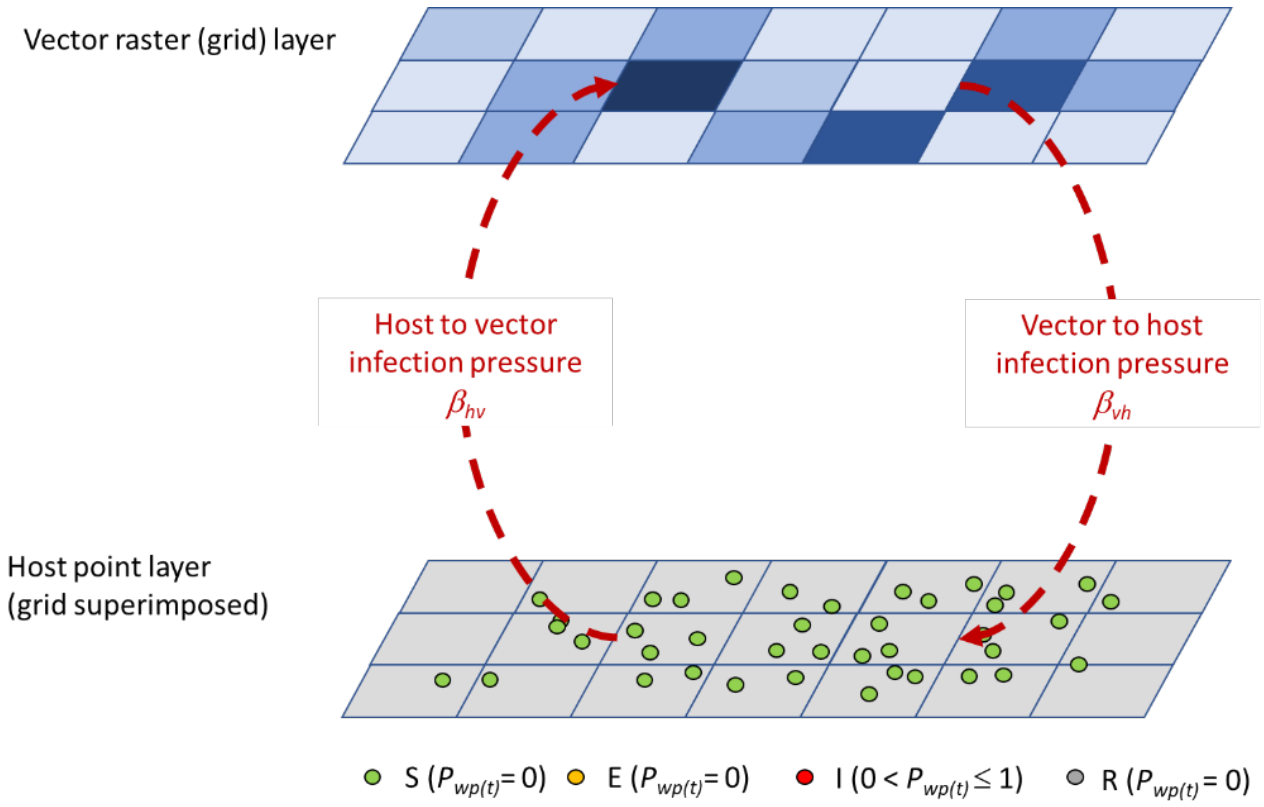


Figure 4.1: A model of the transmission of bluetongue between livestock and insect vector hosts. Schematic diagram of model structure showing transmission of bluetongue virus between insect vectors and cattle hosts. For the simulations presented in this paper we assumed that at time $t = 0$ all animals in all herds were susceptible. Key: S = susceptible; E = exposed; I = infectious; R = recovered.

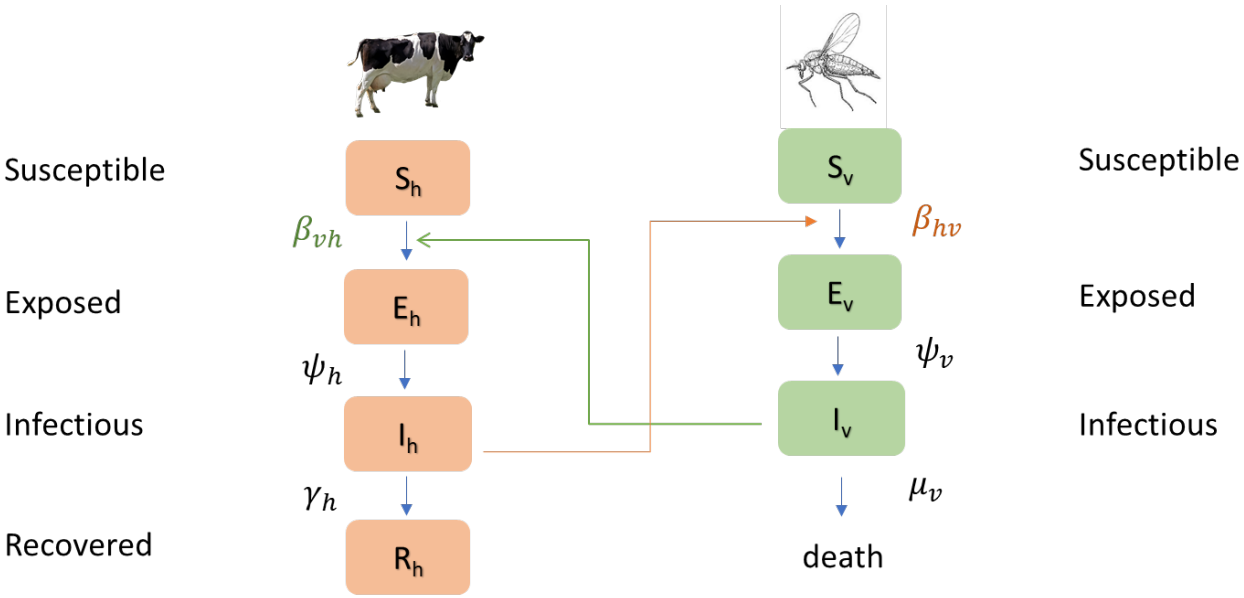


Figure 4.2: A model of the transmission of bluetongue between livestock and insect vector hosts. Diagram showing the susceptible, exposed, infectious and recovered states for hosts and susceptible, exposed and infectious states for insect vectors.

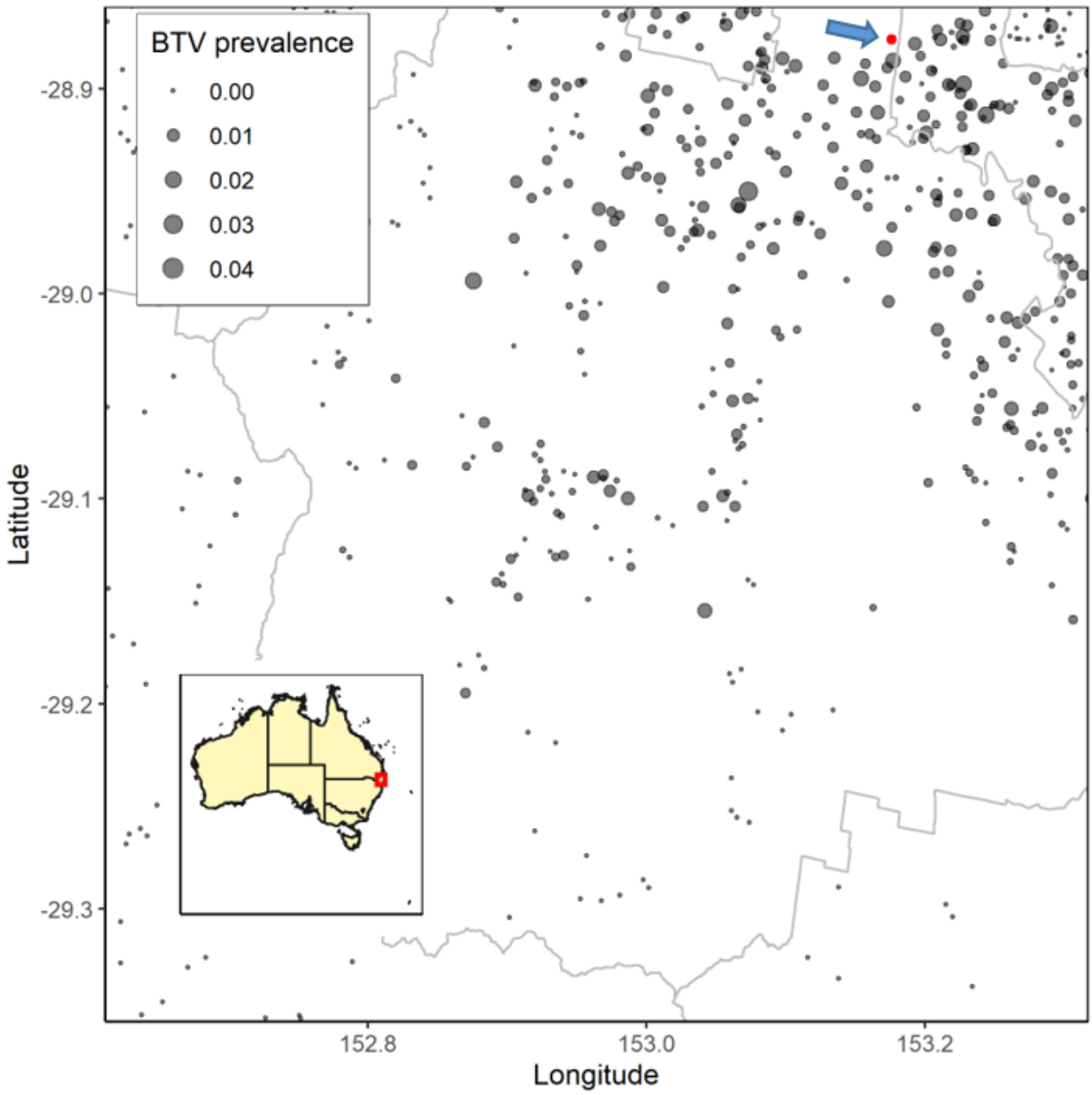


Figure 4.3: A model of the transmission of bluetongue between livestock and insect vector hosts. Map of the study area showing the location of cattle herds as points and the location of the first infected herd (red). In the above plot the size of each point is proportional to the within-herd prevalence of bluetongue at the end of the 12-month simulation period. The red point shows the location of the first infected herd.

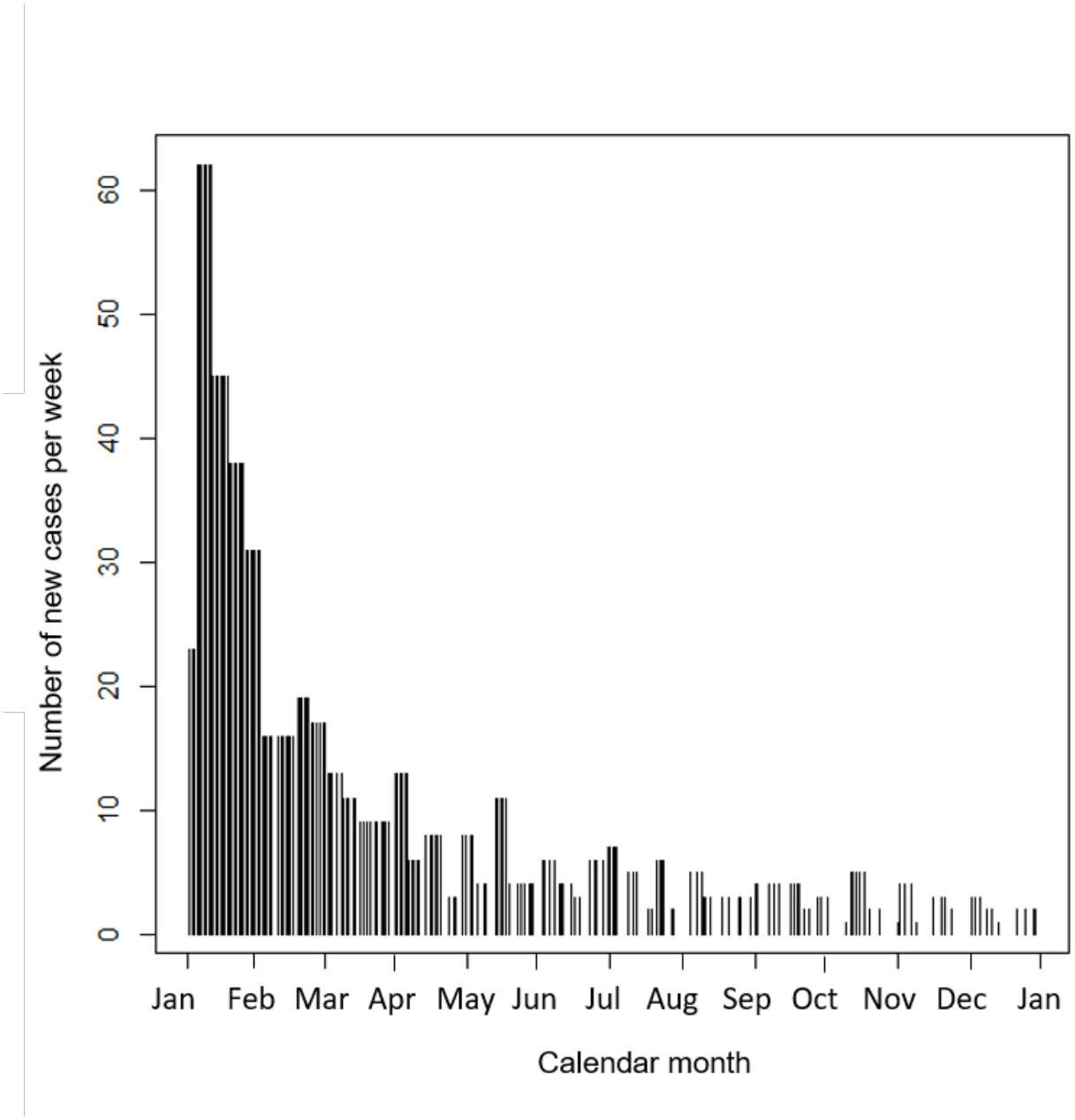


Figure 4.4: A model of the transmission of bluetongue between livestock and insect vector hosts. Frequency histogram showing the number of incident infected herds per week as a function of calendar date, 1 January 2015 to 31 December 2015.

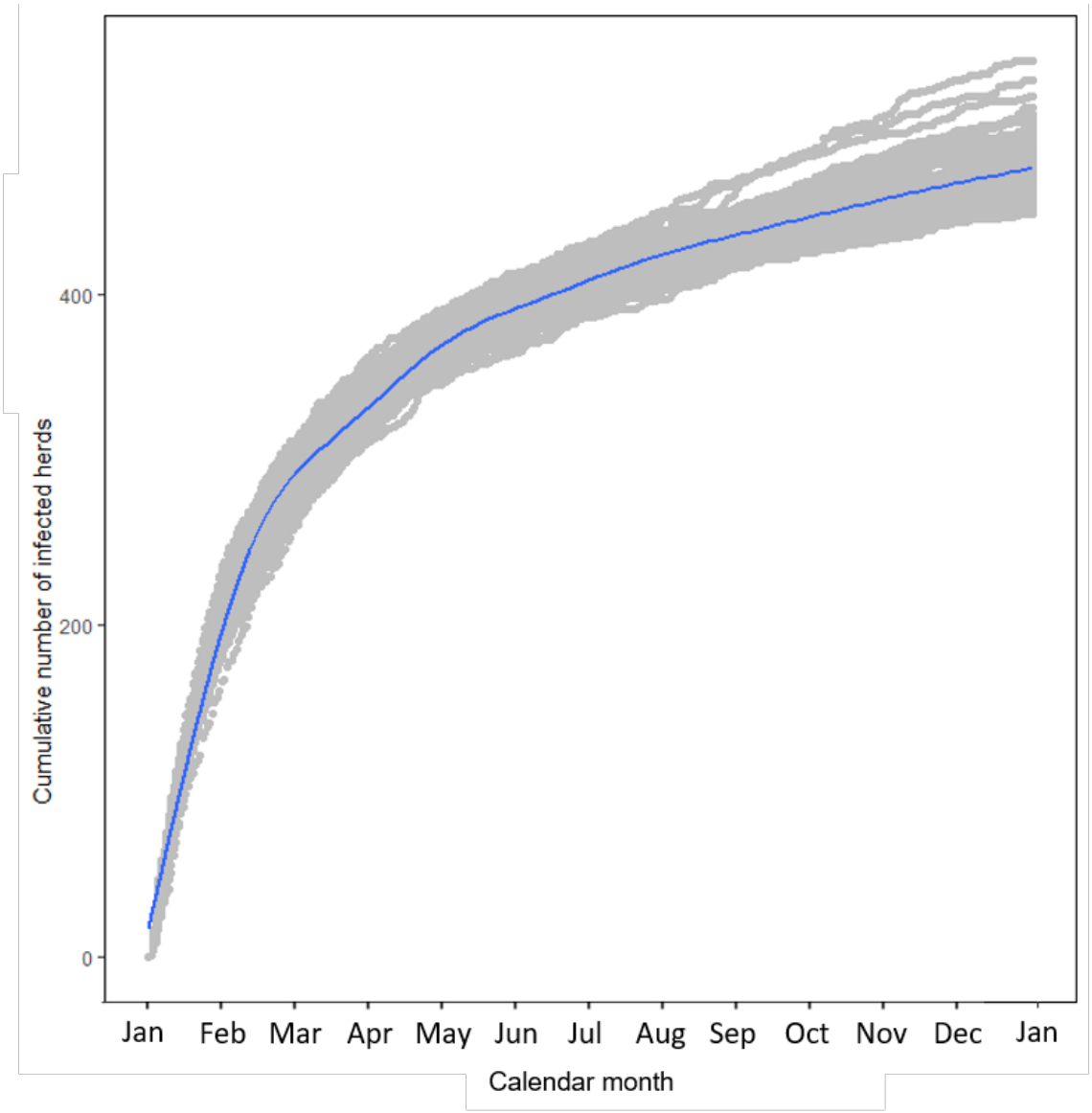


Figure 4.5: A model of the transmission of bluetongue between livestock and insect vector hosts. Line plot showing, for each of 100 simulations, the predicted cumulative number of infected herds as a function of calendar date, 1 January 2015 to 31 December 2015.

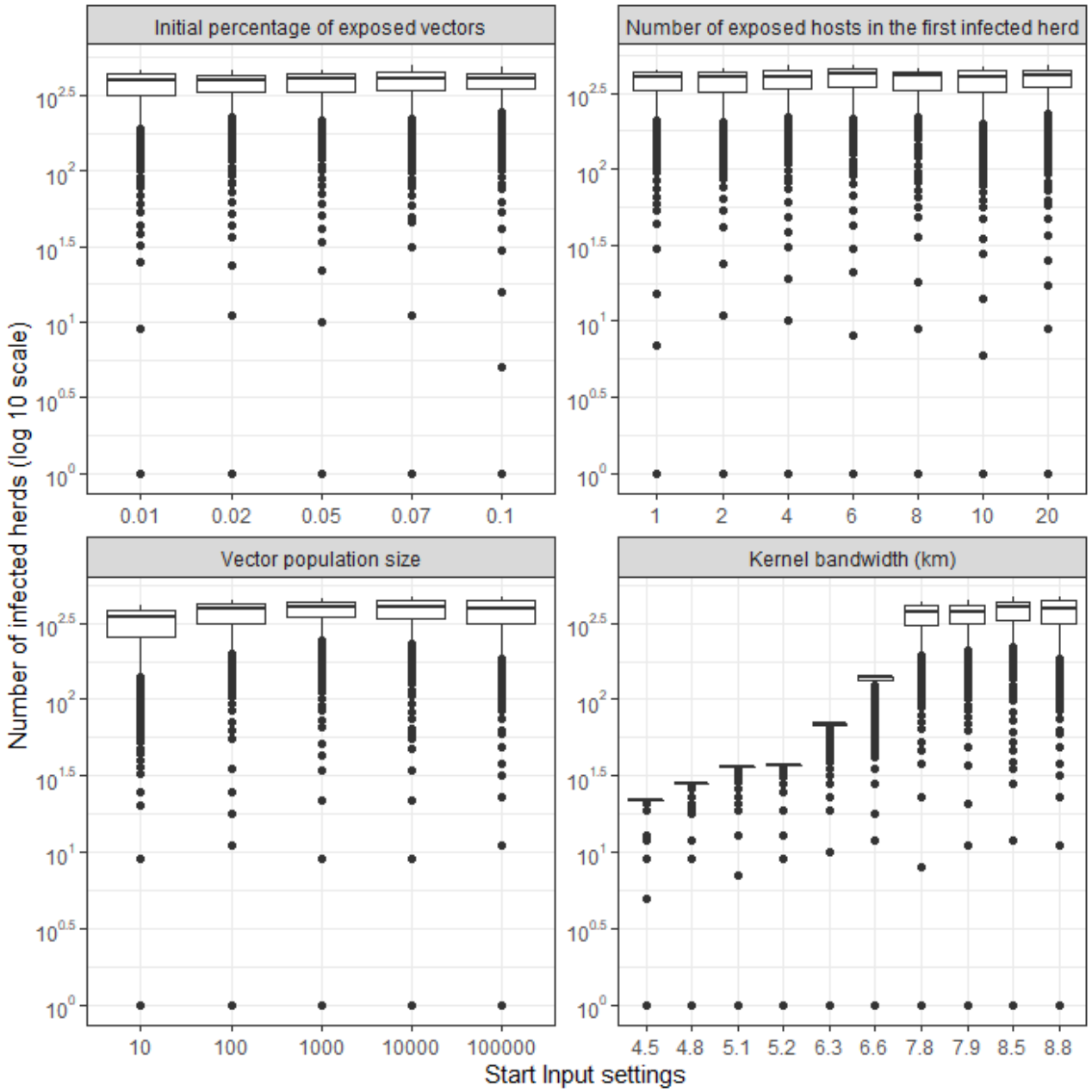


Figure 4.6: A model of the transmission of bluetongue between livestock and insect vector hosts. Box and whisker plots showing the number of bluetongue-positive herds after a 12-month simulation period as a results for bluetongue simulation model. Each distribution is based on 100 simulations for different start input settings.

4.4 Discussion

The model presented in this paper integrates current knowledge of BTV, factors influencing the geographic distribution of insect hosts (and how the distribution of hosts changes over space and time) and empirical data on the animal (host) population at risk. The design of this model has been informed by previous models of BTV spread in the United Kingdom and Denmark (Gubbins et al. 2007, Szmaragd et al. 2009).

Here we have accounted for a single insect vector species and a single host species. We have implicitly assumed that a *Culicoides brevitarsis*-like organism is the competent vector for bluetongue for two reasons: (1) its widespread distribution across Australia (Bishop et al. 1995, Kirkland 2004); and (2) *Culicoides* spp. are capable of transmitting BTV (Kirkland 2004, Standfast et al. 1978). Cattle are assumed to be the primary host: the reason being that *C. brevitarsis* preferentially feed on cattle and cattle dung is a preferred breeding site for *C. brevitarsis* (Animal Health Australia 2015). Moreover, cattle are generally considered to be the major reservoir for BTV due to their prolonged period of viraemia (Bonneau et al. 2002). While sheep have not been included in the model presented in this paper we acknowledge that sheep can play an important role in the epidemiology of bluetongue because, for some seroptypes, sheep can show severe clinical signs in situations where cattle show no obvious signs of disease. In Australia, the presence of susceptible animal populations at risk, competent vectors and the presence of BTV suggests that there is a high probability that an outbreak of clinical bluetongue could occur at some time in the future. Moreover, there has been a spread of some BTV serotypes in susceptible sheep in Queensland and New South Wales but no clinical disease has been reported (Johnson & Flanagan 1992). Our model could be easily refined to include a second host species such as sheep. Similarly, the model could be refined to include additional vectors conditional (of course) on the ability to define suitable model parameters for each.

A key challenge in the development of any model is the presence and availability of data of sufficient quality to allow the model to be validated. Our model was developed using empirical data describing the location and composition of cattle herds in northern New South Wales. Initial parameters were based on a review of the BTV modelling literature, mostly based on the outbreak of BTV-8 that occurred in northern Europe in 2006 (). The model was structured in such a way to include components to define the within-herd spread of disease, combined with a kernel based approach to allow disease to be spread from one herd to another by insect vectors. An additional feature was that the abundance of insect vectors was allowed to change over space and time, in response to changes in environmental temperature (Chapter 3). Environmental temperature was important in this model because it influenced the frequency of contact between insect vectors and hosts, with increases in environmental temperature increasing the probability that virus will be transferred from the insect vector layer to the herd population, through its effect on the infection pressure exerted by the insect vector layer on the animal host layer β_{vh}. In addition, temperature is a determinant of the rate of transmission with an infected herd whereas the risk of transmission between herds (given appropriate temperatures) depends largely on the locations of farms and the distances between groups of animals

(i.e. herds) within those farms. Each of these variables, mortality rate, biting rate and the extrinsic incubation period, were strongly associated with temperature (Gubbins et al. 2007): in the warmer months of the year midges will bite more often and start transmitting virus sooner after infection, however higher temperature results in midges dying sooner.

Our simulation results show that the extent of an outbreak of bluetongue in the study area was dependent on the geographic distribution of the herd population at risk, ambient temperatures and the presence of *Culicoides* spp. vectors. The first infected herd for our simulations was in an area of relatively high herd density on the edge of the of the study area. Our simulations show that the model was most sensitive to the bandwidth (i.e. the radius) of the kernel which determines the distance over which an infected herd poses a bluetongue transmission risk to susceptible herds (Figure 4.6). The predicted number of infected herds was relatively insensitive to changes in bandwidth greater than 7.8 km, most likely due to the dimensions of the raster cells for the insect vector layer (10 km $\times$ 10 km). Given the sensitivity of our model to bandwidth which is, in effect, a proxy measure of *Culicoides* spp. flight distance, a useful area of future research would be to quantify *Culicoides* spp. flying distances under Australian conditions, allowing an appropriate bandwidth setting to be used in the model. Lillie et al. (1981) reported *Culicoides* spp. flying distances of less than one kilometre whereas Murray & Kirkland (1995) reported flying distances of several kilometres. These findings warrant further investigation to determine if they are true differences or (more simply) due to differences in study technique. If *Culicoides* spp. flight distances do vary, the model could be adapted to allow a bandwidth for a given raster cell on a given day to be drawn from a probability distribution.

In most of the bluetongue models published to date parameter settings were derived from the peer-reviewed literature. For example, estimates of biting frequency, insect vector mortality rate and extrinsic incubation period (all of which are temperature dependent) were discussed in detail by Gerry & Mullens (2000) and Mullens et al. (2004). Other parameters were derived from field data derived from past outbreaks. Santman-Berends et al. (2013) collected serology data from sentinel dairy herds over a 12 month period to derive parameter values for their model of BTV transmission. Sumner et al. (2017) used data from a number of surveillance sources to estimate model parameters using Approximate Bayesian Computation. The parameters used in our study (Table 4.1) were mostly derived from the Gubbins et al. (2007) model of bluetongue transmission in the United Kingdom, but also from studies conducted in a range of countries and a range of insect vector species. Parameters relating to infection in the host are likely to be accurate, but those relating to the vector are likely to vary with *Culicoides* species and climate. For example, the extrinsic incubation period for BTV exhibits strong temperature dependence (Gerry & Mullens 2000, Mullens et al. 2004), ranging from from 26 days at 15 °C to 4 days at 30 °C (Wittmann & Baylis 2000). We note that estimates of the extrinsic incubation period are based on laboratory experimental data in which *Culicoides* spp. were maintained at a constant environmental temperatures; temperatures will, of course, fluctuate in the field.

This study was novel in that it used a simulated population of *Culicoides* spp. (as described in Chapter 3) appropriate for Australian conditions. Another novel approach was the separation of host

and vector populations into two spatial 'layers': a raster layer to describe the geographic distribution of the insect vector population and a (geographic) vector layer to represent the herd population at risk. This approach allows the model to be readily adapted for other insect vector-borne diseases such as African horse sickness or other diseases where the precise geographic location of a disease reservoir cannot be defined at the point location level, for example wild boar in the case of African swine fever.

Our model is not without limitations. Firstly, simulation times were markedly longer for large study areas and, for this reason, we elected to use an area that was relatively small (245 square km) compared with the geographic extent of Australia. Simulation times were also longer when the size of the raster cells used for the insect vector layer was reduced. Our choice of a 10 km $\times$ 10 km raster cell size provided a level of spatial resolution of the insect vector layer that was consistent with the spatial resolution of the data used to generate the layer (Chapter 3) while at the same time providing reasonable model run times. Secondly, the absence of an outbreak of clinical bluetongue in Australia means that we have no empirical data to validate our model results. One way of overcoming this limitation would be to validate the model by comparing simulation outputs with data recorded from BTV-8 outbreaks that occurred in Europe (for example, Denmark or Spain). Finally, our model has been developed assuming cattle are managed under a typically Australian system of management where they are kept outdoors at all times of the year. Modifications to the model would need to be made to allow it to be used in other countries where cattle are housed, since housing will influence insect vector-host contact rates.

Chapter 5

Simulation of the spread of bluetongue in Australian livestock

Introduction: Bluetongue is a viral, vector-borne disease that has the potential to cause substantial economic and welfare issues in domestic ruminants. Due to the expected economic impact that an incursion of virulent bluetongue will have on pastoral industries in Australia (mostly arising from the imposition of international trade restrictions) there is a need to develop plans to limit the spread of disease if an incursion were to occur. The Australian Animal Disease Spread (AADIS) model is a national-scale, hybrid model of livestock infectious disease developed to provide decision support for the management of foot and mouth disease. The aim of this study was to extend AADIS to allow it to simulate the spread of a vector-borne diseases such as bluetongue in Australia.

Methods: A series of hypothetical bluetongue incursion scenarios were developed wherein virulent bluetongue was seeded into cattle herds at four geographically distinct sites extending the east coast of Australia. Bluetongue incursions were timed to occur in two seasons (summer and winter) producing eight outbreak scenarios in total. A total of 100 iterations of each of the eight scenarios was run using AADIS. The first set of eight scenarios was run using AADIS's internal model of *Culicoides* spp. population dynamics (Model 1). The second set of eight scenarios was run using externally generated *Culicoides* spread maps (Model 2), as described in Chapter 3. Each of the models were run without imposition of control measures.

Results: Large outbreaks of bluetongue were predicted in Southern Queensland and Far Northern New South Wales with larger outbreaks occurring when incursions occurred during the summer. Outbreaks in Northern New South Wales were smaller compared with the other areas, with a similar seasonal effect. Compared with the other seed locations, the Northern Queensland outbreaks were smaller than those predicted for the other regions but again with a marked seasonal effect. Simulation results for Model 1 and Model 2, across all eight scenarios, were similar.

Conclusion: Biologically plausible estimates of bluetongue spread were generated using AADIS and estimates of bluetongue spread were similar for the two approaches used to estimate the geographic distribution of *Culicoides* spp. This work provides a necessary starting point for response planning for an incursion of virulent bluetongue into Australia.

5.1 Introduction

Bluetongue is a disease of domestic and wild ruminants, caused by a double stranded RNA Orbivirus which is a member of the Reoviridae family (Mertens et al. 2004). Although most domestic, as well as wild ruminant species are susceptible to bluetongue, clinical signs of disease and death are most frequently observed in sheep (Purse et al. 2005, Darpel et al. 2007). Transmission of bluetongue virus (BTV) depends on climatic factors (in particular, temperature and wind) which in turn determine: (1) the geographic distribution of the insect vector of the virus, *Culicoides* spp.; and (2) the inter-relationships between the virus, insect vector populations and susceptible livestock species (Mellor 2000). Bluetongue is generally regarded as a seasonal disease because the numbers of insect vectors and their competence are directly influenced by environmental factors. In endemic countries the incidence of bluetongue is highest in the late summer when insect vector populations are dense and active (Bishop et al. 1995).

Australia has not experienced an outbreak of clinical bluetongue although some strains of BTV are endemic in northern and north eastern Australia (Curtis 2009, Kirkland 2004, White et al. 2019). The most likely route by which a pathogenic strain of BTV might enter Australia is via infected *Culicoides* midges blown on annual northwest monsoon winds from Indonesia or Papua New Guinea to the northern borders of the Northern Territory and Queensland (Eagles et al. 2012, 2014). This conjecture is supported by ongoing detection of BTV of Southeast Asian genotypes (e.g. BTV-12) at sentinel herd surveillance sites in northern Australia (Animal Health Australia 2015).

The direct economic costs of a bluetongue outbreak in Australia will depend on a number of factors including the virulence of the virus serotype involved and the density of animals and herds in affected areas. Additional costs arise from the application of control measures, losses arising from reductions in animal productivity (e.g. the quantity and quality of wool, milk or meat), death of affected animals and losses arising from barriers to international trade that occur following confirmation of the disease (Animal Health Australia 2015). High rates of mortality in sheep are likely to be sporadic in areas that are occasionally populated by insect vectors. Losses due to clinical disease in cattle are likely to be rare.

Due to the substantial economic impact of an incursion of virulent BTV (mostly from international trade restrictions), there is a need to develop plans to limit the spread of disease at the site of incursion and limit long-distance spread of disease over wider geographic areas. According to the Australian Veterinary Emergency Plan (AUSVETPLAN) stamping out would not be justifiable for bluetongue because the disease is not spread by direct or indirect contact between animals and, even if animals were depopulated on identified infected premises, it would not be possible to eliminate infected insect vectors. However, for animal welfare reasons, it may be necessary to slaughter animals showing severe clinical signs (Animal Health Australia 2015). Measures to limit the spread of bluetongue are therefore limited to quarantine of animals in infected herds and the imposition of bans on the movement of animals from one location to another with limitations on movement reducing the likelihood of widespread geographic dispersal of disease. Vaccination would comprise a major component of any

bluetongue control program. Vector control by eradication of insect vectors is not considered possible under Australia conditions but might be appropriate in smaller, well-controlled areas (Saegerman et al. 2008).

The Australian Animal Disease Spread (AADIS) model is a national-scale model of infectious disease of livestock. In AADIS within-herd disease spread is modeled using deterministic, equation-based methods. Between-herd spread is modeled using spatially-explicit, stochastic agent-based methods. While originally developed to provide decision support for managing outbreaks of foot and mouth disease (FMD) in Australia (Bradhurst et al. 2015) the architecture of AADIS is such that it can be readily adapted to model other infectious animal diseases. Indeed, the motivation behind the program of research presented in this thesis has been to provide the necessary preparatory work to allow AADIS to model vector-borne diseases of livestock such as bluetongue.

Two capabilities for representing BTV vector population dynamics were developed. The first was the ability to import externally generated raster data to represent the geographic distribution of an insect vector population and how it changes over time (Chapter 3). The second capability was simulation of vector population dynamics within AADIS itself (Kompas et al. 2017). When simulating the spread of FMD, AADIS uses a raster-based approach to store climate data that informs airborne spread of FMD virus. For our work the AADIS raster architecture was extended to allow it to store the geographic distribution of an insect (indeed any) vector population, similar to the approach used for climate data. This allows the model to account for changes in the geographic distribution of the vector population over time, with conditions in any given raster cell potentially influencing conditions in its neighbours. The process of modelling the distribution of a vector population can be categorised into three components: (1) definition of the geographic distribution of the vector population, dealt within AADIS by using a binary variable to indicate vector presence or absence in each raster cell; (2) definition of the relative abundance of insect vectors in each raster cell, captured by means of an equation-based growth model; and (3) spread, represented by diffusion and jump pathways (analogous to the direct, indirect, local and airborne spread pathways used to model FMD transmission) (Bradhurst 2015, Bradhurst et al. 2015, Kompas et al. 2017).

The first aim of this study was to use AADIS to simulate the spread of bluetongue following incursion of virulent BTV into the cattle population using the model of bluetongue transmission described in Chapter 4 and to describe each simulated outbreak in terms of the number of infected herds and their geographic distribution. With this completed we comment on how the pattern of disease spread might then influence the application of disease control measures. A secondary aim was to compare the spread of BTV using the two options available within AADIS for estimation of the geographic distribution of the insect vector population — those externally generated (Chapter 3) and those generated within the AADIS model itself (Kompas et al. 2017).

5.2 Materials and methods

Geographically, the Australian livestock industry is diverse and spread across a range of climatic zones including the temperate south, the sub-tropical and tropical regions in the north and the far north east and desert areas in the centre of the country (Dunlop & Brown 2008). We selected four regions along the east coast of Australia in which to seed outbreaks of virulent BTV (Table 5.1): Northern Queensland, Southern Queensland, Far Northern New South Wales and Northern New South Wales. In each study area a single first infected herd for each simulated outbreak was selected. BTV was seeded into each of the selected first infected herds on 1 January 2015 (mid-summer) and 1 July 2015 (mid-winter).

5.2.1 Input data

Details of the location of the cattle population at risk were represented using the centroid of each herd location as recorded by the National Livestock Identification Scheme (Australian Bureau of Agricultural and Resource Economics and Sciences 2014). Figure 5.1 is a map of Australia showing the location of each of the four study areas. Figures 5.2, 5.3, 5.4 and 5.5 are maps of each of the four study areas showing the location and size of cattle herds in each.

Within AADIS the geographic distribution of *Culicoides* insect vectors is entered into the model in raster format using grid cells of dimensions 10 km $\times$ 10 km. As described in Chapter 3 parameters governing the birth rate and death rate of *Culicoides* spp. midges were based on the published literature (Kelso & Milne 2014) with modifications to allow changes in the simulated relative frequency of midges as a function of calendar date in a given area to match the temporal pattern of midge capture frequency as recorded by the NAMP (National Arbovirus Monitoring Program 2015). Our rationale for this approach was to ensure that seasonal variations in *Culicoides* midge presence or absence in a given area matched long term trends in empirical data documenting *Culicoides* presence or absence. This approach was particularly important for the New South Wales incursion sites where *Culicoides* presence varies throughout the year, unlike Northern Queensland where *Culicoides* midges are present at all times of the year.

Daily temperature, wind speed and wind direction data for the period 1 January 2015 to 31 December 2015 (used to inform the *Culicoides* distribution model) were obtained in raster format from the Australian Bureau of Meteorology (Australian Government Bureau of Meteorology 2014).

5.2.2 The AADIS model of insect vector dynamics

Here, we briefly describe the within AADIS vector module to represent the geographic distribution of *Culicoides* spp. across Australia and the logistic growth model used to simulate within-raster cell vector population growth.

To represent the vector population biology within AADIS, some simplifications and assumptions were made. Firstly, a spatial automata approach was used to model the diffusion of *Culicoides* spp.

from one raster cell to another. Secondly, the population of midges in each raster cell was represented using a normalised (zero to one) scale, rather than as absolute counts.

A logistic growth model (Equation 5.1) was used to simulate the change in the relative population size of *Culicoides* spp. within each raster cell. This approach is commonly used to represent insect population dynamics and has the advantage of simplicity (Daly et al. 1998).

$$x(t) = \frac{1}{1 + (\frac{1}{x_0} - 1)e^{-rt}} \tag{5.1}$$

In Equation 5.1 $x(t)$ represents the density of *Culicoides* spp. vectors in a given raster cell at day t. The term x_0 equals the initial population density and r is the population growth rate (that is, the population recruitment rate minus the population depletion rate).

The logistic expression shown in Equation 5.1 was extended as follows. Firstly, because vector population density was estimated using a relative scale, the output from Equation 5.1 for each raster cell was multiplied by the normalised cattle density for that cell. Secondly, the population growth rate r was modified each day using mean daily temperature (Kompas et al. 2017).

Agent-based methods were then used to simulate the spread of insect vectors from one raster cell to another, in which raster cells act as agents and can influence the state of other cells through a variety of pathways. The insect vector spread pathways were: (1) short distance movement, consistent with local dispersal; and (2) long distance movement, consistent with wind-borne spread.

The state of a given raster cell (active, quiescent or *Culicoides* spp. free) determines whether it can be a source or recipient of a vector spread event. Only active cells can be a source and only a free cell can be a recipient. Several factors influence the likelihood and nature of *Culicoides* spp. spread. These include the insect vector population density within the raster cell, temperature, wind speed, terrain and cattle density. Local dispersal was based on the existing spatial kernel AADIS diffusion pathway. This pathway can only operate when weather conditions are suitable with a wind speed of less than 8 km.h^{-1}. Long distance spread, on the other hand, was defined by a jump pathway that can cover any type of dispersal event for longer distances. To mimic wind-borne dispersal long distance spread was set to operate only when the temperature was at least 18 °C and wind speed was less than 8 km.h^{-1}. For long-distance dispersal, a higher threshold temperature was used than local dispersal because it was assumed that *Culicoides* spp. vectors would need a higher degree of activity to travel far enough from their hosts to be moved by wind currents. If conditions are suitable, a stochastic approach is used to determine if a spread event occurs and, if so, which grid cells from that source cell are infested.

5.2.3 Outbreak scenarios

Summer (1 January 2015) and winter (1 July 2015) incursions of bluetongue were simulated for each of the four selected study areas (Figure 5.1) returning eight incursions in total. Details of each of the incursion scenarios are provided in Table 5.1. The first set of eight scenarios was run using AADIS's internal model of *Culicoides* spp. population dynamics (Model 1). The second set of eight scenarios

was run using externally generated *Culicoides* spread maps (Model 2), as described in Chapter 3. Each of the models were run without imposition of control measures.

Northern Queensland

The Northern Queensland study area was 100 km north of the Tropic of Capricorn (labelled 'A' in Figure 5.1). This area is characterised by two distinct seasons with low rainfall and warm temperatures (14 – 26 °C) in the winter and higher rainfall and warmer temperatures (24 – 33 °C) in the summer. The area is characterised by, on the whole, relatively low cattle herd density with a markedly higher concentration of herds in the Atherton Tablelands (Figure 5.2).

Northern Queensland is likely to be at higher risk of receiving BTV-positive *Culicoides* incursions from neighbouring islands (Eagles et al. 2012, 2013). The study area was located in the local government area of Mareeba at the base of Cape York Peninsula.

Southern Queensland

The Southern Queensland study area was located in the North Burnett region of southern Queensland (labelled 'B' in Figure 5.1). The North Burnett area has historically had a strong base in beef and dairy production. Intensive beef enterprises (n = 2091) comprise 50% of all farms in the North Burnett (Figure 5.3). The climate is sub-tropical and sub-humid with rainfall concentrated in the late spring to early autumn (October to March). Frosts occur during the winter (June to August). Average temperatures in Southern Queensland range from 5 °C to 32 °C, however temperatures as high as 40 °C can occur over short periods over summer. Sub-zero temperatures regularly occur during the winter.

Far Northern New South Wales

The Far Northern New South Wales study area (labelled 'C' in Figure 5.1) was in the Richmond Valley local government area (Figure 5.4). Agricultural land in the Richmond Valley local government area occupies around 59% of the region (ABARES 2015) and the density of cattle herds in this region, compared with the other study areas, was relatively high. The climate is characterised by warm to hot summers (with average daily temperatures ranging from 19 °C to 30 °C) and cool to mild winters (average daily temperatures ranging from 6.7 °C to 21 °C).

Northern New South Wales

The Northern New South Wales study area (labelled 'D' in Figure 5.1) was in the local government area of Port Macquarie-Hastings. Port Macquarie-Hastings is bordered by Kempsey Shire to the north, the Tasman Sea to the east, the Mid Coast Council to the south and Walcha Shire to the west. The Port Macquarie-Hastings local government area has a humid subtropical climate with warm, humid summers and mild winters, with rainfall throughout the year. Cattle herd density in this area was moderate compared with the other study areas (Figure 5.5).

Following seeding of BTV into a single cattle herd in each of the four study areas AADIS was run for 365 simulation days for a total of 100 iterations. For each scenario, descriptive statistics are reported for the predicted number of infected herds. Counts of the predicted number of infected herds across scenarios were compared using a two-tailed Welch (unequal variance) t test.

5.3 Results

Descriptive statistics of the predicted number of bluetongue infected herds in each of the four study areas for Models 1 and 2 are shown in Table 5.2 (summer incursions) and Table 5.3 (winter incursions). Figures 5.6 and 5.7 show the same data as box and whisker plots. In Figures 5.6 and 5.7 the boxes represent the interquartile range, the horizontal line inside each box represents the median number of infected herds and the whiskers represent the extent of the 95% probability interval for the predicted number of infected herds.

The predicted number of infected herds for Model 1 and Model 2 were relatively similar for each of the eight scenarios where incursions occurred in the summer (Figure 5.6 and Table 5.2) and winter (Figure 5.7 and Table 5.3). The predicted number of infected herds for summer and winter incursions in Northern Queensland did not significantly differ (Model 2: Welch t test statistic: -0.6383; df 122.9; P = 0.52). Incursions that occurred in Southern Queensland and Far Northern New South Wales in the summer resulted in relatively large bluetongue outbreaks with a median of 590 (Q1 552; Q3 631) and 1509 (Q1 1474; Q3 1548) infected herds for Model 2, respectively. In summer, bluetongue outbreaks in Far Northern New South Wales were larger than those in Southern Queensland because of the higher density of herds in Far Northern New South Wales (compare Figure 5.3 with Figure 5.4). There was a marked seasonal effect with winter outbreaks producing a median of one infected herd in both Southern Queensland (Model 2: Welch t test statistic -15.451; df 114.9; $P < 0.001$) and Far Northern New South Wales (Model 2: Welch t test statistic -24.92; df 103.9; $P < 0.001$) due to seasonal effects on the size of the insect vector population.

For the Northern New South Wales scenarios, incursions that occurred in the winter were limited to the first infected herd (Table 5.3). Incursions that occurred in the summer resulted in a median of 198 (Q1 175; Q3 235) infected herds (Table 5.2).

Table 5.1: Simulation of the spread of bluetongue in Australian livestock. Details of each selected of the first infected herds selected for the bluetongue incursion scenarios investigated in this study.

Region	Herd type	Herd size	Longitude	Latitude
Northern Queensland	Beef extensive [a]	1371	145.075	-16.6821
Southern Queensland	Beef intensive [b]	40	151.982	-25.5140
Far Northern New South Wales	Beef intensive [b]	92	153.058	-28.9072
Northern New South Wales	Beef intensive [b]	155	152.686	-31.5341

[a] Systems where cattle graze pasture all year round.
[b] Systems where cattle graze pasture all year round; animals may be confined to receive supplementary feed during the winter months.

Table 5.2: Simulation of the spread of bluetongue in Australian livestock. Descriptive statistics of the predicted number of bluetongue infected herds in each of the four study areas for Models 1 and 2 following incursions of BTV in the summer.

Region	Season	Mean (SD)	Median (Q1, Q3)	Min, max
Northern Queensland:				
Model 1	Summer	14 (27)	8 (5, 15)	1, 192
Model 2	Summer	10 (17)	7 (4, 11)	1, 159
Southern Queensland:				
Model 1	Summer	576 (60)	576 (550, 625)	459, 793
Model 2	Summer	590 (69)	590 (552, 631)	398, 763
Far Northern New South Wales:				
Model 1	Summer	1522 (84)	1502 (1466, 1558)	1387, 1823
Model 2	Summer	1528 (82)	1509 (1474, 1548)	1474, 1922
Northern New South Wales:				
Model 1	Summer	142 (31)	138 (123, 159)	60, 242
Model 2	Summer	205 (46)	198 (175, 235)	106, 347

SD: standard deviation.
Q1: first quantile.
Q3: third quantile.

Table 5.3: Simulation of the spread of bluetongue in Australian livestock. Descriptive statistics of the predicted number of bluetongue infected herds in each of the four study areas for Models 1 and 2 following incursions of BTV in the winter.

Region	Season	Mean (SD)	Median (Q1, Q3)	Min, max
Northern Queensland:				
Model 1	Winter	9 (5)	8 (6, 11)	1, 27
Model 2	Winter	9 (6)	8 (6, 11)	1, 49
Southern Queensland:				
Model 1	Winter	220 (256)	1 (1, 481)	1, 760
Model 2	Winter	200 (242)	1 (1, 447)	1, 703
Far Northern New South Wales:				
Model 1	Winter	185 (504)	1 (1, 1)	1, 1770
Model 2	Winter	215 (520)	1 (1, 1)	1, 1600
Northern New South Wales:				
Model 1	Winter	1 (0)	1 (1, 1)	1, 1
Model 2	Winter	1 (0)	1 (1, 1)	1, 1

SD: standard deviation.
Q1: first quantile.
Q3: third quantile.

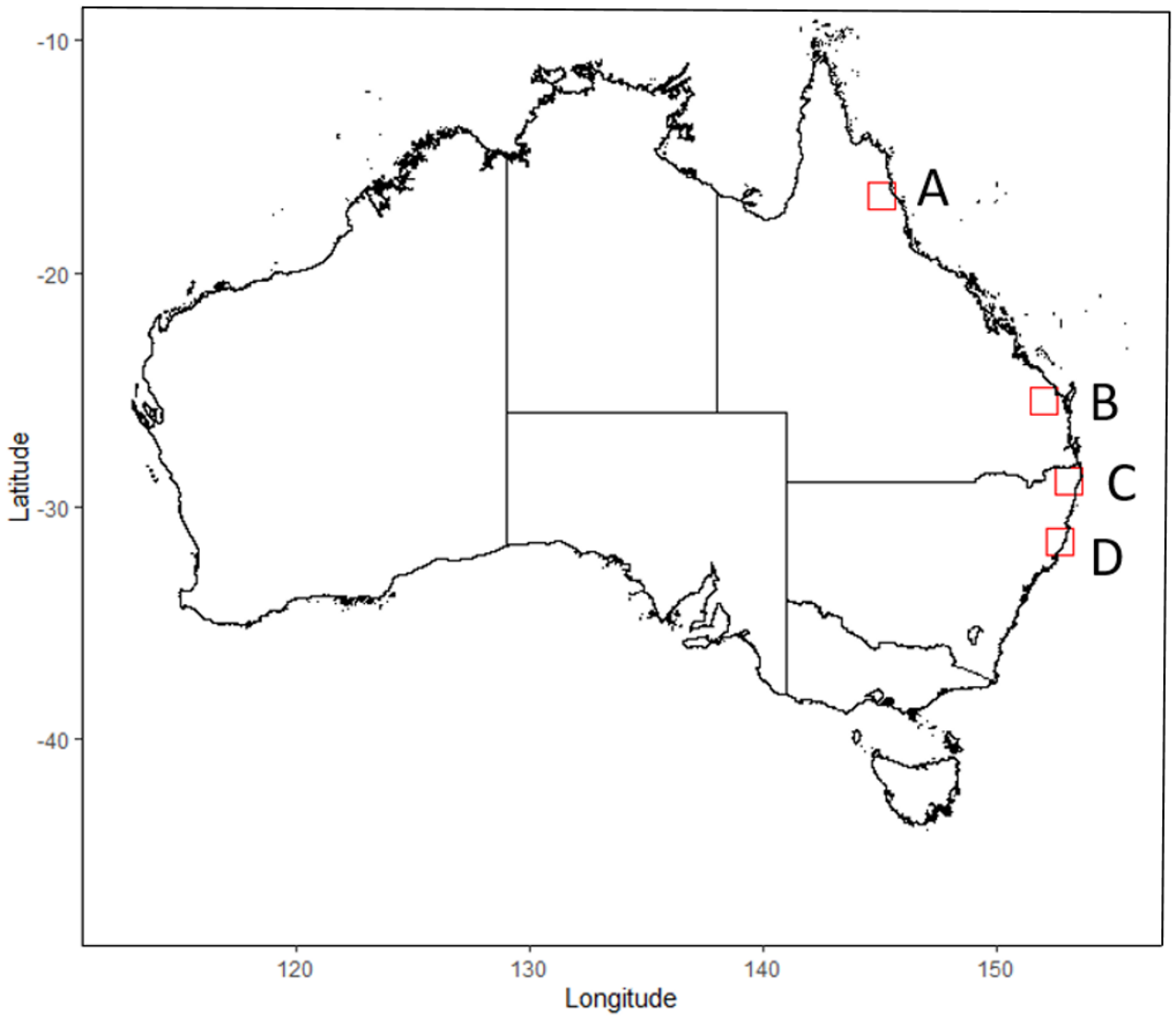


Figure 5.1: Simulation of the spread of bluetongue in Australian livestock. Map of Australia showing the location of the four study areas: (A) Northern Queensland, (B) Southern Queensland, (C) Far Northern New South Wales and (D) Northern New South Wales.

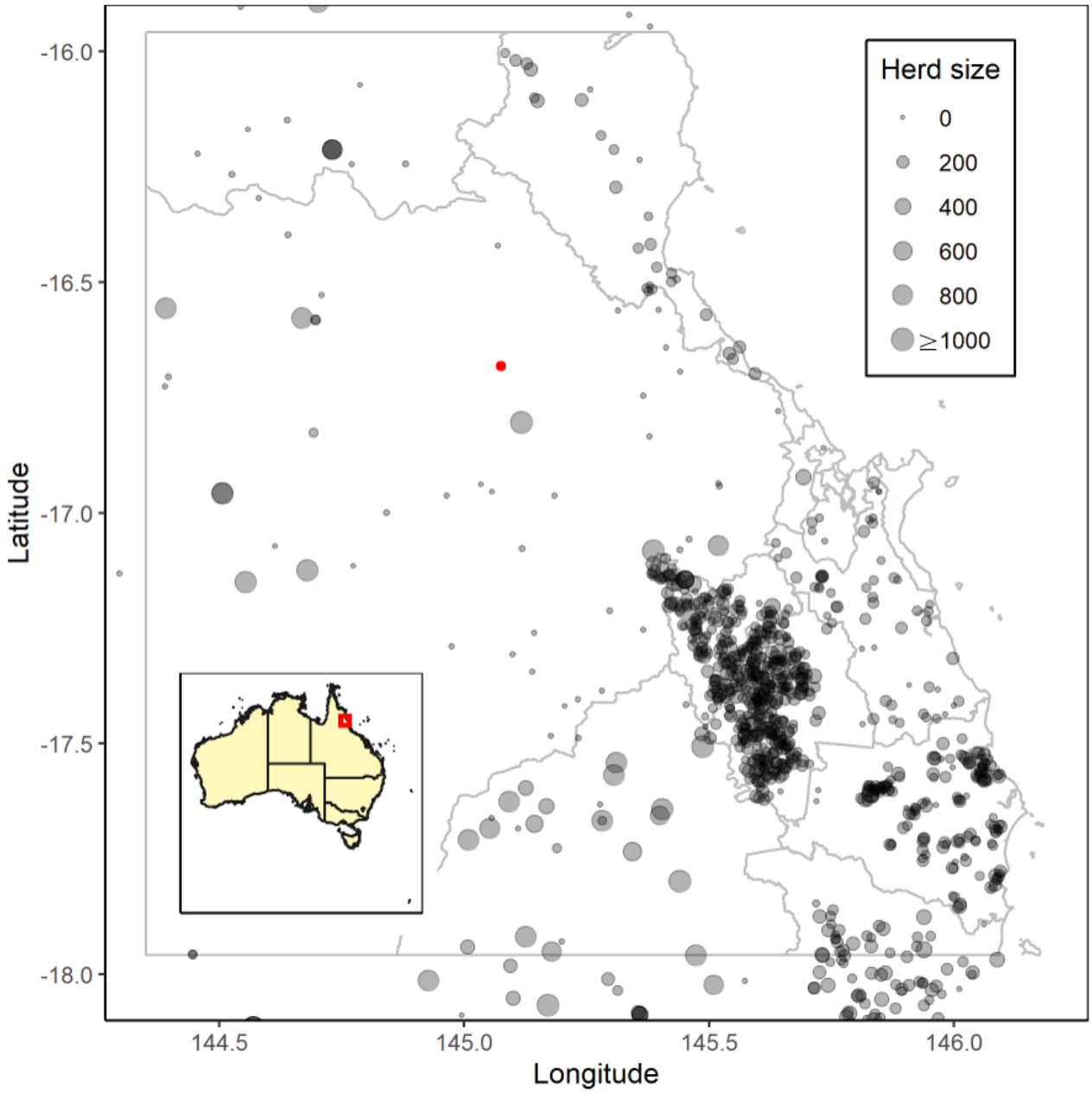


Figure 5.2: Simulation of the spread of bluetongue in Australian livestock. Map showing the location and size of cattle herds in the Northern Queensland study area (labelled 'A' in Figure 5.1). The red point shows the location of the index herd.

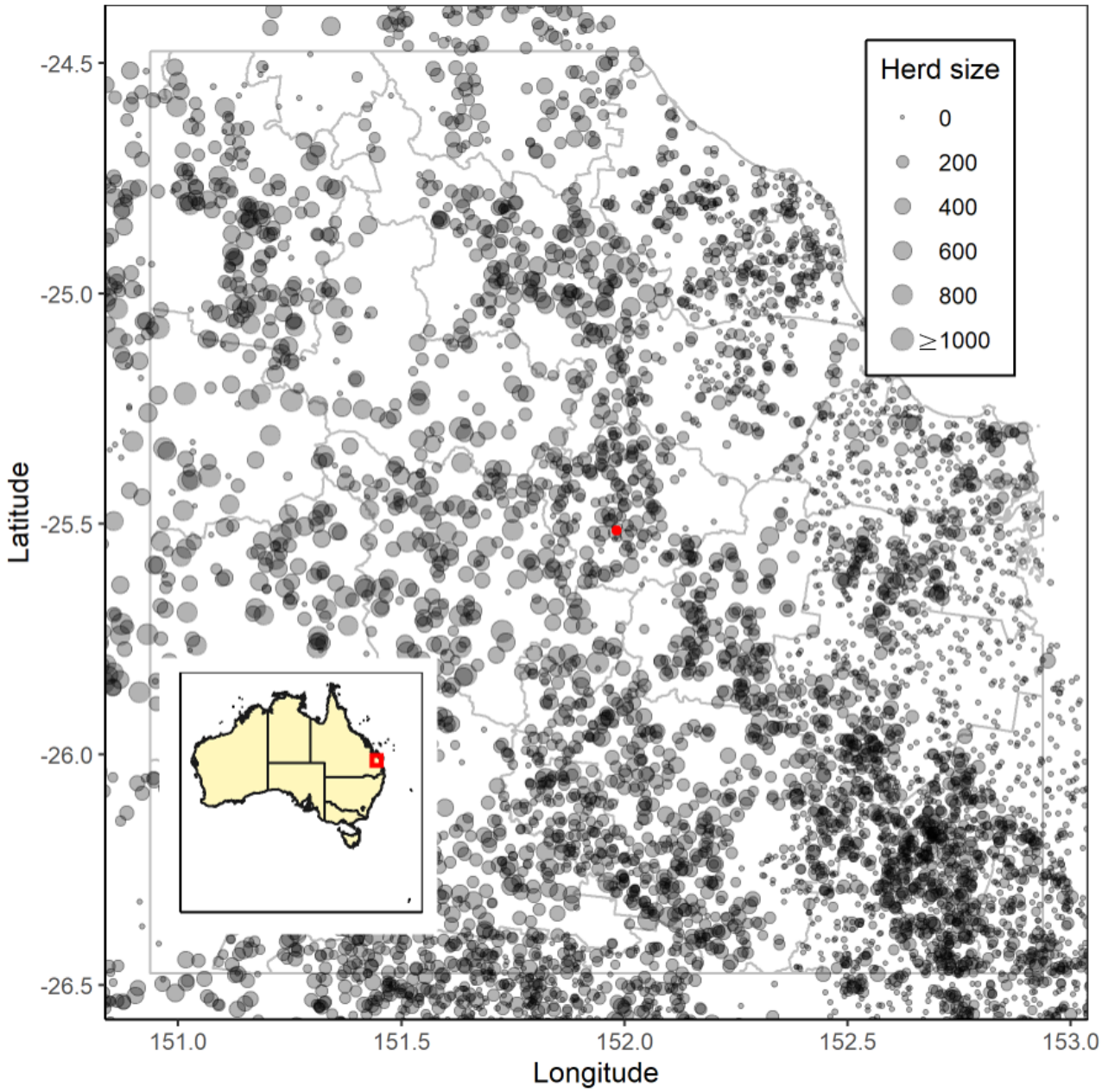


Figure 5.3: Simulation of the spread of bluetongue in Australian livestock. Map showing the location and size of cattle herds in the Southern Queensland study area (labelled 'B' in Figure 5.1). The red point shows the location of the index herd.

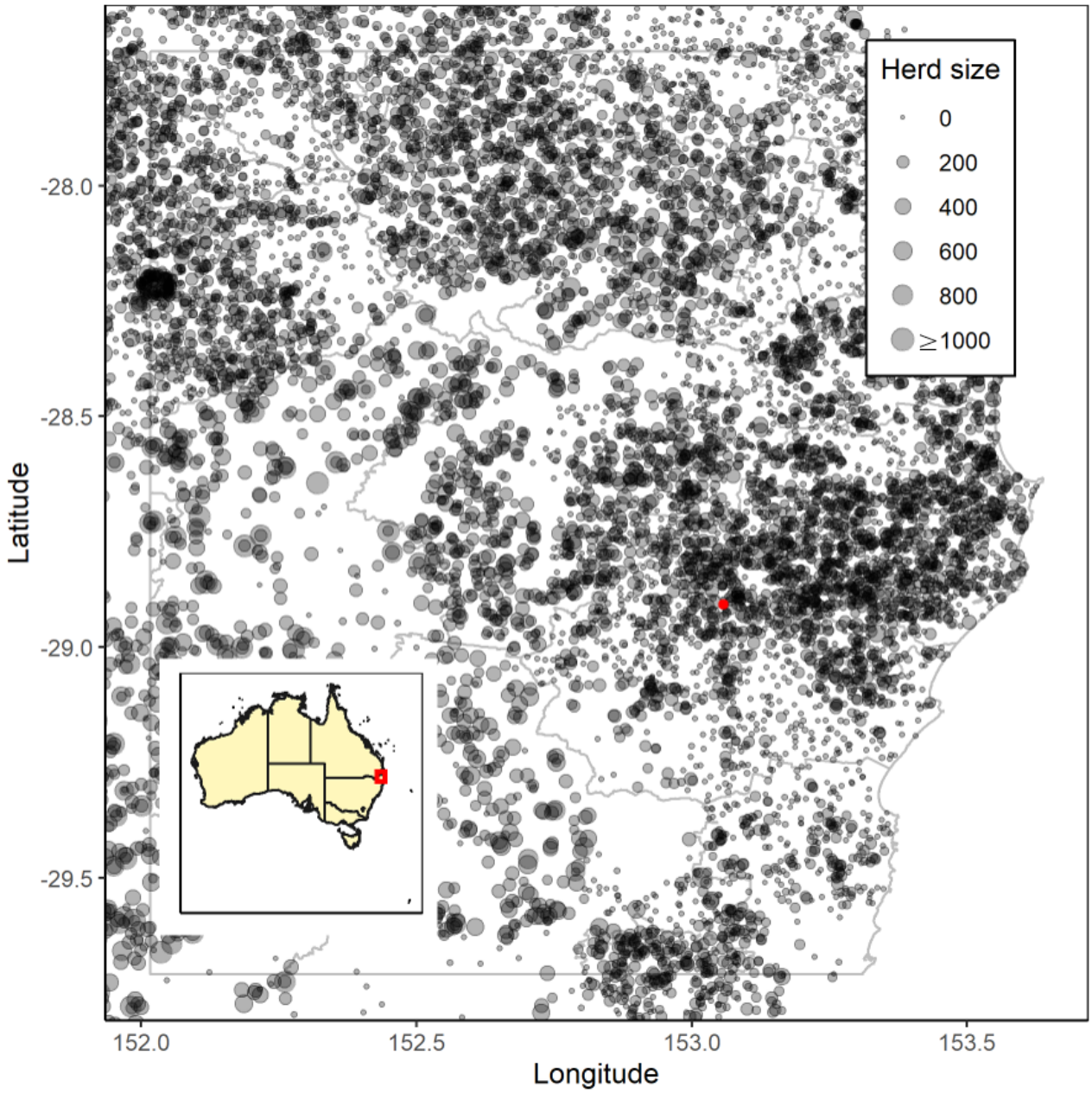


Figure 5.4: Simulation of the spread of bluetongue in Australian livestock. Map showing the location and size of cattle herds in the Far Northern New South Wales study area (labelled 'C' in Figure 5.1). The red point shows the location of the index herd.

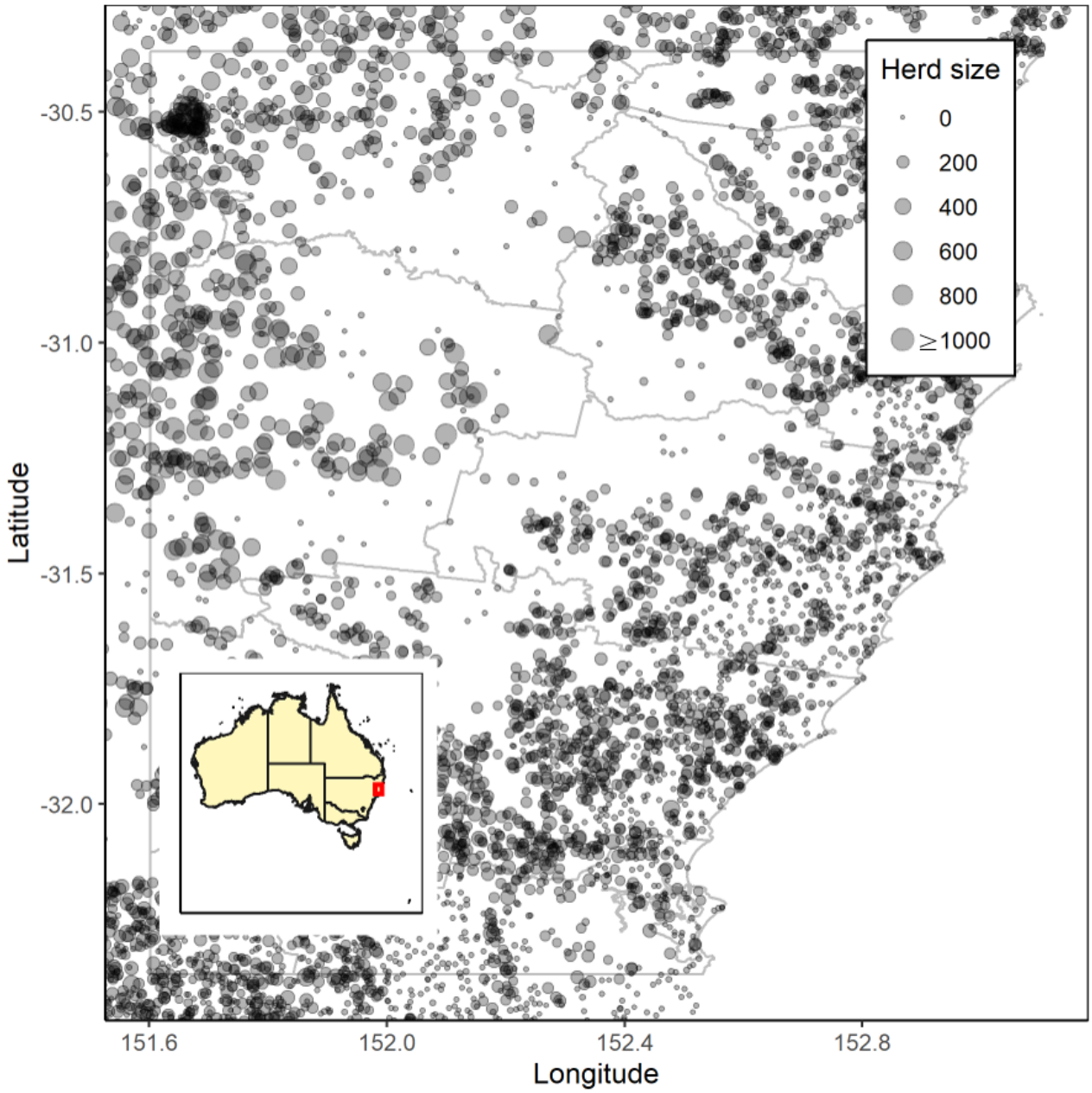


Figure 5.5: Simulation of the spread of bluetongue in Australian livestock. Map showing the location and size of cattle herds in the Northern New South Wales study area (labelled 'D' in Figure 5.1). The red point shows the location of the index herd.

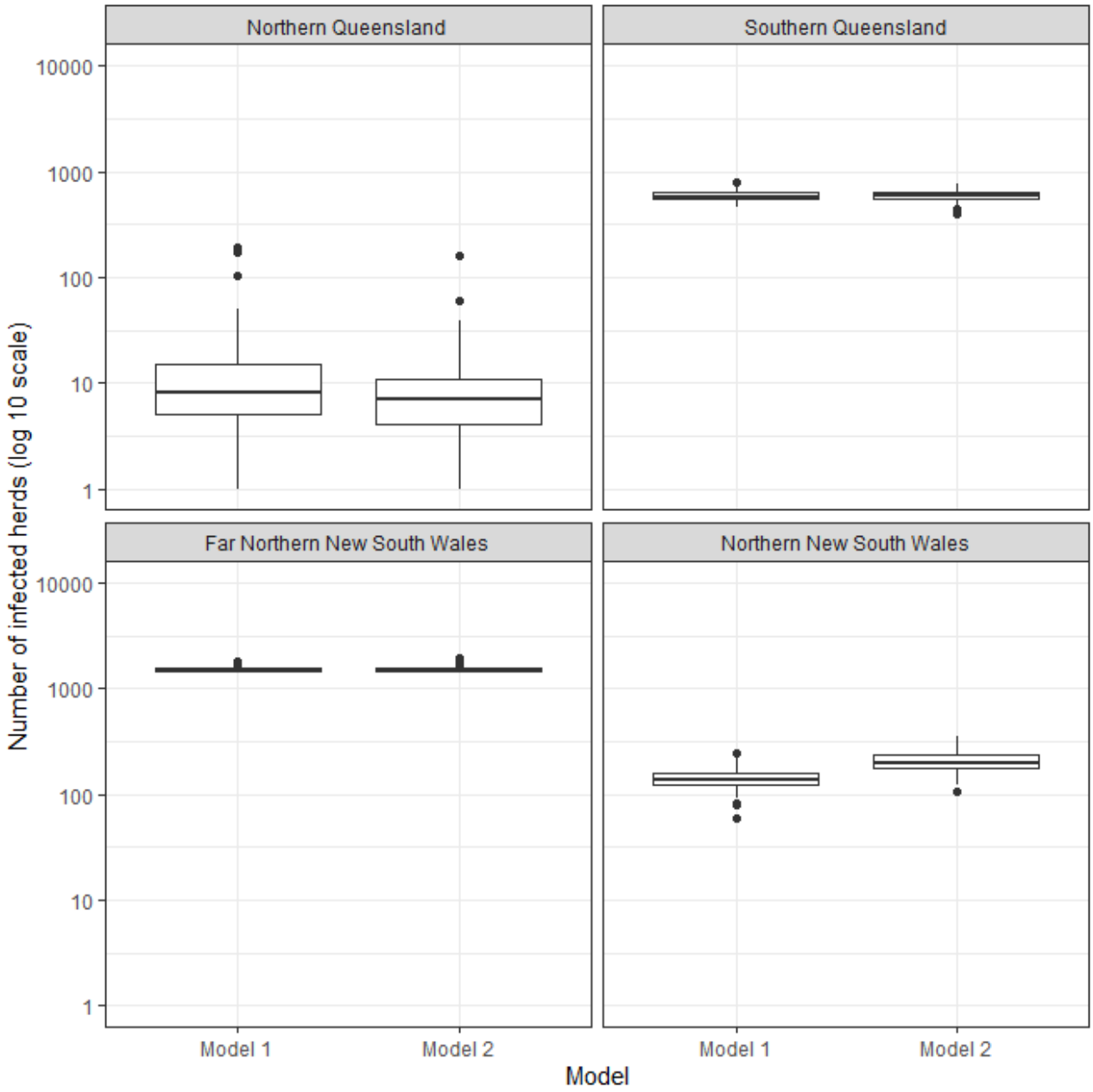


Figure 5.6: Simulation of the spread of bluetongue in Australian livestock. Box and whisker plots showing the predicted number of infected herds for bluetongue incursions occurring in the summer for Models 1 and 2, stratified by study area.

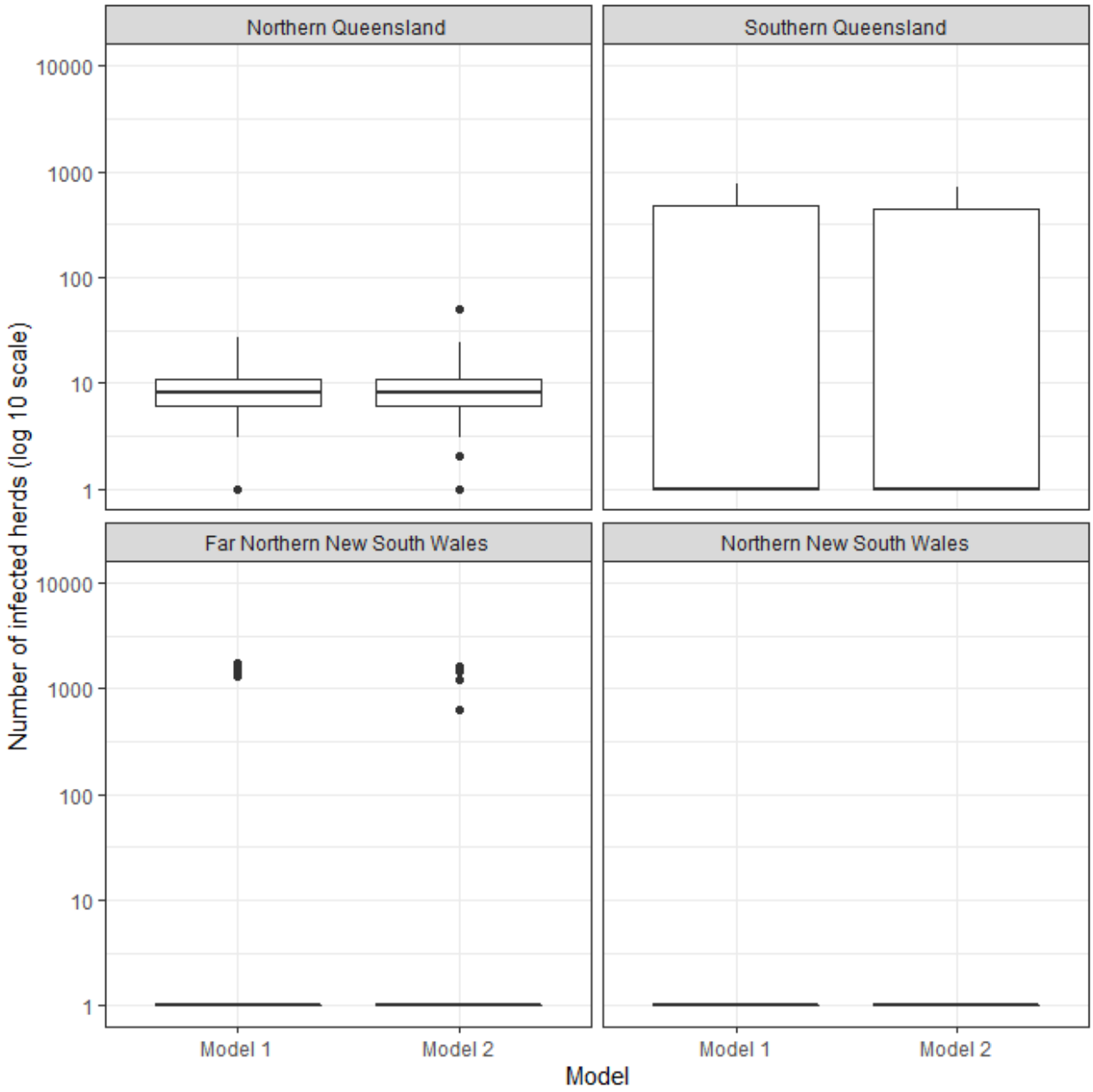


Figure 5.7: Simulation of the spread of bluetongue in Australian livestock. Box and whisker plots showing the predicted number of infected herds for bluetongue incursions occurring in the winter for Models 1 and 2, stratified by study area.

5.4 Discussion

We present simulations of the spread of vector-borne diseases among domestic livestock populations using the Australian Animal Disease Spread (AADIS) model. This work builds on the development of methods to estimate the geographic distribution of insect vectors and how these change over time (Chapter 3 and Kompas et al. 2017) and a model to simulate the transmission of infection between livestock hosts and insect vector populations (Chapter 4).

In the face of an outbreak that needs rapid, national level decisions to be made, insect vector distribution and abundance maps need to be developed quickly and seamlessly incorporated into disease spread models. In this respect the within-AADIS insect vector estimates (Kompas et al. 2017) were well suited for this purpose. On the other hand, the ability to use vector distribution and abundance maps developed independently of AADIS (and presumably by subject-matter experts) recognises the need for a collaborative approach to disease modelling. In the case of model development for vector-borne diseases engagement with entomologists to allow their estimates of insect vector distributions to be included into AADIS provides a mechanism that will allow disease spread simulations to be carried out at a higher level of spatial resolution. In this study the example of bluetongue has been used to provide proof of concept that AADIS can be used as a decision support tool for vector-borne diseases of livestock. We expect that re-configuration of AADIS to allow it to model the spread of other vector-borne diseases of livestock should be a relatively straightforward task.

While BTV is known to be endemic in parts of Australia, to date there has been not evidence of clinical disease associated with bluetongue in Australia (Curtis 2009, Kirkland et al. 2004, White et al. 2019). The main reason for this is that of the nearly 70 million animals that comprise the Australian sheep population (Curtis 2009) only several hundred are kept in BTV endemic areas (Kirkland 2004). Nevertheless, bluetongue has the potential to have a major impact on Australian livestock industries through restrictions on international trade. The risk of incursion of a virulent strain of bluetongue into the country represents a constant threat, particularly via infected midges blown on the annual northwest monsoons from Indonesia to the northern borders of the Northern Territory (Animal Health Australia 2015).

If incursions of a virulent strain of bluetongue into Australia were to occur, there is a need for quick and decisive action to contain the resulting outbreak and to limit disease spread. Fit-for-purpose disease models provide a means for assessing the merits of candidate disease control and eradication strategies, increasing the likelihood that they will be applied effectively in times of crisis. A second benefit of disease spread models is that they provide a means for demonstrating the likely consequences of a disease outbreak to stakeholders. In this way, discussions around disease control measures that might be unpalatable to some sectors (e.g. depopulation in the case of foot and mouth disease) can be had well in advance, reducing the likelihood of non-compliance by stakeholder groups during an outbreak when there is little time available for lengthy debate about the strengths and weaknesses of different control approaches. This study has focused on the risk of BTV incursion occurring under different environmental and geographical areas in livestock and to generate information that can guide

effective policy or mitigation strategies for control and prevention of disease.

Seeding BTV into geographically diverse areas of the country (Figure 5.1) resulted in marked differences in the spread of disease (Table 5.2, Table 5.3) due to a combination of climatic conditions (which influenced the relative abundance of *Culicoides* spp. midges) and cattle herd density. Cattle herd density in Southern Queensland (Figure 5.3) and Far Northern New South Wales (Figure 5.4) was greater than cattle herd density in Northern Queensland (Figure 5.2) which would explain the relatively large outbreaks in Southern Queensland and Far Northern New South Wales compared with Northern Queensland.

Since herds are represented as point locations in AADIS, large farms give rise to a relatively low number of herds per unit area and larger inter-herd distances which in turn leads to a reduction in the probability of between herd spread of disease. This contrasts with rural areas in the more southern regions of Australia where farm areas are much smaller leading to smaller inter-herd distances. This inference is supported by studies from Europe which have shown that between-herd spread of disease occurs more readily when between-herd distances are small (Guis et al. 2007). In the rangelands of Northern Queensland, farms range in size from 1778 to 2500 square km which means that if an incursion of bluetongue were to occur in a single herd, it is possible that spread to nearby herds may not occur simply because inter-herd distances are large. A potentially useful modification of the AADIS model would be to allow the point location of herds to vary within defined boundary ranges in those areas of the country (such as Northern Australia) where farm sizes are extremely large. This would, in effect, mimic the movement of mobs of cattle within a farm over time, giving rise to more realistic estimations of the between-herd spread of infectious diseases such bluetongue as well as foot and mouth disease.

The relatively small outbreaks that occurred when bluetongue was seeded into herds during the winter (Table 5.3) are consistent with the known effect of temperature on vector survival (Mellor et al. 2000, Brand & Keeling 2017). The seasonality of disease outbreaks is associated with annual peaks in both vector numbers and their activity (Baylis et al. 1997). Similar to the findings of other authors (Ward 1994, Turner et al. 2012, Græsbøll et al. 2012), lower temperatures markedly reduced BTV transmission (and therefore outbreak size) in the present study.

Biologically plausible estimates of bluetongue spread were generated using AADIS and estimates of bluetongue spread were similar for the two approaches used to estimate the geographic distribution of *Culicoides* spp. This work provides a necessary starting point for response planning for an incursion of virulent bluetongue into Australia.

Chapter 6

The effect of climate change on the spread of bluetongue in Australian livestock

Introduction: The frequency of vector-borne disease in human and animal populations has increased in recent years leading to concerns that even greater increases will occur as a result of climate change, driven by changes in the geographic distribution of insect vector habitat areas. In this study we investigate the effect of climate change on the expected spread of bluetongue using the Australian Animal Disease Spread model (AADIS).

Methods: Estimates of average daily temperature across Australia for 2015 were obtained from the Australian Bureau of Meteorology. Predicted average daily temperatures using the CanESM2 model (emission scenario RCP 8.5) for 2025 and 2035 at a resolution of 5 km $\times$ 5 km were obtained from the Australian Climate Futures decision-support tool, managed by the CSIRO. Two study areas were selected: the first in North Queensland and the second in Northern New South Wales. A total of 24 outbreak scenarios were run: mid-summer and mid-winter incursions for each study area for 2015, 2025 and 2035 with direct movements disabled and enabled for each.

Results: For North Queensland, there was little change in the median predicted number of bluetongue positive herds for mid-summer and mid-winter 2025 and 2035 incursions (compared with 2015) and a moderate increase in the variability of predicted outbreak sizes when direct animal movements were disabled. For Northern New South Wales there were moderate increases in both the predicted number of bluetongue positive herds and the variability of predicted outbreak sizes for 2025 and 2035, compared with 2015.

Compared with the direct animal movement disabled scenarios, there were marked increases in the predicted number of bluetongue positive herds as a function of simulation year for North Queensland. For Northern New south Wales this trend was not as distinct, but as for the direct movement disabled scenarios, the variability of predicted outbreak sizes for the 2035 incursions were greater than the variability of predicted outbreak sizes for the 2015 incursions.

Conclusion: Climate change will result in a greater portion of the land area of Australia with conditions suitable for *Culicoides* midges. Our findings show that under conditions of climate change and an outbreak of virulent bluetongue in Australia, the rapid imposition of effective restrictions of animal movement will be the single most important control measure to limit further spread of disease.

6.1 Introduction

Climate change is considered to be one of the greatest threats to human health by the World Health Organization (McMichael et al. 2003). The environmental consequences of climate change which include sea-level rise, increased frequencies of flood and drought, more intense hurricanes and storms, heat waves and degraded air quality are predicted to have substantial impacts on human well-being (Field 2014).

Over the past decades, global warming has already caused pronounced and often complex changes in the incidence and prevalence of vector borne infectious diseases of humans and animals (Harvell et al. 2009, Baker-Austin et al. 2013, Garrett et al. 2013). Vector control activities, the use of antimicrobial treatments and infrastructural change can dampen or even mask the negative impact that climate change can have on the frequency of disease in humans. Diseases of domestic animals, wildlife and plants are generally less uniformly influenced by these control measures, making the negative effects of climate change on disease frequency easier to detect in these sectors (Harvell et al. 2009).

Following the emergence and re-emergence of vector borne diseases of humans in many parts of the world in recent years (e.g. Zika virus and malaria) the global spread of arboviruses has received research attention from international public health organisations (Purse et al. 2005, Dash et al. 2013). There is a strong association between climate change and the geographic distribution of vector-borne diseases because insect vector ecology and their rate of development are often dependent on environmental conditions. Generally, larval development stages are dependent on the presence of bodies of water and/or specific conditions of humidity and temperature. Vector biting rates are positively associated with temperature up to a species-specific threshold (Birley & Boorman 1982, Braverman et al. 2003). The amount of time taken for pathogens to replicate within insect vectors (the extrinsic incubation period) is known to decrease when temperatures are higher (Gerry & Mullens 2000, Wittmann & Baylis 2000) and survival times are increased with increases in environmental temperatures (Birley & Boorman 1982).

Given the sensitivity of arthropods to changes in climatic conditions it is reasonable to expect that climate change will result in marked changes in the geographic extent of vector-borne disease and marked changes in the seasonality of vector-borne disease occurrence (Caminade et al. 2014). In human medicine studies estimating the changes in the geographic distribution of malaria has recently received the bulk of research attention at both the global (Béguin et al. 2011, Van Lieshout et al. 2004) and regional (Tanser et al. 2003, Ermert et al. 2012) level. Yet, a lesser number of studies have addressed the importance of socioeconomic factors (Gething et al. 2010, Van Lieshout et al. 2004, Rogers & Randolph 2000), economic development and intervention which might be developed to offset or counteract climate-induced trends (Béguin et al. 2011). These studies are unable to account for the influence of other drivers for disease for two reasons: (1) there is often little or no quantitative evidence to define how the frequency of disease will be affected by change in a non-climate driver; and (2) there are few models available to predict how these non-climatic drivers could change in the future. A recent study assessed changes in vector abundance, factors influencing vector population dynamics,

host density and land use, qualifying that the changes in disease frequency that were observed were likely to be due to observed changes in climate (Sanders et al. 2019). This conflicts with the relative simplicity of climate disease modelling where observational or experimental data are used to associate weather or climate variables with the frequency of disease. Combining the two allows climate-sensitive disease patterns or distributions to be predicted under future climate scenarios.

Bluetongue is likely to be one of the most important diseases of animals influenced by climate change due to expected changes in the geographic distribution of *Culicoides* midges (Rogers & Randolph 2006). In Europe, a series of bluetongue outbreaks occurred after 1998 (Mellor et al. 2008) resulting in the death of millions of ruminants and substantial economic losses. Between 1998 and 2010 more than 110,000 bluetongue outbreaks in Europe were reported to the World Organisation for Animal Health (OIE). Over 80,000 of these were due to bluetongue virus (BTV) serotype 8. In 2006, bluetongue occurred for the first time in northern Europe (Wilson et al. 2008). In 2007 bluetongue spread to the United Kingdom most likely via wind-borne infected midges blown across the English Channel from mainland Europe (Gloster et al. 2008). In 2015, bluetongue re-emerged in France (Brown et al. 2016). An outbreak of BTV-4 that started in the French Alps (in the south east of the country) in 2017 had spread as far as Normandy (in the far north west) by 2018 (Gauntlett et al. 2018). Expansion of the geographic distribution of bluetongue in southern Europe has been hypothesised to be associated with change in the geographic extent of the Afrotropical midge vector (Calvo et al. 2009). It is possible that climate has played a role in both routes of expansion (Purse et al. 2005, Wilson & Mellor 2008, Guis et al. 2012).

Several disease simulation models have been developed for bluetongue, all of which account for the effect of environmental temperature on the rate and geographic distribution of disease spread (Gubbins et al. 2007, Saegerman et al. 2008, Græsbøll et al. 2012, Turner et al. 2012). While these models provide an opportunity to quantify the effect of climate change on the epidemiology of bluetongue, predictions are likely to be imprecise due to uncertainties in climate change projection data and uncertainties in factors driving the epidemiology of the disease itself (Allen et al. 2000, Hawkins & Sutton 2009, Oppenheimer et al. 2016). This said, the results of modelling, if based on a valid conceptual design, provide useful information to guide animal health decision making (Garner & Hamilton 2011).

Bluetongue virus is already present in Australia and the strains that are present are less virulent than strains that occur overseas (Hooper et al. 1996). There is a risk that a novel or virulent BTV strain may be introduced into the country which would then have a substantial impact on animal health. To investigate this risk in detail the objectives of this study were to: (1) use climate change projection data to simulate the spread of bluetongue in Australia using the Australian Animal Disease Spread model (AADIS); and (2) provide recommendations on the way surveillance and outbreak management plans for bluetongue should be changed in the short to medium term future in response to climate change.

6.2 Materials and methods

6.2.1 Bluetongue transmission model

We configured AADIS using the spatial and temporal model of *Culicoides* spp. densities documented in Chapter 3 and the model of bluetongue transmission presented in Chapter 4, as described in Chapter 5.

Predictions of the spatial and temporal spread of bluetongue following incursion of the virus into single herd locations in 2015 provided a reference from which bluetongue spread scenarios under conditions of climate change (2025 and 2035) could be compared. BTV was seeded into two geographically distinct locations during the mid-summer (1 January) and mid-winter (1 July): (1) Mareeba at the base of Cape York Peninsula in North Queensland (labelled 'A' in Figure 6.1); and (2) Heron's Creek which borders Kempsey in Northern New South Wales (labelled 'B' in Figure 6.1).

We selected North Queensland as a study area because it is well known to be within the BTV transmission zone defined by the National Arbovirus Monitoring Program (NAMP) (National Arbovirus Monitoring Program 2015). Northern New South Wales was selected because of its location within the BTV transmission zone and its temperate climate with markedly different seasonal (spring-summer, autumn-winter) temperatures.

6.2.2 Climate model data

Climate change is defined as alteration in the pattern of weather with related changes in the physical characteristics of oceans, land surfaces and ice sheets, occurring over time scales of decades or longer. Climate is known to change in response to both natural and anthropogenic drivers (Clark et al. 2016).

Emissions of carbon dioxide (CO_2), methane (CH_4) and other greenhouse gases are the predominant anthropogenic drivers of climate change (Knutson et al. 2017). Atmospheric carbon emissions arising from human activities has increased by around 2.0 parts per million (ppm) per year since 2009 manly a result of industry (Raupach et al. 2007, Le Quéré et al. 2009). Climate change is caused by an imbalance between incoming and outgoing radiation in the atmosphere. As radiation from the sun enters the atmosphere some of it is absorbed by the earth's surface with the remainder re-emitted as infrared radiation. Re-emitted radiation is absorbed by greenhouse gases in a process that generates heat, with the amount of heat generated directly proportional to the amount of atmospheric greenhouse gas present. Because warmer air retains more moisture than cooler air, global warming alters the earth's hydrologic cycle so that while some areas experience more rainfall others experience drought and extreme weather events.

Previous climate change scenarios were developed using a process that accounted for factors that influence greenhouse gas emissions to atmospheric and climate processes. In a revised process emissions and socioeconomic scenarios (at the time of writing) are developed in parallel (called 'Representative Concentration Pathways', RCPs) which build on estimates of different assumptions about radiative forcing and how they change over time (Van Vuuren et al. 2011). As opposed to starting

with detailed storylines on emission generations which then lead to different climate change scenarios, the new process begins with a limited number of alternative trajectories of radiative forcing that are believed to be representative of the emissions scenario literature. These trajectories cover a range of resulting greenhouse gas concentrations that then lead to clearly distinguishable climate change scenarios.

Representative Concentration Pathways provide a wider range of future scenarios than the previous emissions scenarios and now specifically include the likely effect of greenhouse gas mitigation strategies. No scenario is deemed more likely than the other, however, some require major and rapid change to emissions to be achieved. There are four RCPs: RCP 2.6, RCP 4.5, RCP 6.0 and RCP 8.5 (with the numbers assigned to each RCP equal to the forcing target level for 2100). The radiative forcing estimates are built on the forcing of greenhouse gases and other forcing agents. RCP 2.6 is a very low forcing level requiring carbon dioxide emissions to start declining by 2020 and reaching zero by 2100. RCP 4.5 and RCP 6.0 are medium stabilisation scenarios and RCP 8.5 is a very high baseline emission scenario (Van Vuuren et al. 2011).

The future climate cannot be predicted on the basis of historical climate observations since it depends on future greenhouse gas emissions. Global climate models (GCMs) are generally regarded as the best tools for climate change projections (CSIRO and Bureau of Meteorology 2015). GCMs represent the atmosphere and bodies of water as a three dimensional grid, with a typical atmospheric resolution of around 200 km $\times$ 200 km and 20 to 50 levels in the vertical direction (CSIRO and Bureau of Meteorology 2015). Models are able to represent large-scale synoptic features of the atmosphere such as the development of high and low pressure systems and large-scale oceanic currents. Important physical processes occur at finer spatial scales including precipitation, cloud development and atmospheric and oceanic turbulence. The factors that influence these processes are included in 'parameterisations' of the models where their effects are accounted-for in approximate form on a coarser model grid. Parameterisations are typically the result of intensive theoretical and observational studies and represent an additional level of detail within the climate model itself.

Most climate projection models perform reasonably well and it is generally accepted that there is no single 'best' climate model or subset of models. The relatively coarse scale of the grid used by the global models limit their ability to represent some important regional and local scale features of climate though model resolution has improved over time. A technique known as down-scaling can be used to allow fine resolution regional models to be embedded within a global model.

Climate change models from the Coupled Model Inter Comparison Project Phase 5, CMIP5 (CSIRO and Bureau of Meteorology 2015) were selected as candidate models for this study. These provide improvements on previous climate models which included an increase in horizontal and vertical resolution of predictions, an improved representation of processes within the climate system (i.e. aerosol-cloud interactions) and use of a larger number of ensemble (i.e. model contributor) members.

For this study, we selected the 'worst' case RCP scenario in terms of temperature rise: CanESM2 model RCP 8.5. Daily average temperature data for the CanESM2 model RCP 8.5 scenario at a

resolution of 0.05 × 0.05 decimal degrees (approximately 5 km × 5 km) were provided by the Australian Climate Futures (ACF) decision-support tool (CSIRO and Bureau of Meteorology 2015). ACF provides Australian climate projection data for 14 future time periods (from 2025 to 2090 in 5-yearly increments) and four scenarios of greenhouse gas concentrations (RCP 2.6, RCP 4.5, RCP 6.0 and RCP 8.5) using the latest CMIP5 models (CSIRO and Bureau of Meteorology 2015).

Southern hemisphere summer (1 January) and winter (1 July) incursions of bluetongue were simulated for each of the two selected study areas (Figure 6.1). Simulations were run in two modes. The first was with direct (i.e. herd-to-herd, herd-to-saleyard and saleyard-to-herd) animal movements disabled; the second was with direct animal movements enabled with movement frequencies and distances by herd type the same as that used for the AADIS model of foot and mouth disease (Bradhurst et al. 2015). Our rationale for this approach was to provide a means to better understand the role of animal movement (as opposed to local spread) as a determinant of predicted outbreak size. In summary, a total of 24 outbreak simulations were run: mid-summer and mid-winter incursions for each study area for each year (2015, 2025 and 2035) with direct movements disabled and enabled for each. AADIS was run for 365 simulation days with 100 iterations used for direct movement disabled models and for the direct movement enabled models.

The results of each of the 24 simulated outbreaks are described in terms of the total number of herds predicted to become infected, the size of the outbreak area (as defined by contour lines delineating 95% of infected herd densities, across all iterations) and the within-herd incidence risk for herds in which outbreaks of bluetongue occurred. Counts of the predicted number of infected herds across scenarios were compared using a two-tailed Welch (unequal variance) *t* test.

6.3 Results

Minimum, mean and maximum daily temperatures for North Queensland and Northern New South Wales study areas are presented in Table 6.1 for 2015, 2025 and 2035, based on the CanESM2 model RCP 8.5 emission scenario. These data are presented as line plots in Figure 6.2. Climate projections show an increase in minimum, mean and maximum average daily temperature for 2025 and 2035, compared with 2015. Maximum daily temperatures are predicted to be 1.9 °C and 1.1 °C higher in 2025 and 2035 (respectively) in the North Queensland study area, compared with 2015. In Northern New South Wales, minimum daily temperatures for 2025 and 2035 are predicted to be 0.8 °C and 1.3 °C higher (respectively), compared with 2015.

Adult *Culicoides* spp. predicted densities are presented as line plots in Figure 6.3 for the North Queensland and Northern New South Wales study areas for 2015, 2025 and 2035, based on the CanESM2 model RCP 8.5 emission scenario. The predictions for 2015, 2025 and 2035 showed similar abundance and activity of *Culicoides* trend for each study area. Scenarios in North Queensland for 2025 and 2035 results showed relatively lower vector populations in winter compared with 2015. In Northern New South Wales, midges population predictions for 2025 and 2035 were higher and re-established quicker after winter than the predictions for 2015.

Descriptive statistics of the number of herds predicted to be bluetongue positive by AADIS after 365 days following incursions of BTV into single herds in North Queensland and Northern New South Wales in mid-summer (1 January) and mid-winter (1 July) with direct animals movements disabled for 2015, 2025 and 2035 are shown in Table 6.2. Numbers of infected herds for the animal movement enabled scenarios are shown in Table 6.3.

Maps of the North Queensland study area showing the point location of herds predicted to become bluetongue positive by AADIS following an incursion of BTV into a single herd in mid-summer (1 January) in 2015, 2025 and 2035 with direct animal movements disabled are shown in Figure 6.4. The same plots for the mid-winter North Queensland incursions are shown in Figure 6.5. Figures 6.6 and 6.7 show the same data for the Northern New South Wales study area. Box and whisker plots showing the distribution of the number of herds predicted to become bluetongue positive for the North Queensland and Northern New South Wales study areas, by season and year with direct animal movements disabled are shown in Figure 6.8.

Maps of Australia showing the point location of herds predicted to become bluetongue positive by AADIS following incursion of BTV into a single herd in North Queensland in mid-summer (1 January) in 2015, 2025 and 2035 with direct animal movements enabled are shown in Figure 6.9. The same plots for the mid-winter North Queensland incursions are shown in Figure 6.10. Similar to the direct movement disabled scenarios, in Figures 6.9 to 6.12 contour lines delineate areas where the predicted number of bluetongue positive herds was greater than 95 per square km. Figures 6.11 and 6.12 show the same data for the Northern New South Wales study area. Figure 6.13 are box and whisker plots showing the distribution of the number of herds predicted to become bluetongue positive for the North Queensland and Northern New South Wales study areas, by season and year with direct animal movements enabled.

For the North Queensland, direct animal movement disabled scenarios our predictions showed there was little change in the median predicted number of bluetongue positive herds for the mid-summer and mid-winter incursions (Table 6.2, Figure 6.4 and Figure 6.5) although the variability of predicted outbreak size for the 2035 incursions (summer: minimum 1, maximum 336; winter: minimum 1, maximum 249) was greater than the variability of predicted outbreak size for the 2015 incursions (summer: minimum 1, maximum 192; winter: minimum 1, maximum 27). For Northern New South Wales there were moderate increases in predicted outbreak size for the summer incursions with a median of 142, 274 and 288 bluetongue positive herds for 2015, 2025 and 2035, respectively. Similar to North Queensland, the variability of predicted outbreak size for the 2035 incursions (summer: minimum 139, maximum 465; winter: minimum 1, maximum 348) was greater than the variability of predicted outbreak size for the 2015 incursions (summer: minimum 60, maximum 242; winter: minimum 1, maximum 1).

For the predicted number of bluetongue positive herds for the direct movement enabled scenarios were (predictably) much higher than the predicted number of bluetongue positive herds for the direct movement disabled scenarios (Table 6.3). Compared with the direct animal movement disabled scenarios, there was a clear trend in the increase in the predicted number of bluetongue positive

herds as a function of simulation year for North Queensland (Figure 6.8). For Northern New South Wales this trend was not as marked, but as for the direct movement disabled scenarios, the predicted number of infected herds and the variability of predicted outbreak sizes for the 2035 incursions (summer: minimum 1096, maximum 12,017; winter: minimum 1, maximum 9156) was greater than the variability of predicted outbreak size for the 2015 incursions (summer: minimum 96, maximum 4218; winter: minimum 0, maximum 1). The predicted number of infected herds for the 2015 summer and 2035 summer incursions were significantly different (Welch t test statistic: -9.49; df 54.42; $P < 0.001$). The predicted number of infected herds for the 2015 winter and 2035 winter incursions were significantly different (Welch t test statistic: -3.31; df 99; $P < 0.001$).

Table 6.1: The effect of climate change on the spread of bluetongue in Australian livestock. Minimum, mean and maximum actual (2015) and predicted (2025 and 2035) average temperatures for the North Queensland and Northern New South Wales study areas described in the text. Numbers in brackets equal the change in temperature relative to 2015. Predicted temperatures are based on the CanESM2 model RCP 8.5 emission scenario.

Year	Average daily temperature (°C)		
	Minimum	Mean	Maximum
North Queensland:			
2015	14.8	23.2	28.9
2025	15.3 (+0.5)	24.1 (+0.9)	30.8 (+1.9)
2035	14.7 (-0.1)	23.9 (+0.7)	30.0 (+1.1)
Northern New South Wales:			
2015	8.6	18.2	27.4
2025	9.5 (+0.8)	19.4 (+1.2)	29.5 (+2.1)
2035	9.9 (+1.3)	19.3 (+1.0)	27.6 (+0.2)

Table 6.2: The effect of climate change on the spread of bluetongue in Australian livestock. Descriptive statistics of the number of herds predicted to be bluetongue positive by AADIS after 365 days following incursions of BTV into single herds in North Queensland and Northern New South Wales in mid-summer (1 January) and mid-winter (1 July) with direct animal movements disabled for 2015, 2025 and 2035. The 2025 and 2035 simulations are based on climate predictions from the CanESM2 model RCP 8.5 emission scenario.

Year	Season	*n*	Mean (SD)	Median (Q1, Q3)	Min, max
North Queensland:					
2015	Summer	100	14 (27)	8 (5, 15)	1, 192
2025	Summer	100	11 (18)	8 (5, 13)	1, 186
2035	Summer	100	12 (34)	8 (4, 13)	1, 336
2015	Winter	100	9 (7)	8 (6, 11)	1, 27
2025	Winter	100	9 (7)	8 (5, 13)	1, 59
2035	Winter	100	15 (33)	8(5, 13)	1, 249
Northern New South Wales:					
2015	Summer	100	142 (31)	138 (123, 159)	60, 242
2025	Summer	100	274 (74)	263 (228, 309)	124, 478
2035	Summer	100	288 (80)	267 (230, 338)	139, 465
2015	Winter	100	1 (0)	1 (1, 1)	1, 1
2025	Winter	100	4 (20)	1 (1, 1)	1, 162
2035	Winter	100	59 (99)	1 (1, 111)	1, 348

n: iterations
SD: standard deviation.
Q1: first quantile.
Q3: third quantile.

Table 6.3: The effect of climate change on the spread of bluetongue in Australian livestock. Descriptive statistics of the number of herds predicted to be bluetongue positive by AADIS after 365 days following incursions of BTV into single herds in North Queensland and Northern New South Wales in mid-summer (1 January) and mid-winter (1 July) with direct animal movements enabled for 2015, 2025 and 2035. The 2025 and 2035 simulations are based on climate predictions from the CanESM2 model RCP 8.5 emission scenario.

Year	Season	*n*	Mean (SD)	Median (Q1, Q3)	Min, max
North Queensland:					
2015	Summer	100	531 (796)	187 (15, 753)	1, 3860
2025	Summer	100	1062 (1435)	535 (109, 1246)	1, 5814
2035	Summer	100	1196 (1696)	592 (50, 1465)	1, 9035
2015	Winter	100	2005 (2792)	652 (75, 3434)	1, 10132
2025	Winter	100	2640 (1435)	594 (29, 4718)	1, 12342
2035	Winter	100	5098 (5468)	2268 (27, 10477)	1, 15982
Northern New South Wales:					
2015	Summer	100	1035 (922)	672 (469, 1279)	96, 4218
2025	Summer	100	2354 (1744)	1961 (955, 3121)	250, 7757
2035	Summer	100	4879 (2789)	4872 (2262, 6890)	1096, 12017
2015	Winter	100	0.05 (0.2)	0 (0, 1)	0, 1
2025	Winter	100	14 (103)	1 (1, 1)	1, 1013
2035	Winter	100	368 (1111)	1 (1, 2)	1, 9156

n: iterations
SD: standard deviation.
Q1: first quantile.
Q3: third quantile.

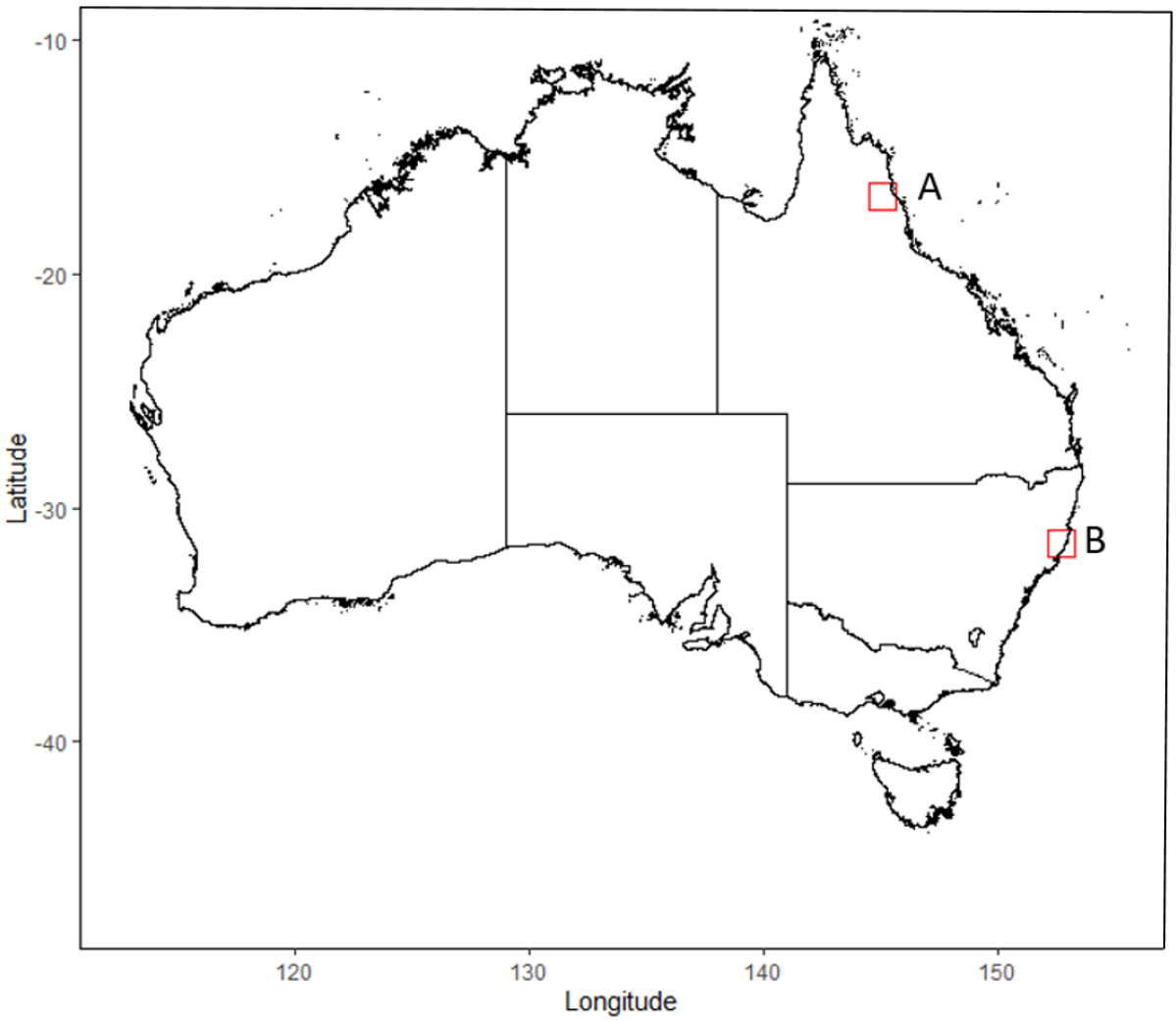


Figure 6.1: The effect of climate change on the spread of bluetongue in Australian livestock. Map of Australia showing the location of the study areas: (A) North Queensland, (B) Northern New South Wales.

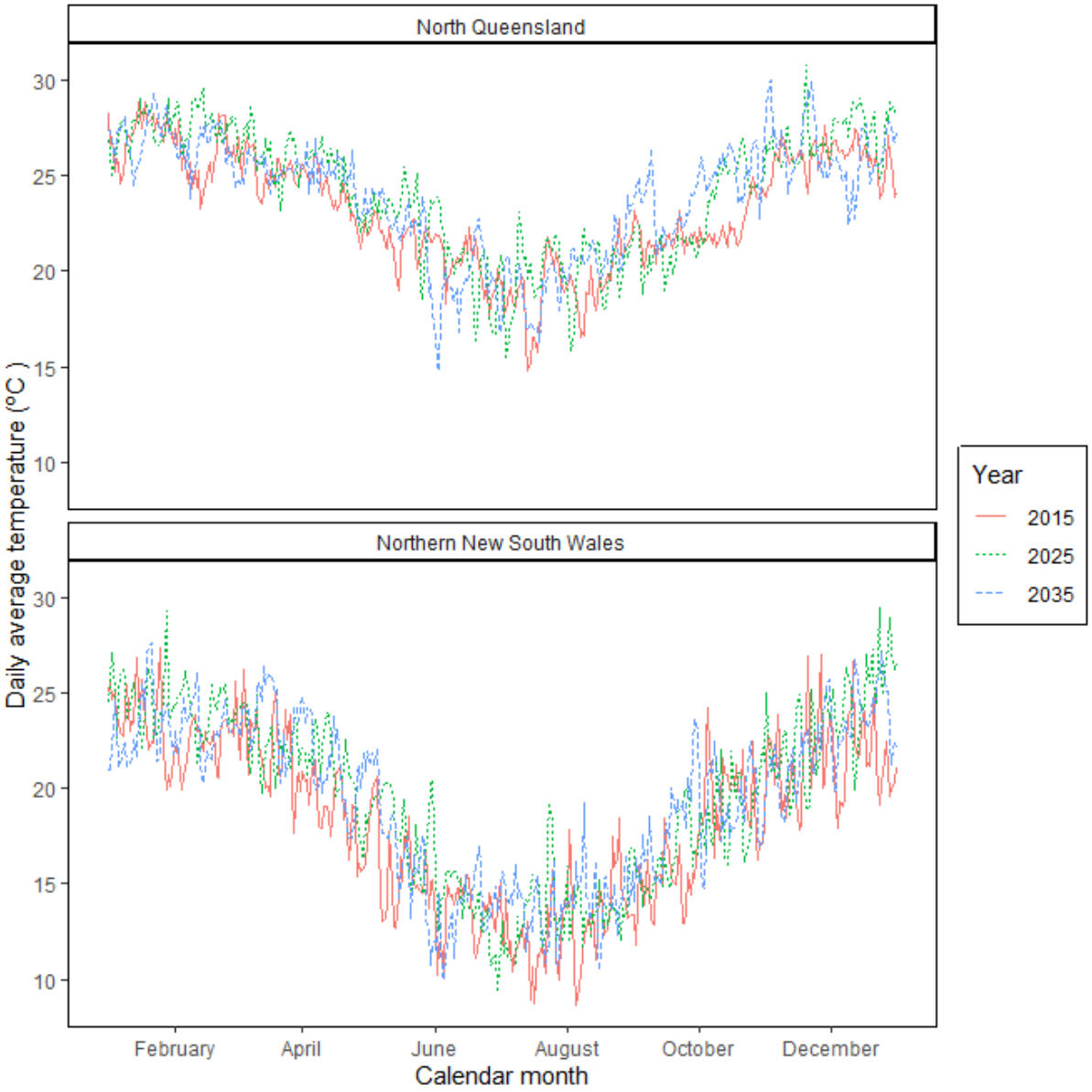


Figure 6.2: The effect of climate change on the spread of bluetongue in Australian livestock. Line plots showing average daily temperature as a function of day of the year for 2015, 2025 and 2035 for the North Queensland and Northern New South Wales study areas. The 2025 and 2035 scenarios are based on climate predictions from the CanESM2 model RCP 8.5 emission scenario.

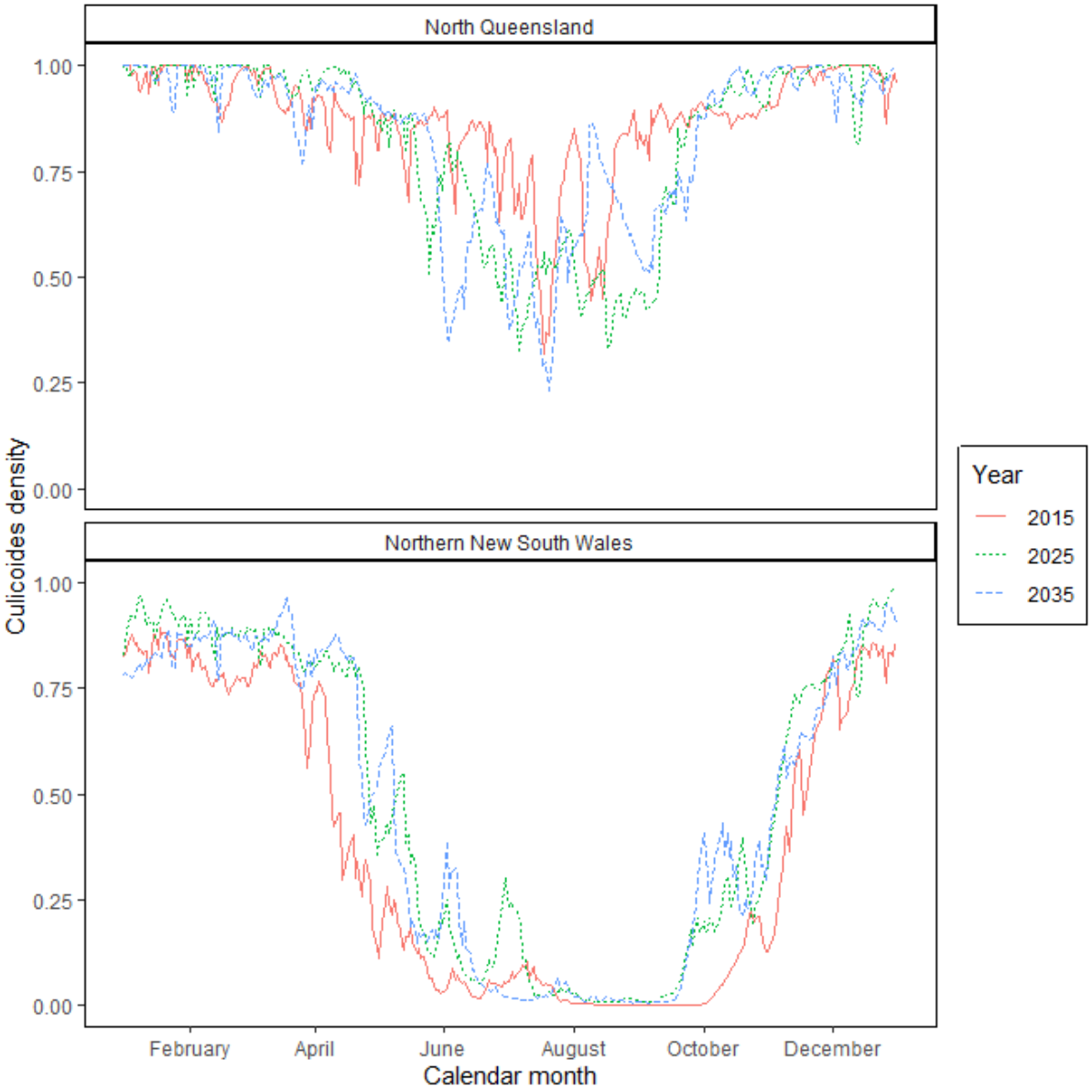
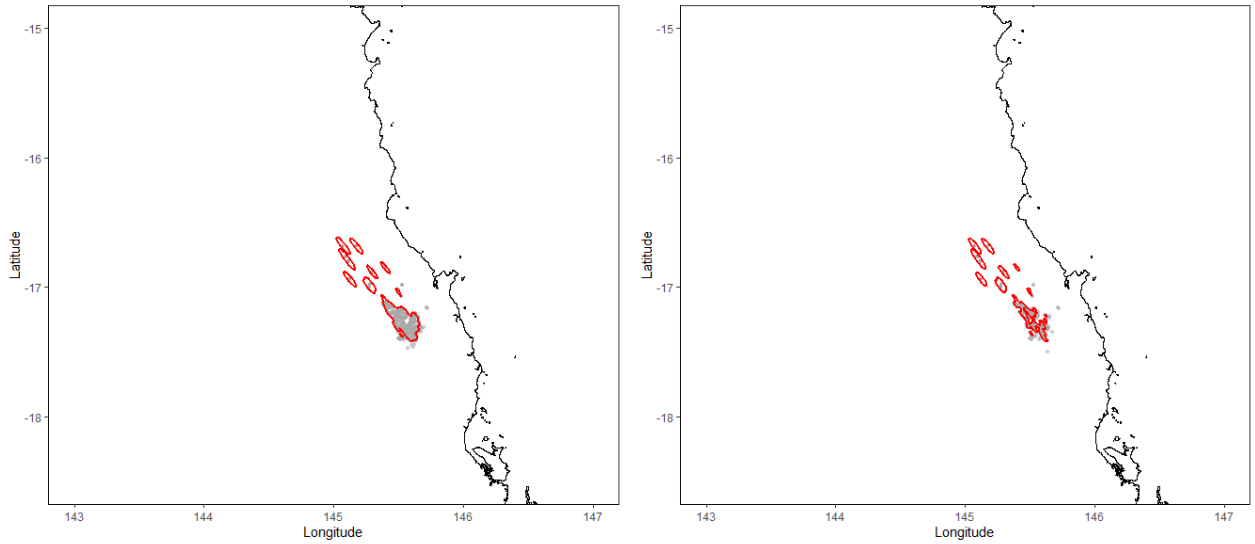
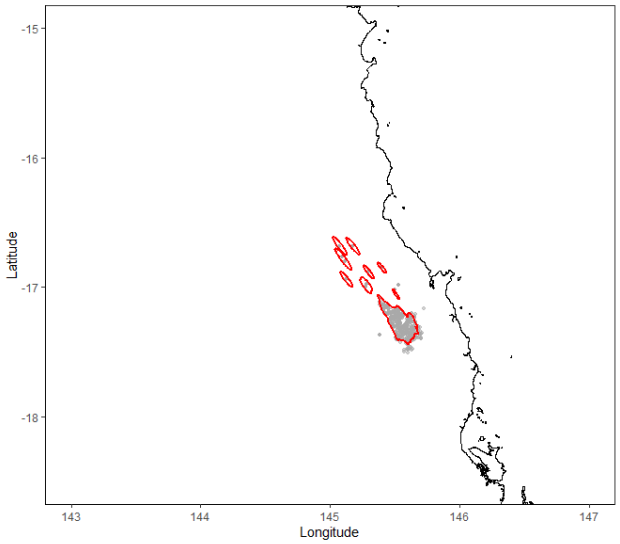


Figure 6.3: The effect of climate change on the spread of bluetongue in Australian livestock. Line plots showing average daily *Culicoides* spp. population density as a function of day of the year for 2015, 2025 and 2035 for the North Queensland and Northern New South Wales study areas. The 2025 and 2035 scenarios are based on climate predictions from the CanESM2 model RCP 8.5 emission scenario.



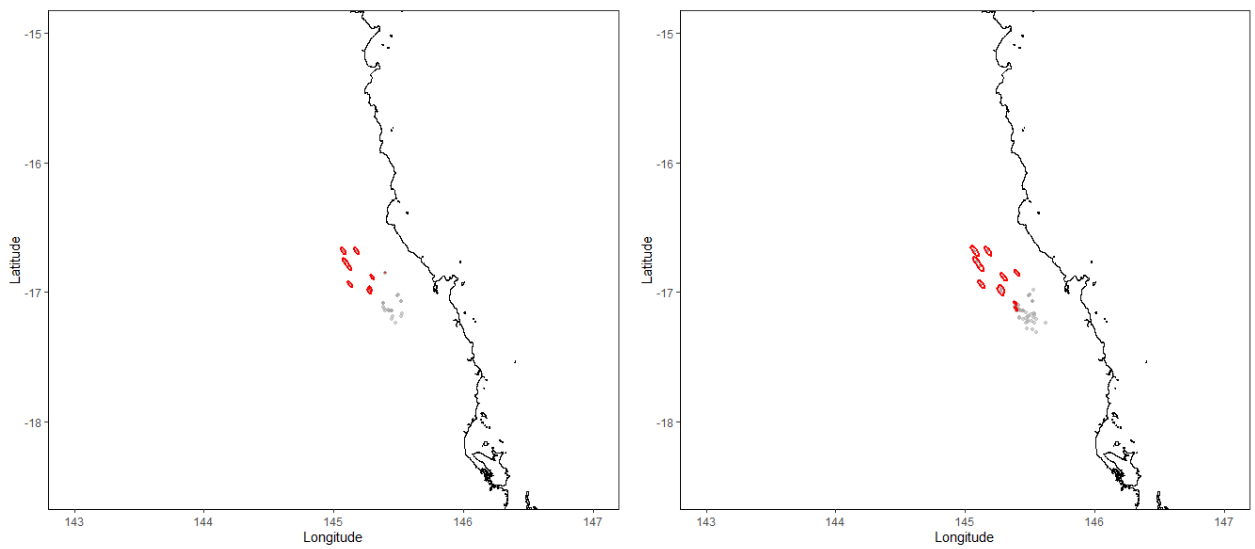
(a) 2015

(b) 2025



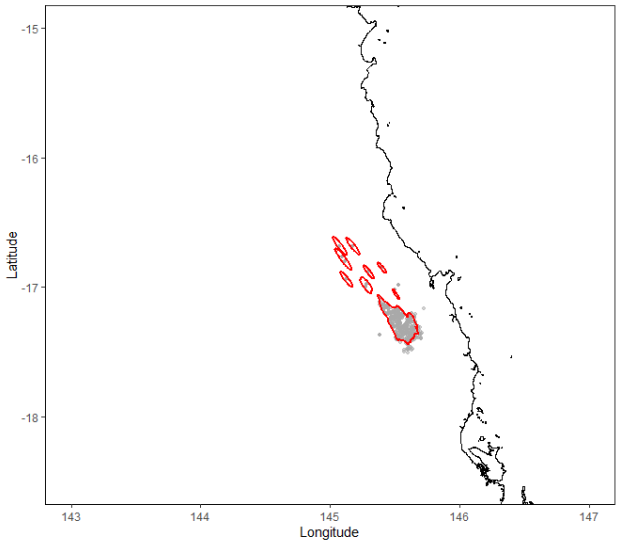
(c) 2035

Figure 6.4: The effect of climate change on the spread of bluetongue in Australian livestock. Map of **North Queensland** study area showing the point location of herds predicted to become bluetongue positive by AADIS following incursion of BTV into a single herd in **mid-summer (1 January)** with direct animals movements **disabled** for: (a) 2015; (b) 2025; and (c) 2035. Contour lines delineate areas where the predicted number of bluetongue positive herds was greater than 95 per square kilometre. The 2025 and 2035 simulations are based on climate predictions from the CanESM2 model RCP 8.5 emission scenario. Predictions are based on 100 simulations of the AADIS bluetongue model, as described in the text.



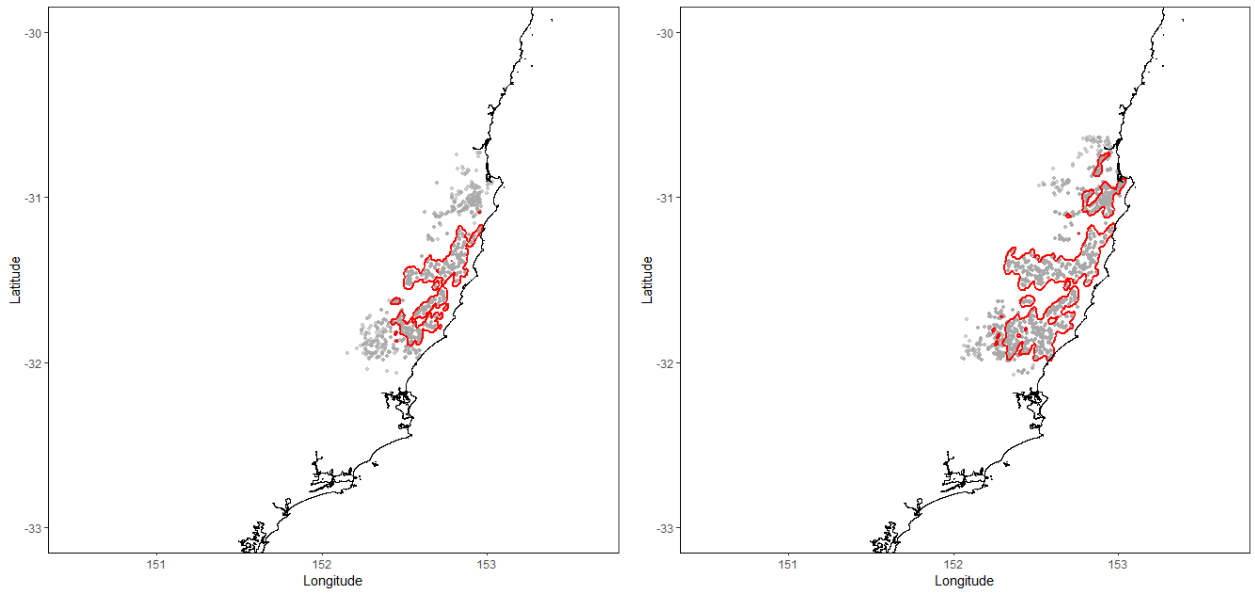
(a) 2015

(b) 2025



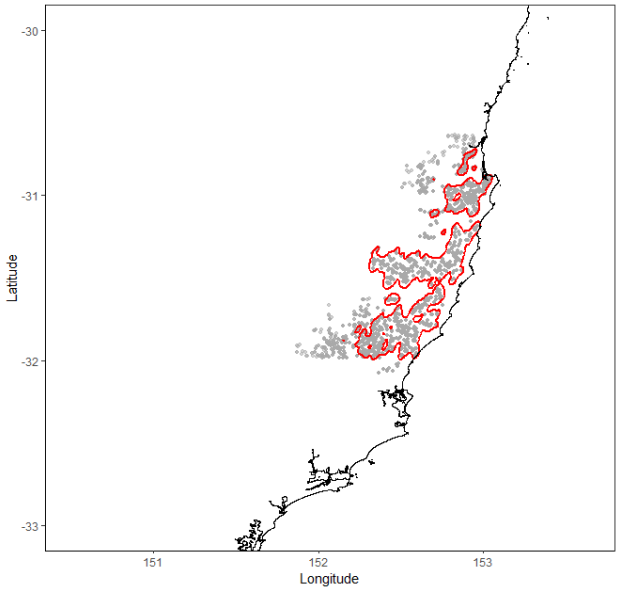
(c) 2035

Figure 6.5: The effect of climate change on the spread of bluetongue in Australian livestock. Map of **North Queensland** study area showing the point location of herds predicted to become bluetongue positive by AADIS following incursion of BTV into a single herd in **mid-winter (1 July)** with direct animals movements **disabled** for: (a) 2015; (b) 2025; and (c) 2035. Contour lines delineate areas where the predicted number of bluetongue positive herds was greater than 95 per square kilometre. The 2025 and 2035 simulations are based on climate predictions from the CanESM2 model RCP 8.5 emission scenario. Predictions are based on 100 simulations of the AADIS bluetongue model, as described in the text.



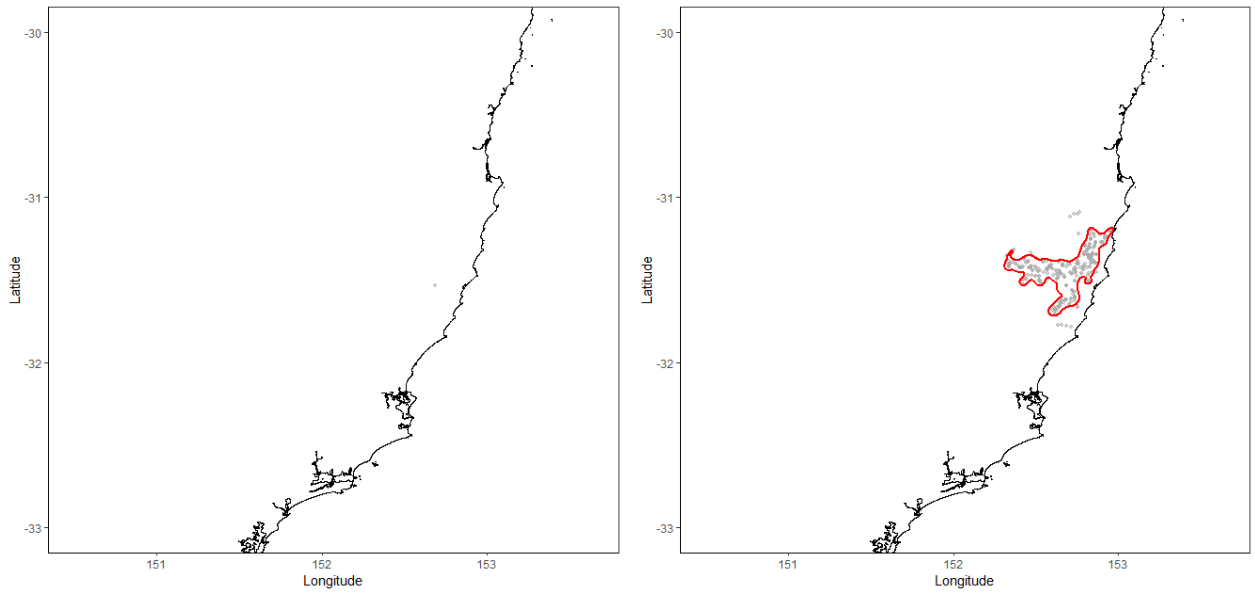
(a) 2015

(b) 2025



(c) 2035

Figure 6.6: The effect of climate change on the spread of bluetongue in Australian livestock. Map of the **Northern New South Wales** study area showing the point location of herds predicted to become bluetongue positive by AADIS following incursion of BTV into a single herd in **mid-summer (1 January)** with direct animals movements **disabled** for: (a) 2015; (b) 2025; and (c) 2035. Contour lines delineate areas where the predicted number of bluetongue positive herds was greater than 95 per square kilometre. The 2025 and 2035 simulations are based on climate predictions from the CanESM2 model RCP 8.5 emission scenario. Predictions are based on 100 simulations of the AADIS bluetongue model, as described in the text.



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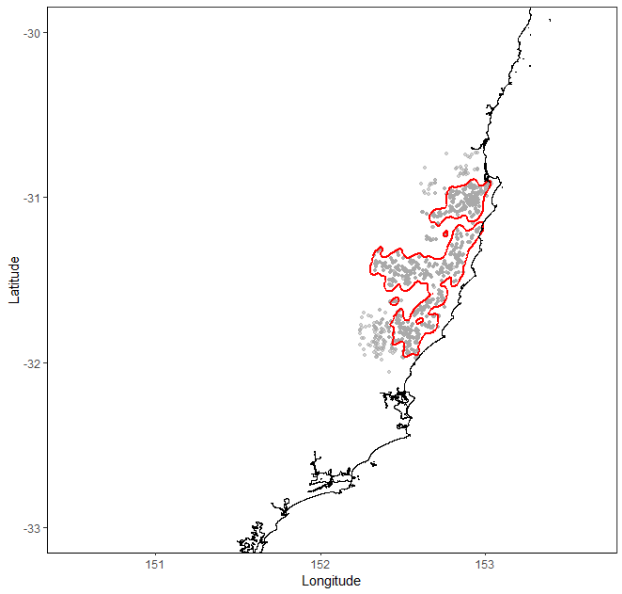

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Figure 6.7: The effect of climate change on the spread of bluetongue in Australian livestock. Map of the **Northern New South Wales** study area showing the point location of herds predicted to become bluetongue positive by AADIS following incursion of BTV into a single herd in **mid-winter (1 July)** with direct animals movements **disabled** for: (a) 2015; (b) 2025; and (c) 2035. Contour lines delineate areas where the predicted number of bluetongue positive herds was greater than 95 per square kilometre. The 2025 and 2035 simulations are based on climate predictions from the CanESM2 model RCP 8.5 emission scenario. Predictions are based on 100 simulations of the AADIS bluetongue model, as described in the text.

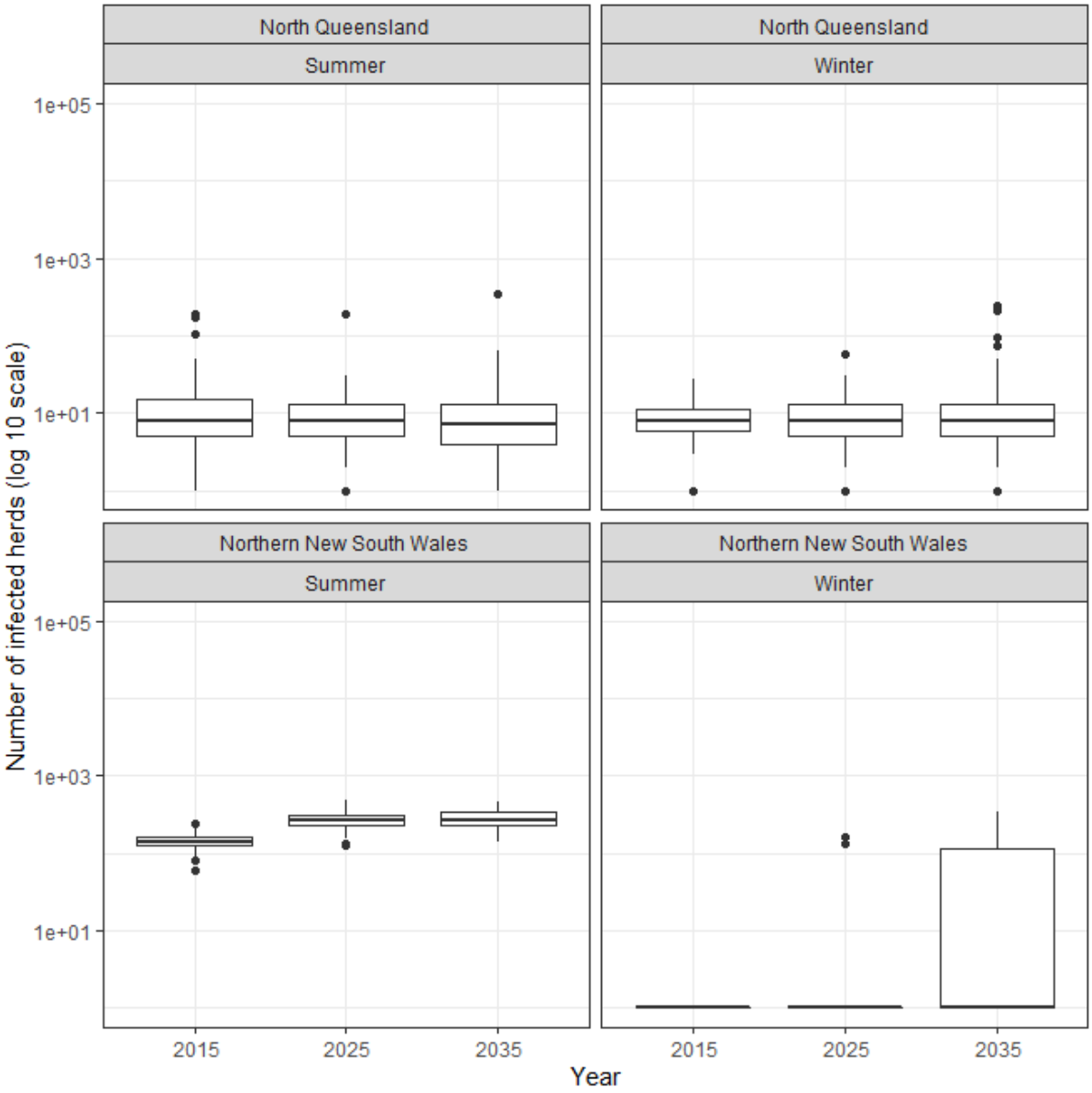
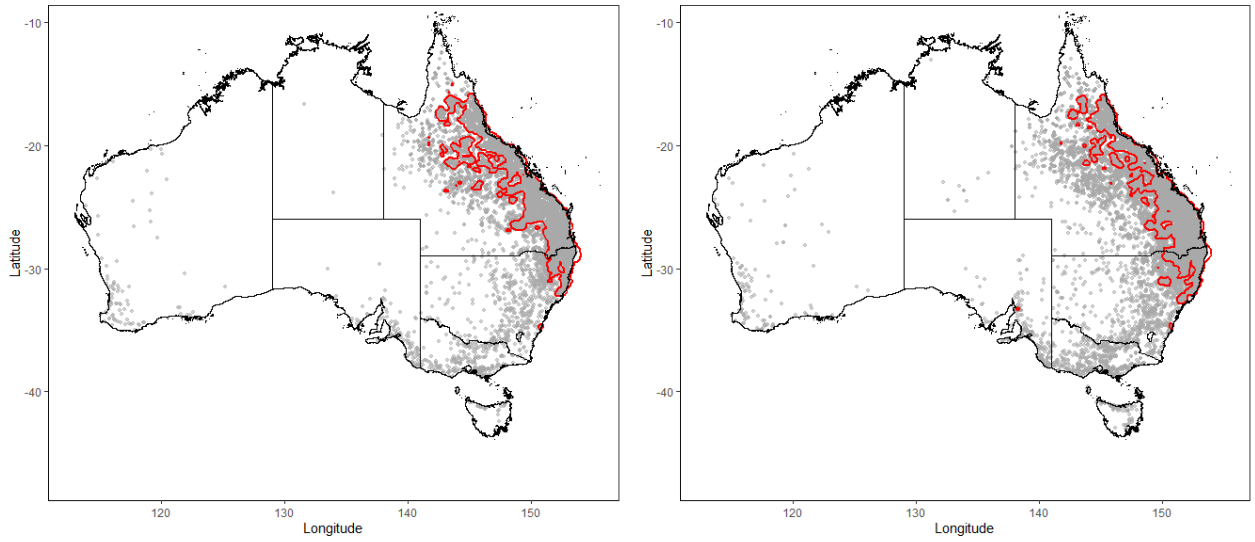


Figure 6.8: The effect of climate change on the spread of bluetongue in Australian livestock. Box and whisker plots showing the distribution of the number of herds predicted to become bluetongue positive by AADIS following incursion of BTV into single herds in North Queensland and Northern New South Wales in mid-summer (1 January) and mid-winter (1 July) with direct animals movements disabled for 2015, 2025 and 2035. The 2025 and 2035 simulations are based on climate predictions from the CanESM2 model RCP 8.5 emission scenario. Predictions are based on 100 simulations of the AADIS bluetongue model, as described in the text.



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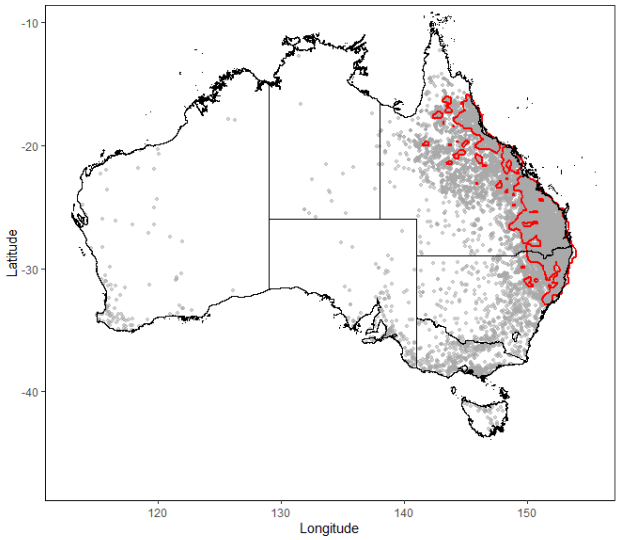

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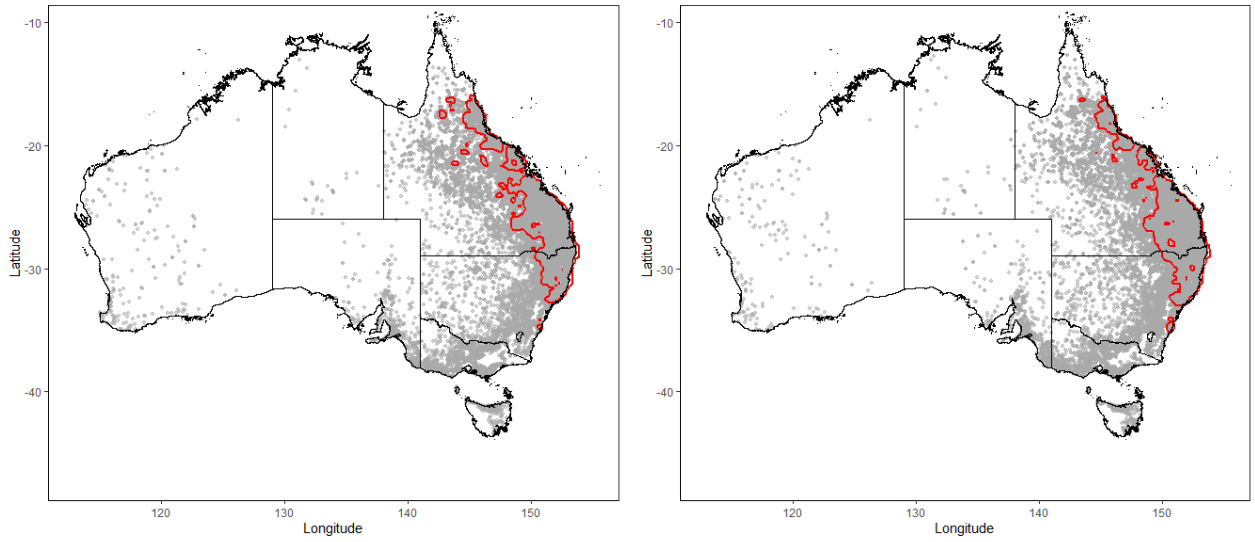
Figure 6.9: The effect of climate change on the spread of bluetongue in Australian livestock. Map of Australia showing the point location of herds predicted to become bluetongue positive by AADIS following incursion of BTV into a single herd in **North Queensland** in **mid-summer (1 January)** with direct animals movements **enabled** for: (a) 2015; (b) 2025; and (c) 2035. Contour lines delineate areas where the predicted number of bluetongue positive herds was greater than 95 per square kilometre. The 2025 and 2035 simulations are based on climate predictions from the CanESM2 model RCP 8.5 emission scenario. Predictions are based on 50 simulations of the AADIS bluetongue model, as described in the text.



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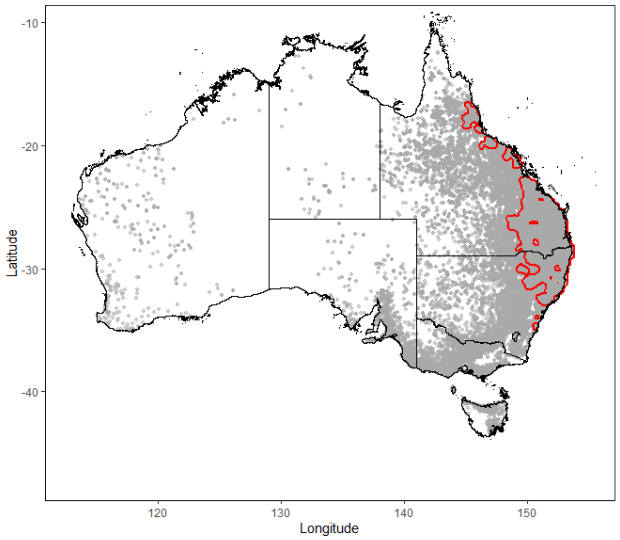

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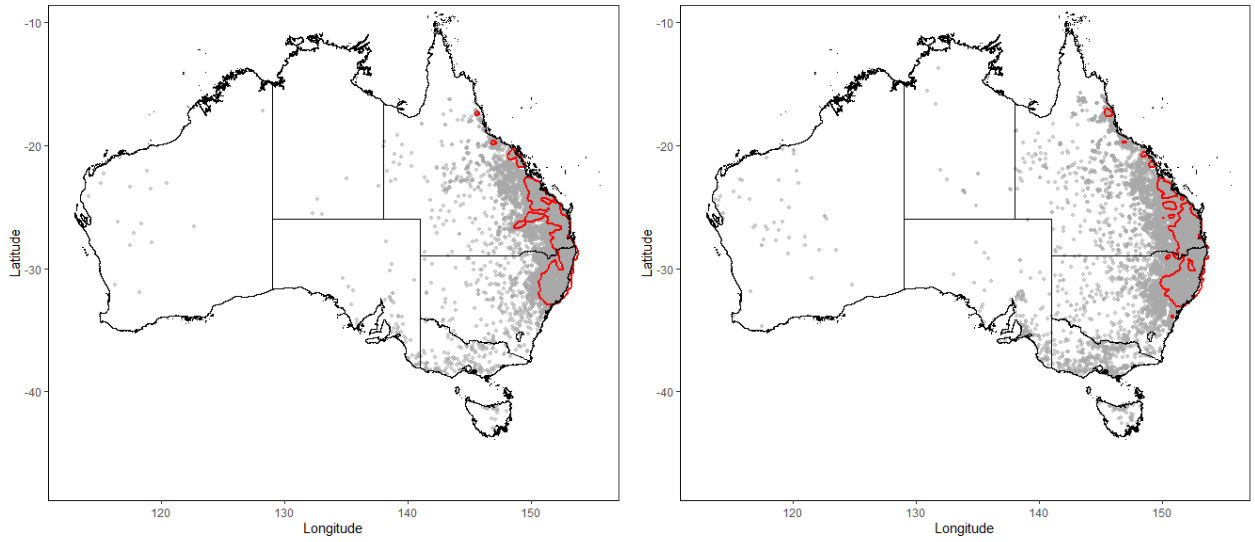
Figure 6.10: The effect of climate change on the spread of bluetongue in Australian livestock. Map of Australia showing the point location of herds predicted to become bluetongue positive by AADIS following incursion of BTV into a single herd in **North Queensland** in **mid-winter (1 July)** with direct animals movements **enabled** for: (a) 2015; (b) 2025; and (c) 2035. Contour lines delineate areas where the predicted number of bluetongue positive herds was greater than 95 per square kilometre. The 2025 and 2035 simulations are based on climate predictions from the CanESM2 model RCP 8.5 emission scenario. Predictions are based on 50 simulations of the AADIS bluetongue model, as described in the text.



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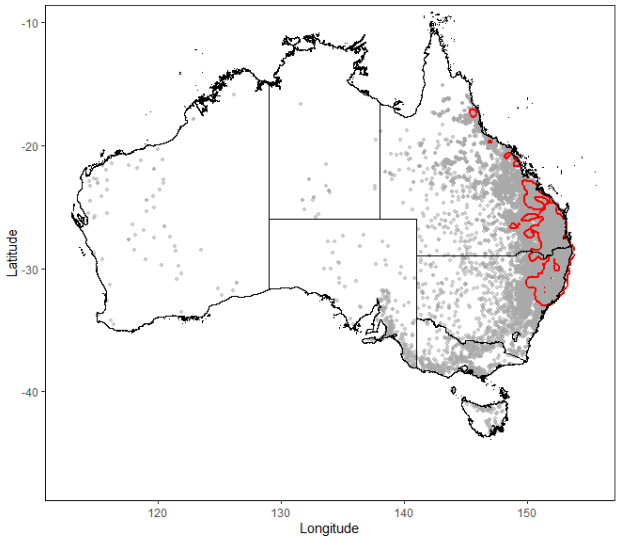

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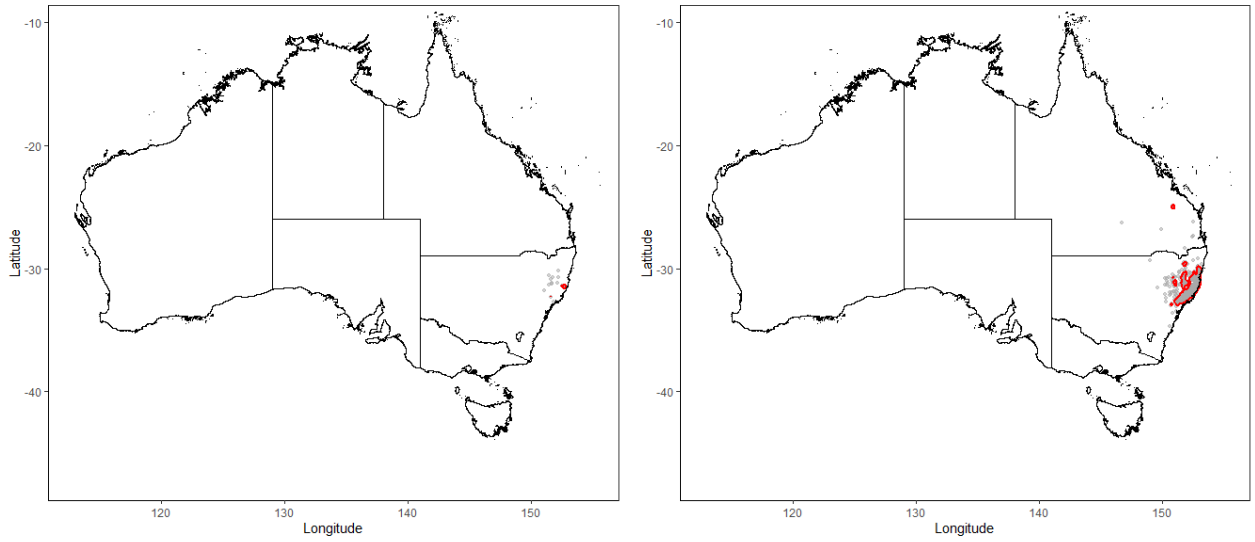
Figure 6.11: The effect of climate change on the spread of bluetongue in Australian livestock. Map of Australia showing the point location of herds predicted to become bluetongue positive by AADIS following incursion of BTV into a single herd in the **Northern New South Wales** in **mid-summer (1 January)** with direct animals movements **enabled** for: (a) 2015; (b) 2025; and (c) 2035. Contour lines delineate areas where the predicted number of bluetongue positive herds was greater than 95 per square kilometre. The 2025 and 2035 simulations are based on climate predictions from the CanESM2 model RCP 8.5 emission scenario. Predictions are based on 50 simulations of the AADIS bluetongue model, as described in the text.



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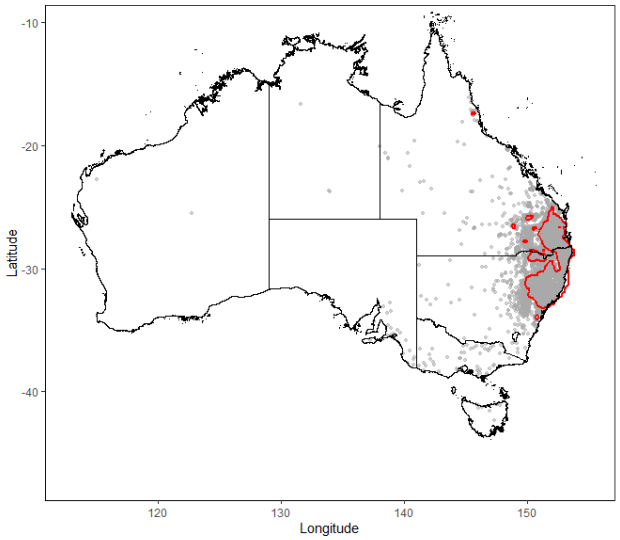

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Figure 6.12: The effect of climate change on the spread of bluetongue in Australian livestock. Map of Australia showing the point location of herds predicted to become bluetongue positive by AADIS following incursion of BTV into a single herd in the **Northern New South Wales** in **mid-winter (1 July)** with direct animals movements **enabled** for: (a) 2015; (b) 2025; and (c) 2035. Contour lines delineate areas where the predicted number of bluetongue positive herds was greater than 95 per square kilometre. The 2025 and 2035 simulations are based on climate predictions from the CanESM2 model RCP 8.5 emission scenario. Predictions are based on 50 simulations of the AADIS bluetongue model, as described in the text.

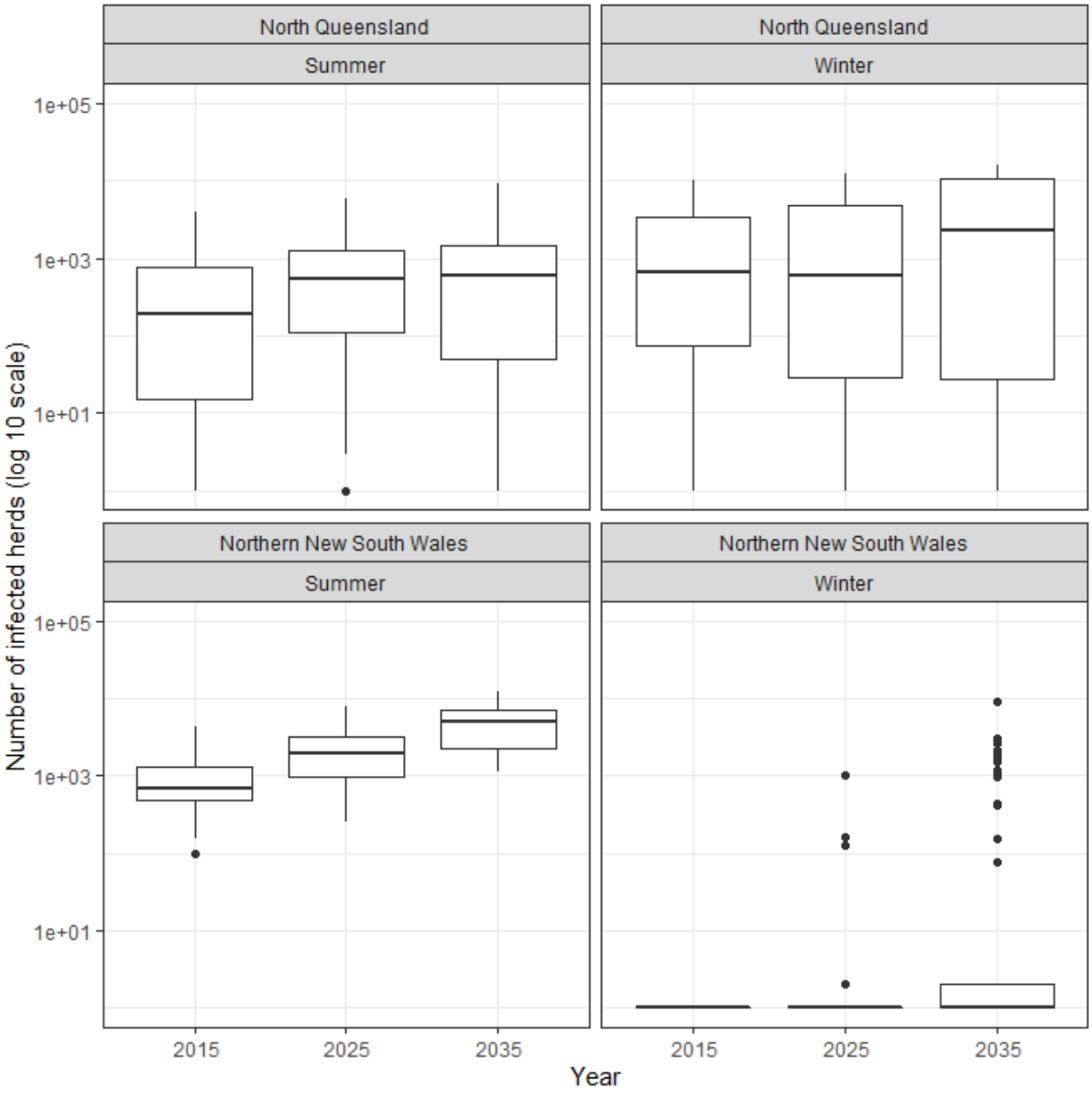

Figure 6.13: The effect of climate change on the spread of bluetongue in Australian livestock. Box and whisker plots showing the distribution of the number of herds predicted to become bluetongue positive by AADIS following incursion of BTV into single herds in North Queensland and Northern New South Wales in mid-summer (1 January) and mid-winter (1 July) with direct animals movements enabled for 2015, 2025 and 2035. The 2025 and 2035 simulations are based on climate predictions from the CanESM2 model RCP 8.5 emission scenario. Predictions are based on 50 simulations of the AADIS bluetongue model, as described in the text.

6.4 Discussion

The aim of this study was investigate the effect of climate change on BTV spread in Australia. Estimates of the geographic distribution of *Culicoides* spp. across Australia (Chapter 3) were combined with a model of bluetongue transmission (Chapter 4) which was then implemented within an existing model of infectious animal disease (AADIS).

Assuming the worst case scenario for greenhouse gas emission (RCP 8.5) our key findings were that, compared with incursions seeded into North Queensland and Northern New South Wales in 2015 and in the absence of direct animal movements, there were only modest increases in the predicted number of infected herds for incursions into the same herd that occurred in 2025 and 2035 (Table 6.2). For the winter incursions in Northern New South Wales in 2025 and 2035 there were substantial numbers of bluetongue positive herds, compared with winter incursions that occurred in 2015. This could be related to the higher abundance and quicker seasonal recovery of *Culicoides* spp. driven by climate change (Figure 6.3).

AADIS allowed us to develop a better understanding of the role of direct animal movements as a determinant of outbreak size (compare the predicted number of infected herds in Table 6.2 with the predicted number of infected herds in Table 6.3). Importantly, the variability in the predicted size of bluetongue outbreaks was greater for the 2025 and 2035 incursions, compared with 2015. When direct animal movements were enabled, there was a substantial increase in the number of infected herds for the 2025 and 2035 incursions, compared with 2015, with greater numbers of infected herds when incursions occurred during the winter (see Table 6.3 and Table 6.2). The most likely reason for this is that in North Queensland off-farm movement events are more frequent during the winter and early spring (May to November) period (Iglesias & East 2015). Seeding of viraemic cattle into areas with a competent insect vector population (particularly in herd dense areas) meant that a new host-vector-host cycle of transmission could be established, further increasing infected herd numbers (Figures 6.9 to 6.12).

Previous European studies using climate-based ecological niche or $R_0(T)$ models identified an increase in bluetongue risk over time (Samy & Peterson 2016, Brand & Keeling 2017) and a marked increase in herd level bluetongue incidence risk in 2006, consistent with the onset of the European BTV serotype 8 outbreak (Guis et al. 2012). Although $R_0(T)$ models provide useful estimation of bluetongue transmission potential (with values of $R_0(T) > 1$ indicative of sustained virus transmission) such models are unable to predict which herds will become infected during an outbreak or which combination of disease control measures will be successful.

Climate change is expected to have a marked effect on the geographic distribution of the insect vector for bluetongue in Australia, *Culicoides* spp., given a temperature range of 13.5 °C to 35 °C is compatible with *Culicoides* survival (Bishop et al. 2015) and it is expected that with climate change a greater proportion of the land area of the country will have temperature conditions that satisfy this criteria for longer periods of the year. Furthermore, the tendency for *Culicoides* spp. midges to feed on mammalian hosts increases as a function of temperature, as does the length of time taken for *Culicoides*

midges to become infectious once they have been exposed to BTV (Wittmann & Baylis 2000, Baylis et al. 2017). However, an increase in the number of extreme temperature days during the warmer months of the year may actually lead to decreased vector abundance by increasing the probability of exceeding the optimal temperature range for growth and development, and thereby decreasing survival probabilities (Bishop et al. 2015).

Environmental temperature is not the only factor that determines the changing risk of BTV outbreaks but the emergence of bluetongue in Europe supports the conjecture that climate change was a contributory factor (Baylis et al. 2017). Modelling studies show that in recent decades Europe's warming has allowed *C. imicola* to extend beyond its established geographic range (Acevedo et al. 2010). This conclusion was supported by our study where the size of the summer and winter outbreaks that occurred in Northern New South Wales were greater for the 2025 and 2035 incursions, compared with 2015. In a study of the effect of climate change on the global distribution of bluetongue Samy & Peterson (2016) predicted a marked increase in the geographic distribution of bluetongue for RCP 8.5 compared with RCP 2.6. Increases in vector abundance does not necessarily lead to increases in the size of predicted bluetongue outbreaks but instead depends on an interaction between herd and animal density, vector abundance and animal movement frequencies.

An additional factor to consider is that climate change is more than likely to result in a change in the geographic distribution of the domestic livestock population at risk. In brief, it is conceivable that areas of the country with high densities of livestock may not be high dense areas in the future because of a change in environmental conditions leading to outcomes such as an impaired ability to produce high quality pasture throughout the year. This possibility needs to be considered when interpreting the results of this study. On balance, it is our assessment that the change in the geographic distribution of the livestock population over time is likely to be relatively small compared with the more widespread effect of climate change. Continued collection of livestock census data and using contemporary livestock census data to inform models of the type presented in this chapter are advised.

The finding that home-bred, bluetongue-exposed cattle were detected in Echuca, Victoria in 2017 (Department of Agriculture, Water and the Environment 2020) provides indirect empirical (albeit indirect) support of the findings presented in this study. Under the effect of climate change and in the event of an incursion of virulent bluetongue in Australia, early detection and rapid imposition of effective restrictions on animal movement provide the best opportunity for rapid disease control. The data presented in this study permits a somewhat more refined assessment of how climate change may alter bluetongue risk in Australia and allows bluetongue surveillance and bluetongue incursion response planning in the coming years to be adapted accordingly.

Chapter 7

General discussion

The overall aim of the work presented in this dissertation has been to provide a means for estimating the transmission of bluetongue among cattle herds in Australia and to implement the proposed approach within the animal disease decision support tool, AADIS. In this chapter, the major findings of each of the studies presented in this thesis are briefly summarised and commentary is provided on key aspects of the methodological approaches developed during the course of this work. Recommendations are then provided for future research including how the techniques developed in this thesis might be adapted for other vector-borne diseases.

7.1 A model of the spatial distribution of a *Culicoides*-like midge

In Chapter 3 a model was developed to allow the spatial and temporal distribution of *Culicoides* spp. across Australia to be described. The model of *Culicoides* spp. population growth in response to ambient temperature was adapted from Kelso & Milne (2014) and we extended this work by using the Hybrid Single Particle Lagrangian Integrated Trajectory Model (HYSPLIT) to estimate dispersal of *Culicoides* spp. to capture the effect of 'windborne' dispersal of midges from populated source sites. A second novel feature of this chapter was that we compared the spatial and temporal distribution of our *Culicoides* spp. predictions with data collected over 24 years by the National Arbovirus Monitoring Program. Comparisons of our predictions of *Culicoides* spp. with empirical data collected by NAMP showed good agreement in endemic areas and poorer agreement at more southern latitudes of the country (Figure 3.4). A profitable area of future research would be adjustment of the model to allow the input parameters to vary according to latitude.

By design, the distribution of *Culicoides* spp. in the model was dependent on temperature, wind speed and the presence of cattle. A raster-based approach was used with each cell of the raster given a binary classification of being either suitable/eligible or unsuitable for midge flight activities. For development and prototyping of the model a raster grid cell of size 10 km $\times$ 10 km was used which meant that inference from the model were only appropriate at broader geographic scales — either the state or national level. A more refined approach would be to capture variation in cattle density at a

finer spatial scale (using, for example, a raster grid cell size of 1 km $\times$ 1 km) which would then allow inferences to be made at more localised (e.g. local government area) levels.

7.2 A model of bluetongue transmission

The outcome of Chapter 4 was a model of bluetongue disease spread that could be used to simulate the geographic distribution of vector-borne disease among domestic livestock. Here the incidence and prevalence of bluetongue was highly dependent on the distribution and abundance of *Culicoides* spp. Also, the geographic extent of bluetongue outbreaks was smaller when the local flight distance of *Culicoides* spp. was small and herd density was low. It is important to clarify that these findings are conditional on temperature that influences biting rate, the survival rate of midges and the extrinsic incubation rate. At the time of writing there have been no outbreaks of clinical bluetongue in cattle in Australia so, for this reason, parameter estimates from overseas studies had to be used. It is proposed that as part of response planning details should be provided on what information needs to be collected during an outbreak to allow credible estimates of bluetongue transmission model parameters.

A novel approach applied in Chapter 4 was that we used the simulated midge population from Chapter 3 to be used as the source population of insect vectors for the bluetongue disease spread model. A second novel approach was the separation of host and vector populations into two 'layers' of different spatial format: a raster layer for the insect vector population and a spatial vector layer (i.e. points) to represent the cattle herd population at risk. This approach allows our model to be readily adapted for other insect vector-borne diseases where the precise geographic location of a disease reservoir cannot be defined at the point location level, for example mosquitoes in the case of Rift Valley fever. This approach would also be suitable for diseases with a wildlife reservoir such as wild boar in the case of African swine fever. In this situation the raster layer providing estimates of the distribution of insect vectors would be replaced with a raster layer providing estimates of the geographic distribution of the wildlife vector, which (in the case of wild boar) will vary on a seasonal basis.

7.3 Simulation of the spread of bluetongue

The Australian Animal Disease Simulation model has been designed to be adaptable and flexible (Bradhurst et al. 2015) and this flexibility was exploited in Chapters 5 and 6. Here, a variation of the model of *Culicoides* spp. distribution (Chapter 3) and the model of bluetongue transmission (Chapter 4) was deployed within AADIS, taking advantage of AADIS's existing architecture to account for the geographic distribution of the herd population at risk and direct and indirect movements between herds. The methodological sequence used in Chapters 4 and 5 — development and prototyping of a model using a flexible programming environment (R Core Team 2020) and then passing the refined prototype over for deployment within a memory-optimised model with existing capability to handle factors that will influence the distribution of disease (e.g. animal movement) and how disease is controlled

(e.g. movement restrictions, vaccination and/or depopulation) provides an excellent precedent for the approach to be used for animal health model development. The process of prototyping allows a working model to be developed and refined, in consultation with subject-matter experts. Once a working prototype has been developed the pseudo code (as shown in Appendix B) provides an unambiguous description of the methodology that is able to be re-engineered for use within a memory optimised, national scale model such as AADIS (Garner & Hamilton 2011).

Chapter 6 provides an example of how the preparatory work presented in Chapters 3, 4 and 5 can be drawn together to support real-world animal health decision making in the face of an outbreak that requires rapid, national level decisions to be made. In Chapter 6 the AADIS bluetongue model was re-parameterised using climate change temperature estimates provided by CSIRO (2020).

In Chapter 6 for the climate change scenarios the geographic extent of bluetongue outbreaks in the area immediately surrounding the site of incursion were substantially different from those estimated under the non-climate change scenario. An important finding was bluetongue being able to establish itself in previously non-endemic areas after being seeded into those areas following the incoming movement of infectious cattle. Under conditions of climate change *Culicoides* spp. were more widely distributed across the country and, in some areas, were able to survive over the winter leading to further outbreaks.

As a result of climate change, the presence of continued animal movement following an incursion substantially increased the number of infected herds. With the climate change scenarios it was found that infected animals moving into BTV free areas where *Culicoides* spp. were present substantially increased the risk of outbreaks in these areas. These findings have important implications for animal health policy: in the event of an incursion of bluetongue into Australia the single most important control measure is to rapidly restrict the movement of cattle out of affected areas in order to prevent establishment of disease elsewhere. This recommendation becomes even more important under climate change scenarios because the extent of the country with suitable habitat for *Culicoides* spp. will be substantially greater than what it is today.

7.4 Modelling to support decision making in animal health

Epidemiological models in animal health are commonly used as decision-support tools to understand the impact of various control measures on disease spread in susceptible populations. Animal disease models (like any model) are based on various assumptions and decision making (guided by disease model outputs) can be improved if policy makers: (1) are aware of these assumptions and the quality of the data used for model parameterisation; and (2) have a good understanding of how sensitive model outputs are to changes in model inputs and assumptions.

The spread of disease in a closed, homogeneous population is concisely captured by equation-based models (Keeling & Rohani 2011). In order to incorporate the effect of an uneven geographic distribution of an animal population at risk, social factors and jurisdictional differences in the way diseases are controlled and eradicated in addition to the effect of chance (stochasticity), individual-

based modelling approaches are necessary, such as agent-based models (Bradhurst et al. 2015). In animal health examples of individual-based models include AusSpread (Garner & Beckett 2005), InterSpread Plus (Stevenson et al. 2013), NAADSM (Harvey et al. 2007) and AADIS (Bradhurst et al. 2015). While each of these models have been designed to account for the complexities that come into play with animal health decision making, this flexibility has a downside effect in that it makes model parameterisation a complex and data intensive task which in turn reduces the ability of the modeller to succinctly communicate the subtle features of model parameterisation to decision makers.

The only solution to this problem is to ensure (as always) disease models are developed well in advance of the time that they are needed (Keeling et al. 2001, Green & Medley 2002, Taylor 2003) and decision makers are made fully aware of model assumptions, how models can be used to support policy and decision-making and appropriate interpretation of model results. Since the 2001 outbreak of foot and mouth disease in the United Kingdom (Gibbens et al. 2001), the veterinary epidemiological community has done a great deal of work on the preparation of models in advance (the body of work presented in this thesis represents an example of this process in operation). A current gap relates to fine-tuning how modelling results are used by animal health decision makers. This is of immense importance for the example of bluetongue presented in this thesis which essentially represents a combination of four distinct models: (1) the *Culicoides* distribution model, Chapter 3; (2) the model of BTV transmission between insect vectors and animal hosts, Chapter 4; (3) AADIS, Chapter 5; and (4) climate change, Chapter 6.

The incidence of bluetongue is highly dependent on the geographic distribution of *Culicoides* spp. and their abundance. The five species of *Culicoides* in Australia that are capable of transmitting BTVs are: *C. actoni*, *C. brevitarsis*, *C. fulvus*, *C. brevipalpis* and *C. wadai* (Muller 1985, Standfast et al. 1978, 1985). Apart from *C. brevitarsis* relatively little specific detail is known about the breeding habitats of other *Culicoides* vectors in the Australasian region. For this reason we have taken care not to label our vector distribution model as a *Culicoides brevitarsis* model, but instead a *Culicoides* spp. model with the assumption that the model provides estimates of the distribution of a *Culicoides brevitarisis*-like midge. An important point to be made is that any vector distribution model could have been used and entered into AADIS, if data were available.

This approach has been intentional because it provides the opportunity for subject-matter experts (e.g. entomologists) to contribute information from their specific area of expertise into a wider animal health modelling framework. In turn this encourages a more collaborative approach to animal disease modelling and facilitates a greater level of 'buy in' of modelling of this type by the wider scientific community (Taylor 2003). This support is of critical importance, particularly if disease outbreak management strategies (developed using simulation models) do not align with the business interests of some industry stakeholders. In this situation it would be common for negatively affected groups to seek the opinion of peripheral experts who are often likely to discredit the model if: (1) they are not familiar with it; or (2) they have not played a role in its development. A solution to this problem is to draw in the expertise of a wide range of scientific disciplines when developing a model with the idea that a model that has received input from multiple disciplines is more likely to withstand intense

stakeholder scrutiny.

The issue of the level of spatial inference of model results deserves specific comment. Given the size of Australia, the size of the raster cell layers used for prototyping (10 km $\times$ 10 km) provided sufficient spatial detail to support decision making at the national level. Perhaps more importantly, the relatively large raster grid cell size meant that AADIS simulations could run relatively quickly, allowing alternative disease spread scenarios to be rapidly assessed. In the future, it is likely that each of the animal health jurisdictions in Australia will want to use the AADIS bluetongue model to support local decision making. A important area for future investigation would be to define the process of how (exactly) to best increase the spatial granularity of *Culicoides* insect vector layer, which would then allow models to be developed to support appropriate tactical decision making at (for example) the local government area level, in contrast to more strategic policy decision-making by regional and federal agencies.

Climate projection down-scaling whereby coarse-resolution global climate model outputs are translated into finer spatial resolution climate outputs (CSIRO 2020) are likely to be important for modelling bluetongue spread at local spatial scales. According to CSIRO (2020), statistical and dynamic down-scaling has the most potential to reveal regional detail in climate change signals due to local features such as complex topography or coastlines. A profitable area of future research would be to determine the best way to deploy down-scale climate projection data into AADIS to allow it to be used for tactical, local-level decision making.

One of the limitations of the approach used for this modelling exercise is that the locations of groups of susceptible animals ('herds') are represented as points defined by a set of longitude and latitude coordinates. While valid for livestock production on the east coast of Australia where individual herds are relatively close in space and the density of herds, while variable, is greater than zero in most areas, this approach presents inferential problems in the far north and west of Australia where the size of livestock holdings are very large. In the case of bluetongue transmission modelling (Chapter 4) the use of a 10 km $\times$ 10 km raster grid in these remote areas is questionable because the size of the grid is invariably substantially smaller than the area occupied by the underlying farms at risk. This means that herd-to-herd spread of disease does not occur. One approach for overcoming this problem (not entirely unique to bluetongue modelling) is to allow the point geolocation of herds in these areas to vary stochastically — perhaps within a defined 'home range' specific for each enterprise and proportional to the size of the geographic area for each enterprise.

The design of the bluetongue transmission model presented in this thesis has been informed by models of BTV spread developed in the United Kingdom (Gubbins et al. 2007) and Denmark (Szmaragd et al. 2009). As discussed earlier, the parameters for the bluetongue transmission model presented in Chapter 4 have been based on the cited European studies and there is a need to develop parameters appropriate for Australian conditions. Indeed, while this thesis provides an architecture for modelling the spread of vector-borne disease the ability to successfully apply this architecture to other diseases (e.g. African swine fever) relies on selection of appropriate model parameters which invariably requires collection and analysis of empirical data.

Throughout our model development an assumption has been made that cattle are the only susceptible hosts for bluetongue. The possibility of sheep as susceptible hosts needs to be considered given evidence of the spread of most BTV serotypes in susceptible sheep in Queensland and New South Wales (Johnson & Flanagan 1992). Some studies have shown that vectors are not found as often in stables than in surrounding fields (Baylis et al. 2010), whereas others show the opposite (Calvete et al. 2009), which could depend on the species of *Culicoides* (Meiswinkel et al. 2000). Animal stabling may also influence the abundance of midges, e.g. how manure is handled may affect breeding habitats.

The presence of the virus, susceptible hosts (both cattle and sheep) and competent vectors contributes to a relatively high probability that an outbreak of clinical bluetongue will occur in Australia at some time in the short to medium term future. Parameters from European bluetongue models can be used to inform Australian models prepared for outbreak planning and outbreak response policy development. On detection of a bluetongue outbreak in Australia collection of data relating to herd location, the number of susceptible animals present, details of incoming livestock movement events should be updated (if necessary) and details of serological testing and estimation of the likely source of infection recorded. For herds reared on relatively large farm enterprises grazing history information should also be recorded allowing the location of herds to be defined over time. In this way credible estimates of the geographic range of BTV transmission risk can be estimated which can then inform use of an appropriate numeric value for the transmission kernel bandwidth used in the model presented in Chapter 4.

7.5 Conclusions

The aim of the investigatory work presented in this thesis has been to develop a model that can be used to generate information to guide effective policy for control and prevention of outbreaks of bluetongue in domestic ruminant populations. Process oriented, individual-based models are becoming more frequently used in many fields of disease science (Ross et al. 2011, Dion et al. 2011, Ariuntsetseg & Yom 2013, Paul et al. 2014) and it is to be expected that this trend will continue in coming years given further advances in computing power and reductions in the cost of computing hardware. The generic animal disease simulation model, AADIS (Bradhurst 2015) provides a clear example of these developments and the bluetongue model developed in this thesis provides an excellent example of the way a generic disease simulation model such as AADIS can be adapted to provide decision support for emerging animal disease threats.

Furthermore, greater familiarity with the strengths and weaknesses of such models will allow them to be used for a greater number of purposes. One such purpose would be to run a model 'backwards' so that when an incursion is detected the model can provide estimates of the likely site of incursion (if this is not already known) and, more importantly the location of undetected herds. The process of running a model 'backwards' might also improve forward predictions, as the backward simulations may reveal a number of non-detected herds which could then be influential as spreaders of virus and determinants of forward disease spread.

An interesting expansion to the model would be to explore and test different control measures and their effectiveness on limiting the spread of vector-borne diseases. An example could be vaccination of animals in a herd that are a recipient of incoming animals from identified endemic areas or if the *Culicoides* model predicts the herd is in a hot spot for midges. Many critical components in bluetongue (and other vector-borne disease) are allied with our lack of basic understanding of bluetongue vector ecology and particular attention is needed to disentangle the uncertainties that arise from the exact understanding of the biology of *Culicoides* spp. in Australia. This could be done by including more data and field-based and laboratory research on *Culicoides* spp. vectors.

In conclusion, the series of studies presented in this thesis make a substantial contribution to the body of scientific knowledge related to the modelling of infectious diseases of animals by providing approaches for: (1) estimating the geographic distribution of disease vectors and how this changes over time (Chapter 3); and (2) simulating the spread of disease from animal hosts and disease vectors and *vice versa* (Chapter 4). Model prototypes were implemented in AADIS providing examples of how such a model could be used in practice (Chapter 5), particularly for the difficult task of developing strategies to deal with climate change (Chapter 6). While bluetongue has been the disease of interest for the studies presented in this thesis it is emphasised that the approach that has been developed is sufficiently generic to allow it to be adapted for any vector-borne (i.e. insect or wildlife) disease of livestock.

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Appendix A

Appendix A

Table A.1: Description of the abbreviations used in the *Culicoides* spp. population dynamics model described in Chapter 3.

Symbol	Description
adt	Adult population.
juv	Juvenile population.
b	Birth (oviposition) rate, function of temperature.
d_j, d_a	Death rate, function of temperature.
m	Maturation (emergence) rate, function of temperature.
$\varepsilon_j, \varepsilon_a$	Temperature at below which declining populations become extinct, immature and adult.
pj_{max}	Immature population density at which oviposition becomes zero.

In Table A.1 the rate parameters b, d_j, d_a and m are assumed to be functions of temperature however they are categorised based on temperature, as described in Table A.2.

Table A.2: Parameters used in the *Culicoides* spp. population dynamics model described in Chapter 3.

Parameter	Temperature range	Parameter value	Reference
b	< 7 °C	0 eggs/day	Bishop et al. (1996)
	7 °C to 18 °C	0 – 1.1 eggs/day	Campbell & Kettle (1975)
	18 °C to 25 °C	1.1 – 3.96 eggs/day	Gerry & Mullens (2000)
	> 25 °C	3.96 eggs/day	-
d_j	< 7 °C	1.0 (1 day)	Bishop et al. (1996)
	7 °C to 17 °C	0.0328 (30.5 days)	-
	> 17 °C	0.0328 (30.5 days)	-
d_a	< 12 °C	0.1 (10 days)	Gerry & Mullens (2000)
	12 °C to 5 °C	0.45 (2.2 days)	-
m	< 7 °C	0 days	Bishop et al. (1996)
	7 °C to 18 °C	0.091 (11 days) to 0.027 (37 days)	-
	> 18 °C	0.091 (11 days)	-
ε_j	-	0.0010	-
ε_a	-	0.0005	-

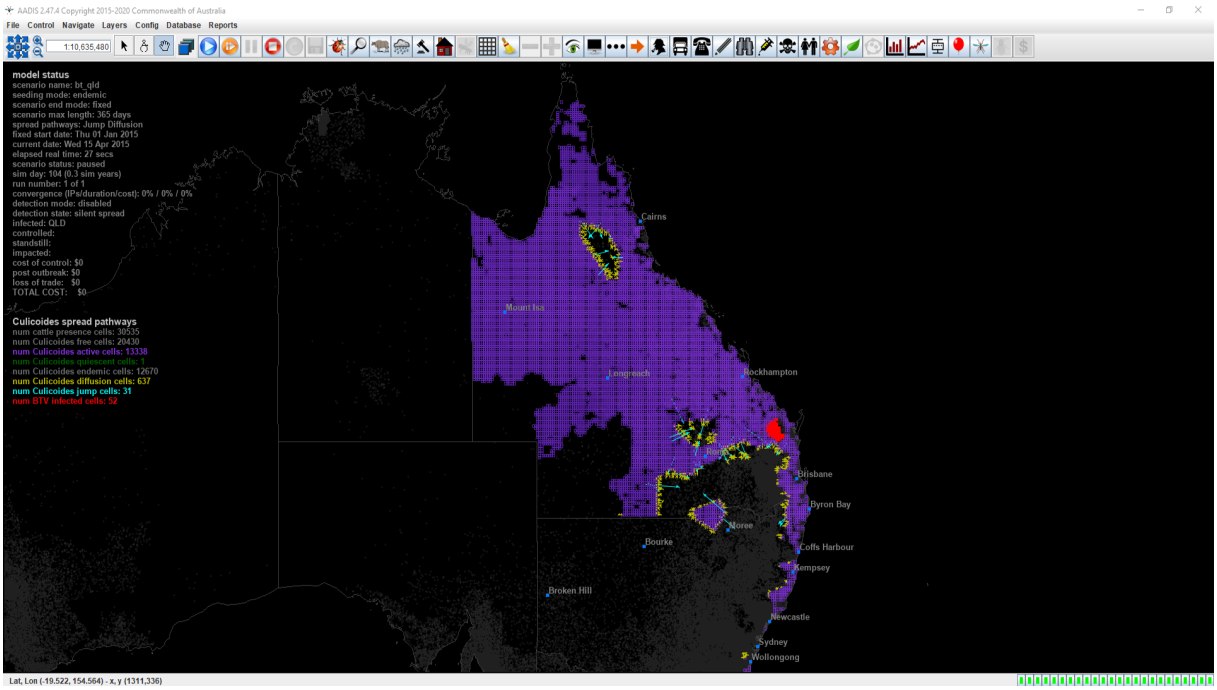

Figure A.1: Screenshot of the AADIS graphic user interface showing the distribution of *Culicoides* spp. during summer. Key: *Culicoides* spp. active cells (purple); BTV infected cells (red).

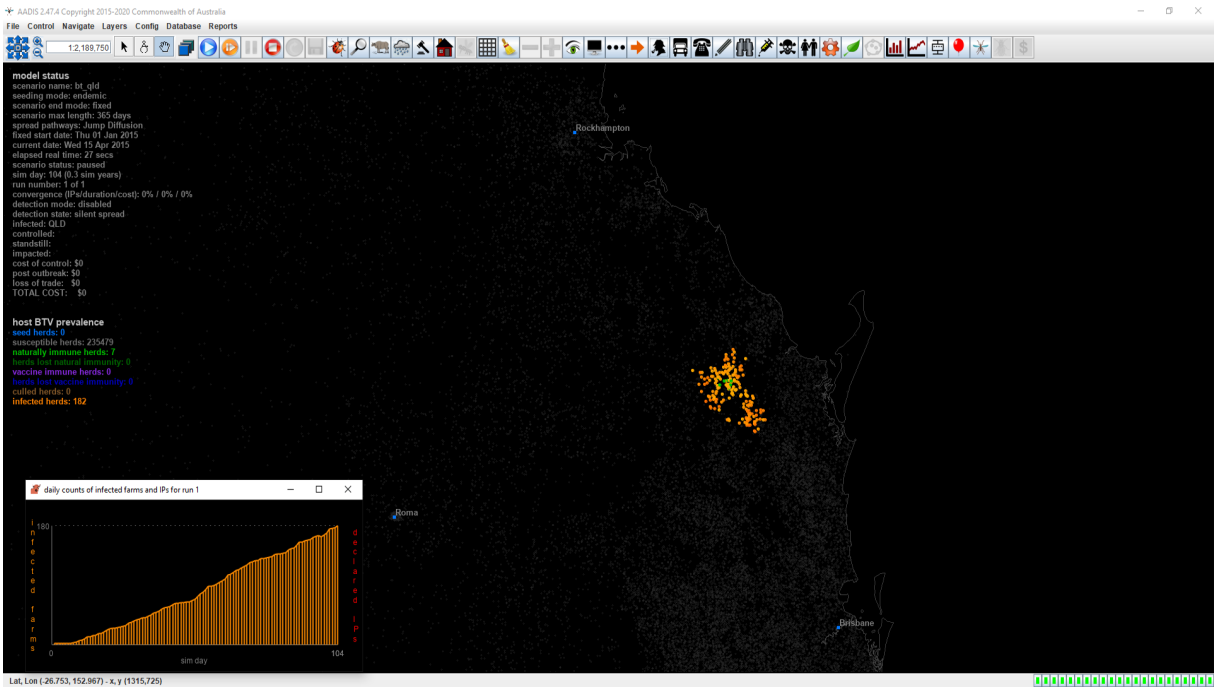

Figure A.2: Screenshot of the AADIS graphic user interface showing the location of BTV positive herds in the Southern Queensland study area, as described in Chapter 5. Key: BTV infected herds (orange); naturally immune herds (green).

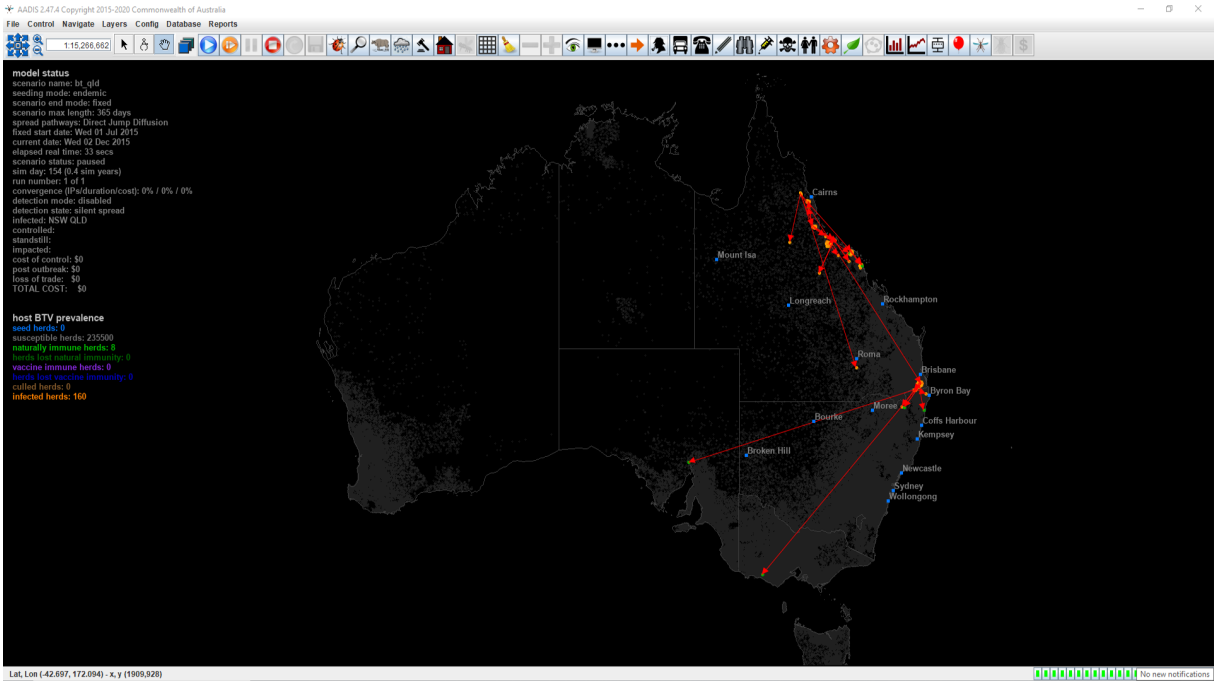

Figure A.3: Screenshot of the AADIS graphic user interface showing source and destination of animal movements events used in the simulations of BTV as described in Chapter 6. Key: BTV infected herds (orange); naturally immune herds (green); animal movement events (red arrows).

Appendix B

Appendix B

This section provides the pseudocode for the *Culicoides* spp. population dynamics model described in Chapter 3 and the bluetongue transmission model described in Chapter 4. The R code (R Core Team 2020) for both models are included in the electronic support files that accompany this thesis document.

B.1 Pseudocode for modelling *Culicoides* spp. population dynamics

```
1
2  Populate the raster map with adult and juvenile Culicoides midges in each cell (as
       starting values)
3
4   each simulation day {
5     - read in the adult and juvenile Culicoides counts and the mean temperature maps
          for each grid cell.
6      - generate adult and juvenile Culicoides counts (based on temperature) using the
           function "culicoides"
7       - update adult and juvenile population using changes calculated in previous step
             and save into pop folder
8        - spread Culicoides to adjacent cells of the raster using function cellauto.
9         - update adult count using changes calculated in previous step and save into
              cauto folder
10         - select the eligible Culicoides cells to be used for HYSPLIT.
11          - update the eligible cell in previous step and save into eligible folder
12           - create HYSPLIT control file using function hysplit.ctl.
13            - pass the control file created by hysplit.ctl to HYSPLIT using
                 HYSPLIT_CONTROL.bat
14              - select the eligible cells adutls to disperse adults by wind via HYSPLIT
15                - update adult count using changes calculated in previous step and save
                       into hsplit folder
16                 - updated Culicoides counts for all steps and save into final folder
17            }
```

B.2 Pseudocode for modelling blue the transmission of bluetongue between *Culicoides* spp. vectors and livestock hosts

```
1
2  Seed an index herd as source of BTV infection
3
4  Each simulation day
5
6  for (each exposed or infectious herd) {
7
8    - select the insect vector grid cells and temperature values corresponding to the
       point location of exposed or infected herd(s) for the current day
9    - determine the prevalence of BTV in insect vector population if there are any
       infectious insect vectors in insect population in the corresponding grid cell
10   - calculate insect vector biting rate activity
11   - calculate the infection pressure exerted by the insect vector layer on the
       population of livestock hosts
12   - transmit BTV within herd (SEIR) for current day
13
14     while (each infected herd on current day) {
15      - define the insect vector grid cell that lay inside the assigned radius range
          around the infectious herd
16          - compute the transmission risk rate of BTV between the infectious herd(s)
              and the insect grid cell based on distance using Gaussian smooth kernel
              density (function density.ppp from package spatstat)
17
18         For (each insect vector grid cell lay inside the radius {
19           - sample the number of insect vectors that would be exposed to BTV from
               binomial distribution with the probability of transmission risk of BTV
               from infectious herd(s)
20
21             While (each exposed or infectious insect grid cells) {
22                - calculate the biting rate activity
23                - determine the prevalence of BTV of animal population of the
                    corresponding grid cell
24                - calculate the infection pressure exerted by the animal host layer on
                    the insect vector layer
25                - calculate the extrinsic incubation period for bluetongue
26                - calculate insect vector mortality rate
27                - transmit BTV within insects (SEI) for current day
28
29                    If (insect grid cell is infected) {
30                      - define the herds within each infected insect grid cell
31                      - sample the number of susceptible animals that will expose to
                          BTV in each susceptible herd from binomial distribution with
                          probability of transmission risk
32     }
33           }
34               }
35                   }
36                        }
```