PREDICTING IMPACTS OF CLIMATE CHANGE ON LIVESTOCK PARASITES

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Abstract

The changing abundance and distribution of parasitic helminths has been identified as one of the greatest threats to animal health in the UK under climate change. This is due to the strong influence of abiotic conditions on parasites' free-living stages. Planning adaptation and mitigation strategies requires predictions of parasite risk, and understanding of subtle interactions between abiotic conditions and parasite transmission. This requires development and application of a range of different modelling approaches.

This thesis includes the first long-term forecast showing potential impacts of climate change on a parasitic helminth in the UK. By combining a correlative parasite risk model with UKCP09 climate projections, risk maps are generated identifying which areas of the UK are predicted to experience unprecedented levels of fasciolosis (liver fluke) risk in the future.

Correlative models provide warnings of future risk, indicating where resources for monitoring and control should be targeted. To address more complex issues, and foresee consequences of subtle interactions between various components of a system under climate influence, a drive towards process-based mechanistic models is required. Consequently, a spatially explicit mechanistic model is developed, for the transmission of gastro-intestinal nematodes in a controlled grazing system. This allows investigation into how climate impacts on different elements of transmission. A non-linear relationship between climate change and parasite risk is revealed, with a distinct 'tipping point' in outbreaks when temperature driven processes exceed critical rates. This indicates that climate change could lead to sudden and dramatic changes in parasite risk.

Through combining the models developed here with improved empirical data and a broader view of livestock systems, our understanding of future risks and opportunities can be increased. This will allow improved control of these physically and economically damaging parasites, reducing deleterious impacts on production efficiency and animal welfare.

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Author's Declaration

Host movement and grazing behaviour elements of the mechanistic model used in chapters three and four were developed and coded by Glenn Marion and Ross Davidson (prior to the inclusion of parasitism in the system). With this exception, I declare that the work contained in this thesis is my own and has not been submitted for any other degree or award.

Naomi Fox

Chapter 1

General Introduction

Climate change has been identified as an important factor driving changes in the prevalence and distribution of important livestock pathogens. There is an urgent need to understand the potential impacts of climate change on livestock health. In the first part of the introduction, the potential impacts of environmental change on animal health are discussed in relation to established, and new and emerging pathogens. This review (in combination with a review of the direct impacts of climate change on livestock growth and production) formed the animal health section of the report "*A Strategic Review of Recent, Past and Current Research Programmes Relating to the Effects of Environmental Change on Animal, Plant and Human Health*". This review was undertaken to assist the LWEC (Living with Environmental Change) programme in identifying future research requirements relating to the health impacts arising from global environmental change.

The second part of the introduction explores the approaches to predicting future parasite risk in livestock. This review formed the basis of the publication: Fox, N.J., Marion, G., Davidson, R.S., White, P.C.L., Hutchings, M.R. (2012). *Livestock Helminths in a Changing Climate: Approaches and Restrictions to Meaningful Predictions*. Animals. Special issue on Climate Change and Livestock Management. 2; 93-107.

1.1 The effects of climate change on diseases of UK livestock

To appreciate the potential for climate change to impact on livestock pathogens, projected changes in climate need to be understood. Since 1970 a global increase in temperature of 0.7^{o}C has been observed, by the end of the century a further increase of between 1 and 6^{o}C is projected (IPCC, 2007). UKCP09 projections indicate future changes in the UK's climate, with an expected increase in UK summer temperatures between 1 and 8^{o}C by 2080, and temperatures projected to rise faster in summer than in winter (UKCP09, 2009a). In conjunction with increased temperatures, variations in the hydrological cycle are predicted.

With a 6% increase in moisture held in the air for every 1^{o}C temperature increase, higher temperatures may intensify the hydrological cycle (Epstein *et al*., 1998). In parts of the UK total winter precipitation has already increased by up to 50% since 1961 (UKCIP, 2002). Further changes in rainfall patterns are expected, with projected increases in winter rainfall of up to 70% by 2080, and projected changes in summer rainfall between a 70% decrease and a 10% increase (UKCP09, 2009a). The frequency and intensity of extreme hydrological events are set to increase, with heavier but less frequent rainfall and higher evaporation rates leading to an increase in floods and droughts (Githeko *et al.*, 2000; Patz *et al.*, 2008; Sutherst, 2001). It is postulated that there will be an increase in cloud cover (Patz *et al.*, 2000), leading to a reduction in daytime warming and night time cooling (Epstein *et al.*, 1998). There has already been a rise in the intensity of extreme weather events (Epstein, 2001) and a further increase in weather variability is predicted (Hansen *et al.*, 2012; Planton *et al.*, 2008).

Climate change will have a direct impact on the transmission of a range of pathogens. The extent to which climate change will impact on specific pathogens is, in part, dependent on their mode of transmission and the amount of time that the pathogen spends outside the host. The changing prevalence and distribution of pathogens in the UK has been the focus of many studies, with environmental change being implicated as one of the driving forces for recent range expansions.

1.1.1 Established micro-parasites

1.1.1.1 Directly transmitted pathogens

A number of climatic factors influence the survival of directly transmitted micro-parasites including moisture, temperature and UV levels. The influence of abiotic conditions is partly determined by the amount of time that the pathogen spends outside the host; as a majority of directly transmitted micro-parasites survive for only short periods outside the host disease levels are governed by non-climatic factors. However, direct impacts of abiotic conditions have been explored for a number of directly transmitted micro-parasites which can persist in the environment. For example, Whittington *et al.*, (2004) found that the causative agent of paratuberculosis, *Mycobacterium avium* subsp. *paratuberculosis*, can survive in soil for up to 55 weeks in dry fully shaded conditions, and for 24 weeks in 70% shade, whilst only surviving two weeks in unshaded plots. Whittington *et al*., (2004) also demonstrated that increased rainfall will not decrease the levels of bacteria in the soil. The work on

M.a.paratuberculosis also demonstrates the importance of vegetation levels on disease transmission. In plots where vegetation provided the only shade *M.a.paratuberculosis* survived for 32 weeks, whilst in plots with vegetation removed all bacteria perished in two weeks (Whittington *et al*., 2004).

One harmful bacterium that is present in the UK and can survive for years in the external environment is *Bacillus anthracis* (anthrax). The survival and germination of vegetative *B. anthracis* spores is governed by temperature and humidity (Giorno *et al*., 2007; Turnbull, 1998). Although *B. anthracis* can spend a great proportion of its lifecycle in the external environment, and temperature affects spore formation, it is unlikely that climate change will have an impact on disease prevalence. National programmes have resulted in a global decrease in livestock cases over the past few decades, with middle and northern Europe only experiencing sporadic cases (Turnbull, 1998). As long as there are no dramatic changes in prevention measures a changing climate should not result in more UK outbreaks.

1.1.1.2 Vector-borne pathogens

One subset of micro-parasites particularly vulnerable to climate change, are vector-borne diseases. Arthropod vectors are poikilothermic, with most elements of both their lifecycle and vectorial capacity influenced by abiotic conditions. A majority of vectors are also habitat generalists with high dispersal abilities and reproductive rates, so can track their climate envelope and colonise new areas quickly.

A majority of work on the impacts of climate change on livestock disease spread has focused on Bluetongue virus (BTV), an arbovirus affecting ruminants. BTV provides an example of the impacts climate change can have on vector borne micro-parasite spread, and approaches to understanding and predicting outbreaks.

Changing Bluetongue virus distribution and abundance

BTV is transmitted by biting midges of the genus *Culicoides* (Calvete *et al*., 2009). Due to BTV's dependence on *Culicoides* midges, the spatio-temporal distribution of the disease echoes the distribution of these vectors. Purse *et al*., (2005) and Wilson and Mellor, (2008)

provide good reviews of the impacts of climate change on vector dynamics and BTV transmission, documenting the spread of BTV across Europe since 1998. Prior to 1998, there had only been brief and sporadic outbreaks of bluetongue in Europe.

Climate change has been identified as the main driver of BTV spread, as most stages of the *Culicoides* life cycle are governed by temperature. The relationships between temperature and each development and transmission stage have been extensively studied and quantified (Purse *et al*., 2005; Wilson & Mellor, 2008). In addition to the role that temperature plays in their lifecycle, *Culicoides* vectors have other traits that cause them to be a concern in a changing climate. *Culicoides* utilise ubiquitous habitats and hosts, have high reproduction rates, and high dispersal potential, so are likely to track their shifting climate envelopes (Baylis *et al.,* 2004). Extreme weather events, such as high winds, will aid the passive dispersal of volant vectors into newly viable habitats. Environmental change will also affect the availability of breeding sites e.g. through changes in irrigation, flooding and agricultural practice. Sea level rise, storms and flooding could also lead to an increase in brackish breeding sites for the halophilic *Culicoides pulicaris* groups (Wilson & Mellor, 2008).

Modelling the change in BTV

The need for surveillance and risks maps is evident when the economic impacts of infection are considered. Subclinical infection is characterised by weight loss, lower milk yield, loss of condition, abortion, infertility and veterinary costs. Indirect economic losses are also incurred via export restrictions, surveillance and mitigation costs (Wilson & Mellor, 2008). The spread of BTV may set a precedent for other climate driven vector-pathogen systems. By understanding how and why climate affects the distribution of BTV, the possible impacts of climate change on other pathogens with similar traits can be identified.

As BTV is a notifiable disease and there has been a recent push in collecting live culicoides trap data, distribution of the disease and its vectors is reasonably well documented. As a result correlative models have been developed for predicting BTV risk and vector distribution across Europe, combining culicoides distribution data with satellite derived climate data (Calvete *et al*., 2008, 2009; Purse *et al*., 2004; Racloz *et al.,* 2007; Tatem *et al*., 2003). For different vector species, variation was found in the type of environmental variables that best predicted distribution, with temperature variables having the greatest influence on *C. obsoletus* and *C. newsteadi* distribution, whilst the *C. pulicaris* and *C. imicola* distributions

are best predicted using NDVI (Normalised Difference Vegetation Index) (Purse *et al*., 2004). The correlative models developed for BTV and its vectors show the capabilities of this approach given sufficient surveillance data. This demonstrates what could be possible for predictions of non-notifiable pathogens at a given level of surveillance.

Despite the abundance of vector distribution data, Pili *et al*., (2006) found substantial differences in relative abundance of BTV vectors between field data and prediction maps based on climate variables derived from satellites. This highlights the need for consideration of other explanatory factors including land use and local microclimate when predicting vector distribution and disease risk. In addition to using climate variables, model fit has been found to improve if host availability is incorporated as a covariate (Calvete *et al*., 2009). Additionally, Gubbins *et al.,* (2008) demonstrated that livestock composition influences the course of outbreaks, as sheep have decreased viraemia durations compared to cattle, and have a dilution effect on mixed farms. This indicates that models including additional variables, such as livestock distribution, can provide improved estimates of disease risk.

As BTV is a notifiable disease, the World Organisation for Animal Health (OIE) records all outbreaks. Such spatio-temporal distribution data aid the development of correlative risk models. However, active surveillance has detected BTV and its vectors in areas that were disease free according to the OIE (Calvete *et al*., 2006; Purse *et al*., 2006). This demonstrates the possible undetected transmission of pathogens with a tendency for subclinical infection and highlights the need for active surveillance in determining the true extent of such diseases. Lack of accurate long term data can make it difficult to determine how distributions are changing (Calvete *et al*., 2006), and false absences could affect model creation and validation (Rocchini *et al*., 2011).

As Calvete *et al*., (2006) and Purse *et al.,* (2006) found, there are often limitations to the distribution data of both BTV and its vectors. As the influences of climate on physiological parameters of vector-host transmission are well understood, it has been possible to create process-based mechanistic models to predict disease spread. There are many examples of such process-oriented models of BTV transmission (Caligiuri *et al*., 2004; De Koeijer *et al.,* 2007; Gubbins *et al*., 2008).

In contrast to the use of distinct correlative and mechanistic modelling approaches, Hartemink *et al*., (2009) generated BTV risk maps for the Netherlands, using an integrated approach which combined mechanistic modelling, with correlative predictions of vector abundance

from satellite data. This study highlights the potential of combining correlative distribution models with mechanistic models of transmission dynamics, however the authors considered this a proof of concept of an integrated approach, rather than providing accurate predictions of risk.

The development of climate based BTV models has already enabled control strategies to be targeted (Charron *et al.*, 2011; Ducheyne *et al*., 2011). For example, Ducheyne *et al*., (2011) developed a predictive model through wind-mediated and wind-independent vector movement using data from the 2006-2007 BTV8 and 2008 BTV1 epidemics in southern France for model parameterisation. The model was used to determine risk in Belgium in 2009, and informed BTV control strategies. Risk maps can also show prime locations for sentinel herds (Racloz *et al*., 2007).

Despite recent advances, climate-driven mechanistic models of BTV still need refining. The key parameters affecting transmission are: extrinsic incubation period, biting rate, vector mortality rate, host to vector transmission probability and vector to host ratio. Each of these elements is influenced by climate. To improve model accuracy, reliable estimates of each parameter's dependence on temperature and moisture levels are required.

Of the climate driven disease expansions threatening the UK, BTV has been the focus of many predictive studies. The creation of risk maps is facilitated by fine-scale distribution data, and detailed understanding of the ecology of its volant vectors.

1.1.2 Established macro-parasites

In comparison to a majority of micro-parasites, macro-parasites spend a large proportion of their lifecycle outside their definitive hosts, where the development and survival of these free-living stages are susceptible to abiotic conditions. The impacts of climate change on macro-parasites of livestock in the UK are discussed below, for both endo-parasites (focussing on helminths), and ecto-parasites (focussing on blowfly-strike).

1.1.2.1 Helminths

Helminths have an extensive impact on the UK livestock industry. Direct welfare and economic costs are incurred from subclinical infection due to weight loss, loss of condition, decreased milk yield and abortion, and heavy infections can cause host mortality (Bisset, 1994; Mckellar, 1993). Gastro-intestinal helminths cost the British sheep industry alone an estimated £84 million per annum from direct costs (production losses and veterinary costs) (Nieuwhof & Bishop, 2005).

The UK's most economically important parasitic helminths include the nematodes *Ostertagia ostertagi, Cooperia oncophora, Trichostrongylus spp, Haemonchus contortus, Teladorsagia circumcincta* and *Nematodirus battus*, and the trematode *Fasciola hepatica* (Kenyon *et al.,* 2009b; Van Dijk *et al.,* 2010). Helminths are transmitted via the faecal oral route, with non-infective stages released from the definitive host in the faeces. These exogenous, free-living stages develop into their infective stages either on pasture (for major livestock nematodes), or in an intermediate host (for trematodes), before being re-ingested by their definitive host.

Survival and development of the parasites' free-living stages are governed by environmental conditions (Stromberg, 1997). Consequently, spatial distribution, intensity of parasite burdens, and seasonal patterns of infection are influenced by climate. A plethora of research has been conducted on the influence of abiotic conditions on survival and development of the main livestock nematodes; these studies have already been extensively reviewed (Chaparro *et al.,* 2011; Kao *et al.,* 2000; O'Connor *et al.,* 2006; Smith & Grenfell, 1994). Morgan & van Dijk (2012) provide a thorough review of how epidemiology of livestock nematodes is currently influenced by climate.

Overall, the development and survival of parasites' free-living stages are primarily governed by temperature and moisture availability. Within their development thresholds, increasing temperatures lead to faster larval development rates. However, free-living stages are vulnerable to extreme temperatures and increasing temperatures can increase mortality rates. Consequently, transmission is optimised at intermediate temperatures, with the optimal range varying between species. For example, favourable temperatures for *H.contortus* development are between 25 and 37^{o}C, whilst *T. circumcincta* transmission is most efficient between 16 and 30^{o}C (O'Connor *et al*., 2006). In addition to the influence of temperature, a majority of parasite larvae are vulnerable to desiccation, with larval survival influenced by both the level of rainfall and its temporal distribution (O'Connor *et al.,* 2007; O'Connor *et al.,* 2008).

Different stages of the lifecycle exhibit varying levels of vulnerability to climatic conditions, with the pre-infective stages most sensitive to adverse abiotic conditions (O'Connor *et al*., 2006). Infective larvae (L3) are more resilient to changing conditions as their protective sheath shields them from desiccation. However, the protective sheath prevents feeding, so an increase in temperatures could diminish L3 survival through raising metabolic rate and depleting energy reserves (O'Connor *et al*., 2006).

Although a majority of studies have focussed on the effects of temperature and moisture availability, other climate variables will influence larval survival and development. Van Dijk *et al.,* (2009) investigated how ultraviolet (UV) light affects Trichostrongyloid nematodes, *H. contortus, N. battus* and *T. circumcinta*, in their infective L3 stages. Mortality rates increased by up to 100 times due to exposure to UV light equivalent to the maximum levels expected for a summers day. There were inter-species differences observed: *N. battus*, with its arctic origins, and *T. circumcincta* were less resistant than the tropically-adapted *H. contortus* (Van Dijk *et al*., 2009).

Changing helminth prevalence and distribution

Previous studies of the effects of climatic conditions on parasite abundance and spread have utilised a range of sources. Mas-Coma *et al.,* (2008) and O'Connor *et al*., (2006) both relied on published literature to determine spread at the national level. To look at national and regional trends in the UK Van Dijk *et al.,* (2008) used the Veterinary Surveillance (VIDA) data from 1975 to present. Pritchard *et al.,* (2005) looked at links between environment and parasite burden using composite faecal samples from farms in East Anglia, local surveillance data and VIDA data, combined with regional climatic data obtained from the Met Office. Kenyon *et al*., (2009b) used examples of outbreaks for each parasite on farms in south eastern Scotland, describing the helminth burden of particular flocks, whilst Mitchell & Somerville, (2005) used data from the outbreaks diagnosed by SAC Veterinary Services. Eysker & Bakker, (2005) used different groups of grazing tracer lambs, and faecal samples collected to determine the impact of the hot summer of 2003 on infective larvae development and survival in the Netherlands. McMahon *et al*., (2012) investigated trends in gastro-intestinal nematode (GIN) infection across Northern Ireland, using veterinary diagnostic data from 1999 to 2009. Burgess *et al*., (2012) determined current trends in helminth outbreaks through analysing faecal samples direct from farms across the UK, in conjunction with information including farm type and management approach.

What is known about changing distributions of key livestock helminths in the UK is outlined below.

Fasciola hepatica

F. hepatica (liver fluke) has a great economic impact on sheep and cattle production as infection leads to weight loss, decreased milk yield, diarrhoea and occasionally mortality (Pritchard *et al*., 2005). Increases in fasciolosis incidence have been reported across Europe (De Waal *et al*., 2007) and this increase has been attributed to changing weather patterns, especially warmer and wetter conditions. There has been a dramatic increase in the number of *F. hepatica* outbreaks in Scotland, in both sheep and cattle. Previously restricted to the wetter west of Scotland, *F. hepatica* has been confirmed in most south east farms since 2002 (Kenyon *et al*., 2009b). There was an exceptional rise in *F. hepatica* infections in 2002/2003 and in the first quarter of 2008, and this is deemed a consequence of climate as these periods were particularly warm and wet, with both temperature and rainfall far higher than the long term average (Kenyon *et al.,* 2009b; Mitchell & Somerville, 2005). Summer rainfall is highly beneficial for the dwarf pond snail intermediate host, and the parasite development period is extended by milder temperatures. The long term changing distribution is attributed to warmer average temperatures year round, increased rainfall in winter and autumn, fewer ground frosts and the 4-week extension of the herbage growing season over the last 40 years (Barnett *et al.,* 2006).

As with Scotland, most cases of fasciolosis in the rest of the UK were previously in the wetter western areas, however the east is now experiencing high prevalence. Pritchard *et al*., (2005) describe the rise in fasciolosis emergence in East Anglia using VIDA data and local farm level surveillance data. Prevalence was particularly high in Norfolk and Suffolk, with outbreaks also occurring in Cambridgeshire, Hertfordshire, Bedfordshire and Essex. This change in distribution has been attributed to warmer, wetter conditions in the East and an increase in the number of sheep brought in for seasonal grazing from areas were fluke is endemic (Pritchard *et al*., 2005).

In addition to increased temperature and rainfall, Pritchard *et al*., (2005) also looked at the influence of changing land management strategies, specifically the Environmentally Sensitive Area scheme (ESA), one of a number of agri-environment schemes that have been introduced over the last 20 years. ESAs aim to maintain suitable habitats for endangered flora, invertebrates and breeding and migrating birds through the creation of wetter grassland

conditions. Unsurprisingly it was found that this land management approach favours the survival of *F. hepatica* and its intermediate hosts and that fluke infection was more common in, though not confined to, ESA grazings (Pritchard *et al*., 2005). The impacts of agri-environment schemes on biodiversity in the face climate change have been discussed, however, aside from this one study, the potential impacts on disease spread have been largely ignored. More work is needed at a broader scale on the impacts of biodiversity protection measures on disease abundance.

Nematodirus battus

N. battus is a highly pathogenic nematode found in the small intestine of ruminants. Unlike other livestock parasites, development of the free-living stages into infective larvae was thought to only occur after prolonged periods of exposure to low temperatures (around $0^{o}C$) are followed by a rise in temperatures (Ash & Atkinson, 1986). *N. battus* infections have increased in some areas of the UK; in Scotland infections have increased since 1995 (Mitchell & Somerville, 2005). There have been regional differences in the patterns of infection: rises in prevalence are primarily in Scotland, with minor increases also observed in Wales and northern England (Van Dijk *et al*., 2008). It is now thought that the ability of *N. battus* eggs to hatch without a chilling period (Van Dijk *et al*., 2008; Van Dijk & Morgan, 2008, 2010), combined with warmer temperatures accelerating development, have led to the considerable increase in infection risk in grazing lambs.

Haemonchus contortus

H. contortus, an abomasal nematode of sheep, is typically a parasite of tropical climes, with haemonchosis in the UK previously confined to the warmer southern regions. However it is now found to be present on around 50% of UK farms (Burgess *et al*., 2012) and its distribution extends to the north of the UK; with infections found on a majority of surveyed Scottish farms (Bartley *et al*., 2003). There is a high prevalence and widespread distribution of *H. contortus*, but low outbreak intensity with few clinical cases across a majority of its geographic range (Burgess *et al*., 2012). However outbreaks of pathological cases are increasing in Scotland (Abbott *et al.*, 2007; Kenyon *et al.*, 2009b; Mitchell & Somerville, 2005), the North and the Midlands, but remaining stable in Wales and the Southwest (Van Dijk *et al*., 2008). This change in outbreak patterns has been attributed to climate change as warm temperatures lead to high larval activity and decreased development time (Mitchell & Somerville, 2005) whilst wetter conditions decrease desiccation. Higher autumn temperatures also encourage the ingested larvae to develop into disease inducing adults rather than enter hypobiosis, increasing the number of eggs released later in the year and extending

the transmission window later into the autumn (Van Dijk *et al*., 2008; Wolstenholme *et al*., 2004). It has been suggested that this increase may be counteracted by the larvae succumbing to desiccation during the hotter and drier summer months, however severe haemonchosis outbreaks followed the unusually warm and dry summer of 2003 in the Netherlands (Eysker & Bakker, 2005).

The increased range of *H. contortus* has also been attributed to other, non climatic, factors such as increased anthelmintic resistance and changing husbandry practices. However the patterns observed, including changing seasonality and range expansion primarily at the limits of their thermal thresholds, point to climate change over other factors (Van Dijk *et al*., 2008).

Those describing the recent changes in distribution of the most economically important helminths have identified many gaps in current knowledge. A majority of conclusions surrounding helminth range expansion are based on passive surveillance data only (Mitchell & Somerville, 2005; O'Connor *et al*., 2006; Van Dijk *et al*., 2008). Changes in many other factors could affect the perceived changes in helminth prevalence including changing laboratory methods, farmer and veterinary motivation and disease awareness (Van Dijk *et al*., 2008). There has been a move towards active surveillance (Burgess *et al*., 2012), however these data are collected across limited timescales. Effective monitoring is needed to determine the changing prevalence and define the current range accurately to use as a bench mark against climate change. The development of evidence-based predictions and control strategies could be realised if national and regional systems for epidemiological monitoring were established.

Overall, there have been a number of papers aiming to link the recent changes in helminthiasis abundance and distribution with environmental change (Kantzoura *et al*., 2011; Kenyon *et al*., 2009b; Mas-Coma *et al*., 2008; O'Connor *et al*., 2006; Pritchard *et al*., 2005; Van Dijk *et al*., 2008). However, the true influence of climate change on changing patterns of outbreaks has yet to be deduced.

Modelling the change

Due to the potential for climate change to further influence shifts in helminth prevalence and distribution, predictions of future risk are required. The use of modelling approaches will enable the extent to which previous prevalence increases can be attributed to climate change

to be explored, as well as providing a framework within which to investigate potential future risks. Models of helminthiasis have mainly been restricted to *F. hepatica* due to a close relationship between weather and fasciolosis outbreaks (De Waal *et al*., 2007) and the worldwide importance of fasciolosis as a zoonosis.

As *F. hepatica* levels are so closely associated with weather, several forecasting systems have been developed. Farmers in the UK are currently provided with short term predictions of the following seasons' fasciolosis risk via the National Animal Disease Information Service (NADIS) (www.nadis.org.uk/parasite-forecast). This forecast uses the Ollerenshaw index, which is dependent on rainfall, potential evapo-transpiration and number of raindays (Ollerenshaw & Rowlands, 1959). De Waal *et al*., (2007) aimed to develop a correlative, GIS-based model using prevalence and environmental data to determine local scale fasciolosis risk in Ireland; however no effective predictive models have been developed. New GIS based systems would enable more accurate predictions of changing risk and help to prepare farmers and inform control strategies.

Due to the global importance of *F. hepatica* and other snail-borne parasites, much work has also been done outside of the UK to determine the current distribution. Kantzoura *et al*., (2011) predicted the spatial distribution of different *F. hepatica* genotypes and haplotypes across Greece and Bulgaria, using environmental data and ecological niche modelling. Formed in 2002 GNOSIS (Global Network for Geospatial Health) is dedicated to the improvement of control programmes and development of computer-based models for snail-borne diseases of medical and veterinary importance. GNOSIS is a network of collaborating earth scientists and health workers using epidemiological databases and environmental data, combined with GIS to match abundance and distribution with environmental parameters, this will help predict distribution and implement control strategies. Fuentes, (2006) reviewed past work on both animal and human fasciolosis forecasting, concentrating on South American countries, concluding that more accurate epidemiological reports and more climate and remote sensing data are required to create reliable prediction models.

Development and validation of new correlative models of helminth risk are dependent on availability of both prevalence and climate data, however there is generally a mismatch between the scale of transmission and the recording of both infection and climate variables. For example, McMahon *et al*., (2012) investigated the changing levels of GIN infection in Northern Ireland, and the potential role of climate. Prevalence data from 1999-2009 were amalgamated into four regions (North, South, East and West), which were then correlated

with climate data from only four meteorological stations, one for each of these regions. Despite the obvious limitations of this approach, this remains one of the most thorough descriptions of recent climate driven changes in parasite prevalence in Northern Ireland, and even at such a coarse scale, links between climate change and parasite levels were still found.

Due to the paucity of models showing the impacts of environmental change on the UK's important helminths, it is useful to look further afield to identify possible changes in parasite dynamics. Kutz *et al*., (2009) argue that the Arctic provides good systems to decipher the influence of climate change on the dynamics of parasites and hosts, as the systems generally contain fewer confounding factors than those in more tropical climates and the rate of warming is more pronounced.

The creation of correlative models for UK helminths is limited by the lack of accurate distribution data. With this lack of data, process-based mechanistic models are a useful tool in making more robust predictions. The creation of such mechanistic models is dependent on an understanding of how environmental variables influence all stages of the helminth lifecycle. The different approaches to modelling changing helminth distribution are discussed in detail in the second part of this introduction

1.1.2.2 Ecto-parasites

Blowfly strike

In addition to influencing endo-parasite abundance and distribution, ecto-parasites of livestock may also be affected by climate change. Cutaneous myiasis (blowfly strike), caused by *Lucilia sericata* (blowfly), is the most widespread ecto-parasite affecting sheep in the UK (Bisdorff *et al.,* 2006) and strike incidence is partly determined by variations in temperature and rainfall. Investigating the risk between cutaneous myiasis (blowfly strike) and climate, Broughan & Wall, (2007) found strike risk to be dependent on high blowfly abundance, higher maximum temperatures and higher rainfall.

Species distribution models have been used to determine correlations between cutaneous myiasis and environmental variables (Morgan & Wall, 2009; Rose & Wall, 2011). Rose & Wall, (2011) used presence only data to train their predictive model, as recorded absences could be due to the use of effective control strategies, rather than climatic conditions not

being favourable. Their resultant risk maps indicate that increased temperatures will drive a rise in strike risk, and extension of the blowfly season. However temperatures are not predicted to increase to the extent where winter cases of blowfly strike are likely (Rose & Wall, 2011). The increase in hot and dry summers predicted for southern England could result in decreased *L. sericata* numbers in the summer months. However, conditions could favour Mediterranean agents of myiasis, such as *Wohlfahrtia magnifica* (Rose & Wall, 2011).

The study of Morgan and Wall, (2009) emphasised the need to take account of changing husbandry strategies in models predicting disease change, suggesting that an increase in blowfly will not necessarily result in an increase in strike when husbandry is also considered (Morgan & Wall, 2009). Ewe susceptibility would be decreased by shearing (removal of the soiled, humid habitat required by the flies) and as a consequence the increase in ewe strike, predicted by the impact of temperature on *L. sericata,* is largely eliminated by a shift in shearing from June to April (Morgan & Wall, 2009). More research is needed on host-parasite systems that take into consideration the impacts of changing husbandry and other anthropogenic responses on disease transmission.

1.1.3 New and emerging diseases

As BTV expansion has demonstrated, viruses that evolve rapidly, lead to subclinical infection of a wide range of hosts and are spread by a plethora of poikilothermic vector species with ubiquitous habitat requirements, are likely to be greatly influenced by environmental changes. Expansion of BTV range warns that other Culicoides transmitted arboviruses could also spread with climate change. Primary examples include epizootic haemorrhagic disease which can cause mortality in wild deer and cattle and is currently found in the western Mediterranean, Israel, Algeria and Morocco, and African Horse Sickness currently circulating northwest Africa and resulting in a horse mortality rate approaching 95% (Wilson & Mellor, 2008).

Gould & Higgs, (2009) reviewed the impacts of environmental change on emerging mosquito borne arboviruses whose vectors are likely to track their climate envelopes. For example *Aedes* Spp. which transmit Rift Valley Fever Virus (RVFV) are expanding their range as temperatures increase. Outbreaks of RVFV are usually preceded by high rainfall, and are associated with floodplains and wetlands. As the number of extreme weather events are set to increase and RVFV can cause fatal infections and high abortion rates in livestock (Gould & Higgs, 2009), its spread could have a great impact on the UK's naïve host population.

The potential impact of new and emerging arthropod borne viruses is exemplified by Schmallenberg Virus (SBV). An orthbunyavirus first identified in 2011, SBV is now widespread across Northern Europe (Lievaart-Peterson *et al.*, 2012), with multiple outbreaks recorded in the UK in both sheep and cattle (Garigliany *et al*., 2012; Tarlinton *et al*., 2012). The detection and response to SBV highlights the benefits of surveillance systems which identify unusual clinical presentations and monitor changing trends in livestock health (Roberts *et al.*, 2012). Thought to be transmitted by Culicoides midges, and/or mosquitoes, there is potential for existing models (developed for determining BTV spread) to be parameterised for SBV and refined as new information is garnered.

1.1.4 Changing distribution of wildlife reservoirs

The abundance and distribution of wildlife is already altering as a consequence of environmental change. Of 120 biodiversity action plan (BAP) species studied in the UK, 90% showed a substantial shift in their climate envelope (Walmsley *et al*., 2007). Generally speaking, the climate envelopes of northern species are predicted to contract in the UK, whilst those with a southern distribution will see their possible range expand. However, the dispersal capabilities of species are rarely considered. Under NERCs Biodiversity Theme Action Plan, the monitoring and valuing of biodiversity, identifying long term biodiversity trends and emerging diseases are all current priorities. There are a number of programmes that have been set up that also address these priority areas including "MACIS" (Minimisation and Adaptation to Climate change Impacts on biodiversity) (http://macis-project.net/index.html) and MONARCH (Modelling Natural Resource Responses to Climate Change).

Changing wildlife ranges and patterns will affect the spread of disease, as wildlife are host to a diverse range of livestock diseases. One example of this is the effect of climate change on highly pathogenic avian influenza (HPAI H5N1). Reported in over 60 countries across Asia, Europe and Africa, migratory birds of the *Anatidae* family are thought to be the primary vehicle of long-distance HPAI spread (Gilbert & Pfeiffer, 2012). Through monitoring migration patterns using Satellite-telemetry, Gaidet *et al*., (2010) demonstrated that wild birds could disperse the virus over extensive distances (up to 2900km) within the duration of asymptomatic infection. It is important to understand the risk of HPAI H5N1 emergence as there will be an immense economic impact if it spreads across the UK. In 2005-2006, 140

million domestic bird deaths were due to HPAI H5N1 virus outbreaks in Southeast Asia alone, with an economic loss totalling around US$10 billion (Gilbert & Slingenbergh, 2008). Climate change will alter migration patterns, impact on the transmission cycle of the virus and influence the survival of the virus outside of the host.

For the understanding and prevention of HPAI H5N1 spread, WCS (Wildlife Conservation Society) recognise the need to monitor wild bird populations. Funded by USAID and the Centre for Disease Control and Prevention (CDC) the WCS-Global Health launched GAINS (the Global Avian Influenza Network for Surveillance). GAINS has developed a data-sharing system with open access and millions of data points from both biological samples and bird surveys. The distributions of many wild bird species are already showing a northward shift and there has been a decline in the number of long distance migrations undertaken. A changing climate has also been implicated in variations in winter arrival time, distribution and breeding and laying dates of many wetland birds (Rehfisch & Austin, 2006). An increase in extreme weather events may further disrupt population movements and cause novel distribution patterns (Gilbert & Slingenbergh, 2008). The factors influencing migration of birds must be better understood before the impacts of climate change on migration can be modelled with any certainty (Rehfisch & Austin, 2006). The knowledge on how environmental factors influence AI epidemiology is limited and largely speculative, so potential impacts of environmental changes on its spread cannot be deduced. To further complicate the picture, AI emergence is also attributed to other factors including globalisation of the poultry market, illegal trading, intensification of the poultry industry and high densities of poultry with homogenous genotypes (Gilbert & Slingenbergh, 2008).

1.1.5 Conclusions

Environmental change will impact on animal health, with some changes already being observed. For certain species of parasites and wildlife, the impacts of environmental change on species' ranges are already being shown, and understanding dispersal abilities is important for predicting further range shifts.

The increase in pathogen ranges over recent years has been mirrored by our increased understanding of the role of climate in transmission dynamics. In order to determine changes in disease levels, this knowledge needs to be drawn on and predictive models developed and refined. To date, the development of predictive models has focussed on vector-borne

pathogens, specifically BTV. This is due to the availability of active surveillance data, and a thorough understanding of the climate sensitive elements of the transmission process.

Helminths spend significant proportions of their lifecycle outside their definitive host, and are very vulnerable to changes in climate. Consequently it has been suggested that climate change has already affected, and will continue to influence, the intensity and distribution of helminth outbreaks. However there has been no definitive link between observed climate and changes in outbreak patterns, and there is a need for long term predictions of future helminth risk under climate change.

In contrast to direct impacts of environmental change on livestock growth and productivity, the effects on parasites and disease, including those mediated by wildlife, are under far less control, and potentially far more severe and acute in their impacts. The patterns of many pathogen outbreaks are governed by environmental conditions, and therefore a very real threat to livestock systems is posed in the context of climate change. The uncertainty of these changes and the difficulty in quantifying risks represents a key challenge to animal health.

1.2. Approaches to predicting future parasite risk in a changing climate

Despite the deleterious impacts of helminths on the livestock industry and their dependence on climatic conditions, predictions of long-term pathogen threats to livestock in a changing climate have so far concentrated on those spread by volant vectors, such as BTV. Although there have been a number of studies aiming to link the recent changes in helminthiasis abundance and distribution with environmental change, there are a lack of predictions for future helminth risk to livestock. Here the optimal approaches to generating long-term predictions of helminth risk in livestock are explored, stratifying modelling approaches as either correlative or mechanistic.

1.2.1. The correlative approach

Predictive models of species distribution, for both epidemiology and conservation, are often based on correlative ecological niche models (Elith & Leathwick, 2009; Engler & Guisan, 2009; Heikkinen *et al*., 2006; Lawler *et al.,* 2006; Leathwick *et al.,* 2006; Pagel & Schurr, 2012; Thuiller, 2003). This modelling approach is used in chapter two of this thesis. These models are based on Hutchinson's ecological niche theory where the current geographic distribution is used to infer the environmental requirements of a species (Bachrach, 2012). The current, past or future distribution of that species is then predicted based on these requirements (Hijmans & Graham, 2006). Insights into the biology of parasite dynamics should be used to systematically build the foundations of these models, and the most proximal environmental predictors should be chosen based on known ecological and physiological theory (Guisan & Thuiller, 2005).

A number of programmes are available to determine a species' climate envelope by matching current distribution with climatic parameters, such as CLIMEX (Sutherst & Maywald, 1985), HABITAT (Walker & Cocks, 1991), DOMAIN (Carpenter *et al.,* 1993) and SPECIES (Pearson *et al.,* 2002). In addition to these generic models, species-specific correlative models have also been developed, primarily for species of conservation importance and invasive alien species.

To date, correlative predictive models of helminthiasis have focussed on *F. hepatica* (liver fluke) due to the close relationship between weather and fasciolosis outbreaks (De Waal *et al*., 2007) and the worldwide importance of fasciolosis as a zoonosis. There are a number of factors that make correlative modelling the preferred approach for determining fasciolosis risk. Firstly, the existence of long term prevalence data facilitated the development of a statistical model (Ollerenshaw & Rowlands, 1959). Secondly, despite their complex life cycle, the distribution of liver fluke is driven by simple proximal drivers – temperature and water availability. It is these drivers that form the basis of the correlative model. Thirdly, their dispersal by wild hosts and speed of colonisation of new regions makes them ubiquitous where livestock are present across their fundamental niche. Consequently, the correlative approach is used in chapter two, to generate the first long term projections of future fasciolosis risk in the UK.

Despite the information that correlative models can provide, there are a number of disadvantages to applying this approach to a wider range of helminths. A prominent bottleneck to the development of correlative models is the lack of current or past parasite distribution data. Data on parasite distribution are often opportunistic, passive surveillance data. Climate parameters used in model training and application are dependent on which measurements and predictions are available, rather than those that are most pertinent to disease transmission. In order to build reliable models, purpose-driven active surveillance data are needed. As climate affects long term, large scale trends, these data must be collected over appropriate scales to observe these trends, rather than the patchy distribution visible at finer scales, which is likely to be a consequence of non-climatic factors. It is equally important to apply predictive models at the right scale. It is often tempting to apply models on as fine a scale as the climate projections allow, as this will lead to detailed maps with an illusion of greater accuracy. However this temptation should be resisted and models based on climatic parameters alone should be applied at the scale at which they were fitted.

The lack of distribution data also impedes validation of these predictive models, as ideally they should be validated with data fully independent from those used to build the model (Austin, 2007; Heikkinen *et al*., 2006; Lawler *et al*., 2006). An issue with validation is that it often indicates the models ability to predict current distribution; models that are effective at predicting current distribution may not be so reliable when predicting future outbreaks (Hijmans & Graham, 2006). Hence there is a need to validate these models with data outside the spatial and temporal range of the training dataset. To make use of existing datasets for both model creation and validation there are ongoing developments in statistical methodology

to account for biases in reported data. Existing datasets can be utilised for modelling distributions if imperfect detection is considered, with irregular sampling intensity and false absences accounted for using hierarchical Bayesian models (Bierman *et al.*, 2010; Elith *et al*., 2006; Elith & Leathwick, 2009; Pagel & Schurr, 2012). Uncertainty in predictor variables can also be addressed through Bayesian analysis (McInerny & Purves, 2011).

Given sufficient data for creation and validation of correlative models, fundamental disadvantages remain. As correlative models are generated using distribution data they are based on the realized niche (Guisan & Zimmermann, 2000) which includes competitive exclusion and biotic interactions (e.g. the presence of hosts and other pathogens), rather than the fundamental niche. As distribution data are usually only available for a limited area or time window, correlative models are generally fitted using data reflecting a snapshot of the current climate-pathogen relationship. An assumption is therefore made that a species has reached equilibrium with its environment (Guisan & Thuiller, 2005). This ignores any non-climatic dispersal constraints that may be restricting the current range, or declining sink populations where presence is recorded but climate is not actually suitable for long-term population survival. This failure to account for non-equilibrium ranges is an inherent weakness in correlative models (Pearson & Dawson, 2003; Sutherst & Bourne, 2009). This weakness could be especially pertinent for emerging parasites which are very unlikely to be in equilibrium with their current environment, so could be absent from climatically suitable areas due to low propagule pressure. Conversely, these models will not identify areas which are not within bounds necessary for pathogen survival but where deleterious levels of parasitism could be reached given sufficient propagule pressure. This issue posed by the non-equilibrium nature of emerging pathogens could be addressed through training models for emerging parasites using distribution data from their long established native range (Bachrach, 2012).

Above all aforementioned limitations, dangers in extrapolating statistical models are especially pertinent to climate projections. The assumption that a species is in equilibrium with its current environment and the reliance on relationships between climate variables that may not exist in novel climate change scenarios leads to equivocal results when models are extrapolated spatially and temporally (Elith *et al*., 2006; Elith *et al.*, 2010; Elith & Leathwick, 2009; Kearney & Porter, 2009). We are likely to experience previously unseen climate combinations and climate parameters exceeding their currently observed ranges; parasites could be well adapted to these novel situations, however correlative models would assume these conditions to be unsuitable (Hijmans & Graham, 2006). Additionally, correlative

models cannot identify points where the system behaviour undergoes a non-linear change. It is this inability to extrapolate that further emphasises the need for a complementary modelling approach.

As a further testament to correlative models' often unreliable outputs, models created using different statistical approaches have been shown to produce conflicting distribution estimates, even when trained with the same distribution and climate data (Ortega-huerta & Peterson, 2008; Pearson *et al*., 2006). Such differences between distribution estimates can be exacerbated when extrapolating to novel climatic conditions (Thuiller, 2003). To address the divergence in model outputs, a framework for selecting the most robust statistical modelling technique has been developed (Thuiller, 2003). This approach would be useful for selecting optimal models for predicting changes in helminth distribution. The differences between distributions predicted by different models could also be informative; discovering why predictions differ could improve understanding of the main drivers, and quantification of the differences could inform decision making and risk analysis (Elith & Leathwick, 2009).

Despite their limitations, correlative models can provide a first indication of how climate will influence helminth distribution, and identify where limited resources and targeted surveillance should be focused. They provide a useful tool when too few elements of the transmission process have been quantified for the creation and parameterisation of mechanistic models. The limitations of correlative models are being addressed through continued development of statistical methodologies, led by work in both conservation and invasive species control; there is scope for these emerging approaches to be applied to predicting livestock parasite risk. Reliability of correlative models will ultimately be governed by the quality of data used for model training and validation, the statistical methods employed, the ecological and physiological knowledge on which inclusion of proximal variables is based, and discrepancies between the realized and fundamental niche.

1.2.2. The mechanistic approach

An alternative approach to understanding and predicting parasite risk is the process-based mechanistic approach. This approach is used in chapters three and four of this thesis. Mechanistic models are based on detailed knowledge of the physiology of the species (Hijmans & Graham, 2006) and attempt to replicate the underlying mechanisms that drive the species' response to environmental variables (Robertson *et al.,* 2003). Given sufficient

understanding of the parasites' physiology, these models can be employed to predict changes in outbreak patterns (Anderson, 1987). Previous mechanistic models have explored the dynamics of helminth infection in livestock (Callinan, Morley *et al.,* 1982; Cornell *et al.,* 2004; Dobson *et al.,* 1990; Gordon *et al.,* 1970; Learmount *et al.,* 2006; Leathwick *et al.,* 1992; Paton *et al.,* 1984; Roberts & Grenfell, 1991; Tallis & Donald, 1970). However these models have not been used to assess the impacts of climate change on helminth transmission.

One element of mechanistic modelling that makes it well suited to assessing the impacts of a changing climate is that it is less prone to extrapolation problems than the correlative approach. The mechanistic approach does not rely on relationships between climate variables that may cease to exist under future climate change (Dormann, 2007; Guisan & Zimmermann, 2000; Hijmans & Graham, 2006; Kearney *et al.,* 2010), making them less prone to breaking down when tested outside current observation limits. Consequently, the mechanistic approach is considered superior in extrapolating beyond current conditions and forecasting the impacts of climate change (Mangal *et al.,* 2008). The mechanistic approach also avoids some of the inherent problems that correlative models have when applied to emerging and invasive parasites since mechanistic models do not typically need to assume the species is in equilibrium with the environment (Pearson & Dawson, 2003). Mechanistic models typically account for non-linear interactions between a number of component parts which lead to emergent outcomes that are difficult to predict *a priori,* for example sudden changes in behaviour as one or more model parameters are varied

The severity of helminth infections is often dependent on intensity, rather than prevalence. The economic and welfare implications of outbreaks would be difficult to evaluate using a correlative approach, as data availability typically constrains these models to only look at prevalence. If data on adult worm burdens are available they are often based on indirect measures such as faecal egg count. It is more feasible to include models of adult worm burden within a mechanistic framework. By incorporating key mechanisms into the model structure more complex questions can also be addressed, such as determining the impact of climate on specific stages of the lifecycle, identifying potential non-linear responses, and assessing the efficacy of different control and mitigation strategies.

Unlike correlative models, mechanistic model development is not restricted by the paucity of accurate distribution data. Instead, the primary restriction to their development is the need for knowledge of the underlying biology, and the extensive physiological data needed for parameterisation (Guisan & Thuiller, 2005).

An oversight in some mechanistic models is that they assume Liebig's Law of the Minimum (Hijmans & Graham, 2006), which presumes that the overall response will be determined by the most limiting factor. This is not necessarily true. For example, larvae on pasture could survive otherwise deleteriously low levels of rainfall if temperatures were not too high. This emphasises the need to look at proximal, rather than distal variables – in this case water availability rather than levels of rainfall. It also emphasises the importance of looking at variables in combination.

In contrast with the correlative approach, mechanistic models are based on measured physiological and behavioural parameters, and reflect the fundamental rather than realized niche (Guisan & Thuiller, 2005). This leads to over estimation of risk showing the whole potential range if dispersal restrictions or biotic interactions are not accounted for (Aurambout *et al.,* 2009; Hijmans & Graham, 2006; Lafferty, 2009; Pearson & Dawson, 2003). The extent of predictive errors will be partly dependent on the proportion of the fundamental niche that the realized niche occupies (Guisan & Thuiller, 2005). This proportion will depend on the parasites' dispersal and competitive abilities; if the discrepancies between the species' fundamental and realized niche could be identified, it could give an indication of how accurate predictive models could be for particular species.

To attain realistic predictions of species distribution, models should ultimately integrate constraints from biotic interactions and dispersal (Guisan & Thuiller, 2005). Projections often assume either complete dispersal, where the parasite can reach all areas with permissive climes, or no dispersal where presence is only predicted in areas of its current range where climate remains within viable thresholds (Guisan & Thuiller, 2005). It is overly simplistic to assume that a species will either fully disperse to fill the fundamental niche, or that they will only survive in areas where the projected fundamental niche and current realized niche overlap (Lawler *et al*., 2006), however, this approach does at least provide (often very wide) bounds on the possible distribution. The importance of incorporating species interactions in prediction models has been demonstrated (Araújo & Luoto, 2007; Davis *et al.,* 1998; Kearney & Porter, 2009), with biotic interactions influencing the predictive power of correlative models even at the macro-ecological scale (Araújo & Luoto, 2007).

The incorporation of dispersal also influences predictive power (Engler & Guisan, 2009; Hooten *et al.,* 2007; Pagel & Schurr, 2012), with the disparity between models that do incorporate dispersal and those that do not increasing under more extreme climate warming

scenarios (Engler & Guisan, 2009). The integration between model projections, biotic interactions and simulated host/pathogen distribution and dispersal patterns would improve the accuracy of predictive models (both correlative and mechanistic). This could be achieved through the adoption of hierarchical Bayesian frameworks (Hooten *et al*., 2007). However, these should take into account that biotic interactions and dispersal abilities could change with time. Due to the high selective pressures that novel conditions are likely to impose, climate change is likely to select for phenotypes with enhanced dispersal capabilities that can track the shift in their climate envelope. This would affect the parameterisation of models that incorporate dispersal.

Mechanistic models provide a powerful tool in predicting the influence of climate change on helminth risk. They are comparatively robust under spatio-temporal extrapolation and can be developed to address complex questions. However, a move towards a mechanistic approach should not be seen as a way of alleviating the need for field data; to develop and validate models and assess their continued reliability under changing conditions, there is a need for ongoing surveillance.

1.3 The thesis

1.3.1 Aims

The overall aim of this thesis is to understand the impacts of climate change on livestock helminths in the UK. In order to address this aim, a species-specific prediction of changes in parasite risk at a coarse spatio-temporal scale is first made, using a correlative modelling approach. More subtle interactions between climate and parasite transmission are then explored at a finer scale, through the development of a process-based mechanistic model.

1.3.2 Structure

The first part of the introductory chapter reviews the broader impacts of climate change on livestock pathogens, identifying disease threats to the UK livestock industry and revealing lacunas in research. This review concludes that macro-parasite transmission is strongly

affected by abiotic conditions, and specifically identifies a need for long-term predictions of future helminth risk. The second part of chapter one explores approaches to generating long-term predictions of helminth risk, highlighting the obstacles to generating meaningful predictions, and identifying optimal approaches based on data availability and model purpose.

In chapter two a correlative model of fasciolosis risk is applied to long-term observed climate data to illustrate how intensity and distribution have already been influenced by climate change. This model is then combined with climate projections to predict future fasciolosis risk across the UK. The resultant maps allow comparison between past and future risk, in addition to highlighting regional differences, and expected changes in seasonal patterns of outbreaks.

To explore more subtle interactions between parasite transmission and climate, a process based approach is required. Chapter three details the development of a mechanistic model which incorporates both the host's immunological response to parasitism and key grazing behaviours. This integrated approach also incorporates other important elements of the transmission process: survival and development of the parasite both within the host and on pasture; spatial heterogeneity of both pathogens and resources; and the interactions between host grazing behaviour and parasitised state. Macro-parasite transmission is then explored in a spatially and temporally heterogeneous environment, demonstrating the importance of both host behaviour and immune response.

Using the transmission model developed in chapter three, chapter four aims to determine how changes in climate sensitive elements of the transmission process influence macro-parasite risk. Specifically, it explores how nematode outbreaks are influenced by 1. Changing parasite development rates; 2. Changing death rates of the free-living stages; 3. Over-winter survival of the parasites' free-living stages; 4. Host resistance under changing conditions; and 5. Seasonal fluctuations in key rates and changes in the timings of livestock management. This approach can help assess the efficacy of different mitigation and adaptation approaches under future climate change scenarios.

Each modelling chapter is preceded by a preface, providing the wider context for the chapter. In chapter five, the main findings are summarised, and limitations of the predictive models are discussed. Potential applications and future developments are also explored.

Chapter 2

Predicting the impacts of climate change on *Fasciola hepatica* risk

2.1 Preface

In the following chapter, the impacts of climate change on *Fasciola hepatic* (liver fluke) risk are explored. Fasciolosis has an impact on livestock production in most regions of the world where sheep and cattle are reared (McIlroy *et al*. 1990). The distribution, magnitude and timing of fasciolosis outbreaks have been changing in the UK (VLA, 2008). The overall increase in fasciolosis has been associated with climate change (Rojo-Vázquez *et al.,* 2012).

Due to the impacts of fasciolosis on livestock, and the close links with environmental conditions, a number of short term prediction models for fasciolosis have been created (Asrat *et al*., 2007; Gettinby *et al.,* 1974; Malone et al., 1998; McIlroy *et al.,* 1990; Ollerenshaw & Rowlands, 1959; Rapsch *et al*., 2008; Yilma & Malone, 1998). Despite the plethora of short-term predictive models, long-term projections of future risk under climate change remain elusive.

The generation of long-term predictions of future *F. hepatica* risk will enable surveillance strategies to be targeted, and long term control strategies to be developed and implemented. In the following chapter, the first long term predictions of liver fluke risk are made using a correlative method which synthesises an existing model with the latest climate change projections.

There are a number of factors that make correlative modelling the preferred approach for determining fasciolosis risk. Firstly, the existence of long term prevalence data facilitated the development of a statistical model (Ollerenshaw & Rowlands, 1959). Secondly, despite their complex life cycle, the distribution of liver fluke is driven by simple proximal drivers – temperature and water availability. It is these drivers that form the basis of the correlative model. Thirdly, their dispersal by wild hosts and speed of colonisation of new regions makes

them ubiquitous where livestock are present across their fundamental niche, so spatial dispersal does not need to be explicitly incorporated.

This chapter formed the basis of the publication: Fox NJ, White PCL, McClean CJ, Marion G, Evans A, Hutchings MR. (2011) Predicting Impacts of Climate Change on *Fasciola hepatica* Risk. PLoS ONE 6(1): e16126. doi:10.1371/journal.pone.0016126

2.2 Summary

Fasciola hepatica (liver fluke) is a physically and economically devastating parasitic trematode whose rise in recent years has been strongly associated with climate change. Climate has an impact on the free-living stages of the parasite and its intermediate host *Lymnaea truncatula*, with the interactions between rainfall and temperature having the greatest influence on transmission efficacy. There have been a number of short term climate driven forecasts developed to predict the following season's infection risk, with the Ollerenshaw index being the most widely used.

Through the synthesis of a modified Ollerenshaw index with the UKCP09 fine scale climate projection data a long term seasonal risk forecast is developed, up to 2070 at a 25km square resolution. Additionally UKCIP gridded datasets at 5km square resolution from 1970-2006 were used to infer the climate-driven component of the increase over this period.

The maps show unprecedented levels of future fasciolosis risk in parts of the UK, with risk of serious epidemics in Wales by 2050. The seasonal risk maps demonstrate the possible change in the timing of disease outbreaks due to increased risk from overwintering larvae. Despite an overall long term increase in all regions of the UK, spatio-temporal variation in risk levels is expected. Infection risk will reduce in some areas and fluctuate greatly in others with a predicted decrease in summer infection for parts of the UK due to restricted water availability. This forecast is the first approximation of the potential impacts of climate change on fasciolosis risk in the UK. It can be used as a basis for indicating where active disease surveillance should be targeted and where the development of improved mitigation or adaptation measures is likely to bring the greatest benefits.

2.3 Introduction

Fasciolosis is responsible for economic loss in most regions of the world where sheep and cattle are reared (Mcllroy *et al.*, 1990). It is a physically and economically devastating disease; heavily infected hosts may die, those with lighter infections may suffer inhibited growth and reduced production efficiency, while the detection of pathological lesions lead to invariable liver condemnation (Goodall *et al.*, 1991; Mcllroy *et al*., 1990; Rapsch *et al*., 2008). Patterns of fasciolosis outbreaks also have wider implications; Claridge *et al*., (2012) found a significant negative correlation between presence of *F. hepatica* and diagnosis of Bovine tuberculosis (BTB), due to the sensitivity of the principle BTB diagnostic test being reduced by the influence of *F.hepatica* on the host's immune response. Therefore changing fluke levels could impact on the efficacy of BTB control strategies (Claridge *et al*., 2012).

Through examining the influence of abiotic factors on each stage of the complex lifecycle, the potential for climate change to impact parasite risk can be appreciated. *F. hepatica* has a multi host lifecycle with its adult stage being a denizen of the definitive hosts bile duct (Sukhdeo *et al.*,1987). Eggs are excreted with the definitive hosts faeces, and the rate that eggs hatch into free-living ciliated miracidia increases with rising temperatures. Survival of the free-living stages is also dependent on moisture levels, due to susceptibility to desiccation. Asexual reproduction occurs inside the intermediate host, *Lymnaea truncatula* (dwarf pond snail), and cercariae are produced. Within *F. hepatica*'s developmental range, temperature increases are coupled with a rise in both rate and quantity of cercariae production (Mas-Coma *et al.*, 2009; Poulin, 2006). This may be a result of the accelerated metabolic rate of the host and the subsequent increase in energy available to the parasite (Mas-Coma *et al*., 2009). Climatic conditions also impact on the survival and development of *L. truncatula*. A temperature range of 10-25^{o}C is needed for snail survival (Rapsch *et al*., 2008) with increased temperatures in this range accelerating development (De Waal *et al*., 2007). Additionally, the snails require areas of standing water, so precipitation and evapotranspiration levels influence habitat availability (Mas-Coma *et al*., 2009). High sunlight levels also aid *L. truncatula* survival as higher levels of solar radiation promote the growth of the algae on which they feed (Rapsch *et al*., 2008). The relationship between rainfall and temperature is important as snails are vulnerable to aestivation if conditions become too dry (Goodall & Menzies, 1995).

Once released from the intermediate host, cercariae encyst as infective metacercariae on vegetation which the definitive host then ingests (Sukhdeo *et al*., 1987). Once within the herbivorous host the larvae take three months to reach sexual maturity (Olsen, 1947). There

is a negative correlation between temperature and metarcercariae survival (O'Connor *et al*., 2006; Rapsch *et al*., 2008), as they become more active at higher temperatures and deplete their finite resources faster. It has been suggested that *F. hepatica* has an optimum development temperature between 15-22^{o}C (Goodall & Menzies, 1995) and an upper limit of 23^{o}C (Malone et al., 1998), with eggs dying when temperatures exceed 30^{o}C (Rapsch *et al*., 2008). However, with an extensive range including the warmer regions of Australia, Africa and India, it is unlikely that *F. hepatica* will be pushed beyond its development threshold in the UK within the time scale considered here.

As with many parasites there is a distinct seasonal pattern in fasciolosis outbreaks, (Altizer *et al.*, 2006; Goodall & Menzies, 1995) with two key periods of infection, summer and winter. Summer outbreaks occur when snails are infected in late spring and early summer, with infections maturing during the summer and disease levels peaking during the late autumn/ winter period (Goodall & Menzies, 1995; Mcllroy *et al*., 1990). Winter infection occurs when eggs excreted during unfavourable winters commence development in early spring, once suitable conditions are encountered, (Goodall *et al*., 1991; Luzon-Pena *et al.*, 1994), with infection typically evident in the host from July to October (Ollerenshaw, 1966).

Being a temperate species *F. hepatica* has a wide geographical range, covering Southern and Northern America, Europe, Africa, India and Australia (Asrat *et al*., 2007). Fasciolosis is increasing across Europe (De Waal *et al*., 2007), and there is evidence to suggest that it is increasing in the UK (VLA, 2008). Changes in timing of outbreaks have also been observed with an increase in acute fasciolosis in sheep by mid-summer in parts of the UK (De Waal *et al*., 2007; Taylor, 2012), suggesting that climate change is already having a measurable influence on disease dynamics through milder winters supporting the development of overwintering larvae (Van Dijk *et al*., 2010). Although the increase in fasciolosis in the UK is thought to be influenced by climate change (Kenyon *et al.*, 2009b; Mas-Coma *et al*., 2009; Van Dijk *et al*., 2010) the link has not been proven due to the paucity of long term studies and lack of consistent disease incidence data (Van Dijk *et al*., 2008).

The strong links between climate and fasciolosis levels have facilitated the creation of short term forecasting models. These short-term forecasts can help to predict fasciolosis incidence and severity at local and regional scales, allowing the development and implementation of improved control strategies (Asrat *et al*., 2007; De Waal *et al*., 2007; McCann *et al.*, 2010), with strategic chemical use helping slow the development of resistance.

Short-term prediction models for fasciolosis have been created for many regions across the globe including the USA (Malone *et al.*, 1987; Malone & Zukowski, 1992; Zukowski *et al.*, 1993), Africa (Asrat *et al*., 2007; Malone *et al*., 1998; Yilma & Malone, 1998), Bolivia (Fuentes *et al.*, 2001) and the UK (Ollerenshaw & Rowlands, 1959). These models are created using various techniques including process-based mechanistic modelling (Gettinby *et al*., 1974), correlative models based on surveillance data (Ollerenshaw & Rowlands, 1959) or liver condemnations (Mcllroy *et al*., 1990), and a trend towards GIS models (Asrat *et al*., 2007; Malone *et al*., 1998, 1987; Malone & Zukowski, 1992; McCann *et al*., 2010; Zukowski *et al*., 1993).

Of all the forecast models the Ollerenshaw index (Ollerenshaw & Rowlands, 1959) was the first widely used system to predict acute outbreaks and manage control strategies in the UK. It was developed using *F. hepatica* prevalence data and climate data from farms and meteorological stations from 1948 to 1957 with a seasonal index derived from measured rainfall, number of rain days and potential evapotranspiration. The National Animal Disease Information Service (NADIS) currently provides farmers with short-term forecasts of fasciolosis risk based on the Ollerenshaw index (NADIS, www.nadis.org.uk).

The emphasis of previous forecast systems has been on predicting risk for the subsequent year to inform the farming industry and facilitate the implementation of appropriate control measures. So far no models have been applied to long-term climate data to illustrate how intensity and distribution may vary over an extended time scale. Showing where the greatest changes are likely to occur will allow surveillance to be most efficiently targeted. The release of UKCP09, with fine scale predictions for a number of climate variables (UKCP09, 2009b), provides the opportunity to make meaningful long term projections. Here a modified Ollerenshaw risk index is combined with the UKCP09 climate data to predict how climate change will influence fasciolosis risk, up to 2070. Risk maps for 1961-2005 are also created to illustrate how climate has already influenced risk. Risk maps for summer and winter infection risk are generated independently to allow changes in timing of disease outbreaks to be considered. The resultant maps allow comparisons between future risk and risk levels experienced to date, in addition to highlighting the regional differences and expected changes in seasonal patterns of outbreaks.

2.4 Methods

To calculate *F. hepatica* infection risk, the Ollerenshaw index was used, with some slight modifications due to the availability of climate data. This model is dependent on the interactions between rainfall and temperature, with the monthly fasciolosis risk value (Mt) calculated as below (Ollerenshaw & Rowlands, 1959):

$$Mt = n\left(\frac{R}{25.4} - \frac{PE}{25.4} + 5\right)$$

Mt = Fasciolosis risk value,
n = Number of rain days per month,
R = Rainfall (mm/month)
PE = Potential evapotranspiration (mm/month).

For the calculation of potential evapotranspiration (*PE*), the Hargreaves equation for evapotranspiration was used, where *Ra* is extraterrestrial radiation (MJ m^{-2} day^{-1}) (Droogers & Allen, 2002), T_{max} is the monthly average of the daily highest air temperature (^{o}C), T_{min} is the monthly average of the daily lowest air temperature (^{o}C):

$$PE = 0.0023 \times 0.408 \times R_a \left(\frac{T_{max} + T_{min}}{2} + 17.8\right)\sqrt{T_{max} - T_{min}}$$

Below, the key elements of the Ollerenshaw index are briefly described. For a full description of the Ollerenshaw index see Ollerenshaw & Rowlands (Ollerenshaw & Rowlands, 1959). An Mt value was first calculated for each month and these monthly values are subsequently summated to give seasonal risk values (summer and winter). Mt was set to zero if the mean monthly temperature was below 10^{o}C, to reflect the development thresholds for both the free living stages of *F. hepatica* and *L. truncatula*. The mean temperature was used as fasciolosis transmission can occur when night time temperatures are below the minimum development threshold of 10^{o}C if they are compensated for by high day time temperatures (Mas-Coma et al., 2009). When the model was originally created mean temperatures were only above 10^{o}C between May and October, hence only these months were included in the model. As temperatures have increased over the past five decades, and are predicted to continue rising (UKCP09, 2009a), the modified method used here includes all

months with a mean temperature greater than 10°C. As with the original model a restriction was applied to the calculation to allow for exceedingly wet years. When the monthly Mt value reaches 100 it can be assumed that the moisture levels, regardless of previous state, have become sufficiently wet to permit parasite development (Ollerenshaw & Rowlands, 1959). Consequently, monthly Mt values are capped at 100. The cap of 100 was always reached when number of rain days per month exceeded 18.

For the risk maps, the seasonally summated summer and winter Mt values were grouped into four risk categories following Ollerenshaw & Rowlands (Ollerenshaw & Rowlands, 1959): $Mt < 300$, little or no disease; $300 < Mt \leq 400$, occasional losses; $400 < Mt \leq 474$, disease prevalent; and $Mt > 474$, serious epidemic.

2.4.1 Climate data

2.4.1.1 Past

For the calculation of past fasciolosis risk, climate data were obtained from the UKCIP gridded datasets (Met Office, 2010). These data are based on interpolations of surface observations, which provide a grid of values for 5km squares across the UK. Each value represents a point at the centre of the 5km square and the Ordnance Survey National Grid was used to identify the grid cells. Monthly data from 1970 to 2006 were used, with the following climate variables: minimum, maximum and mean monthly temperature (°C), number of rain days per month (>1mm), and monthly rainfall (mm).

2.4.1.2 Future

For predicting future fasciolosis risk, the UKCP09 climate data were used from the HadCM3 climate model (UKCP09, 2009b), using monthly climate change averages at 25km square resolution for six 30 year time periods: 2010-2039, 2020-2049, 2030-2059, 2040-2069, 2050-2079, 2060-2089. In the analysis these time periods are referred to as 2020, 2030, 2040, 2050, 2060 and 2070 respectively. The medium emissions scenario (IPCC SRES:A1B) was used. The climate variables used were: Mean temperature (°C), mean daily maximum temperature (°C), mean daily minimum temperature (°C), precipitation (mm/day), total cloud (%) and relative humidity (%).

2.4.2 Comparing past and future risk

For comparison between past and future risk, long term climate averages were used. Past Mt risk was calculated using long term average data from 1961-1990. These data were based on the regional climate model and were downloaded at a resolution of 25km squares (Met Office, 2010). The future long term average was calculated using the modified Ollerenshaw method and average climate data from 2030-2070, at a resolution of 25km squares (UKCP09, 2009b).

2.4.3 Modification for future projection

As there are no projections for rain days, a model was created to calculate a surrogate rain days value using available climate parameters. The model was created using the 1961-1990 long term monthly averages (LTA), from the UKCIP 25km gridded data set covering the whole of the UK (Met Office, 2010). This dataset included the variables: percentage cloud cover (%), maximum temperature (^{o}C), minimum temperature (^{o}C), mean temperature (^{o}C), relative humidity (%), rainfall (mm/day) and number of rain days (days/month). Data from all parts of the UK for all months of the year were included.

To determine a surrogate value for rain days using other climate variables a generalized additive model (GAM) was used as this allows the modelling of non linear relationships (Zuur *et al.*, 2007) with the smoothing functions enabling non-parametric response curves to be fitted separately to each predictor variable (Lawler *et al*., 2006). The gam function from the mgcv library in R was used (Wood & Augustin, 2002).

The GAM was built using the 1961-1990 LTA climate data (Met Office, 2010). The climate data were split spatially with the training data set comprising a randomly selected 80% of the points (n = 4215). The variables with colinearity (minimum temperature and maximum temperature) were removed and the remaining variables were pre-screened by fitting GAM models to each variable in isolation. The remaining parameters included in the model were selected using generalised cross validation (GCV) (Wood & Augustin, 2002). Parameters included were number of rain days, mean temperature, cloud cover, rainfall and humidity with the final model explaining 90.2% of the deviance ($P<0.0001$ (for all variables), GCV = 1.117).

The predictive power of the model was first evaluated using the test dataset, comprised of the remaining 20% of the 1961-1990 long term average climate data (n = 1054). Figure 1 shows

the predicted rain days and the actual rain days put into bins of integer rain days, ± the coefficient of variation. The Ollerenshaw model is capped when rain days exceed 18, as above this value the area is considered moist enough to allow for maximal larval development, and any higher value would not increase infection risk any further.

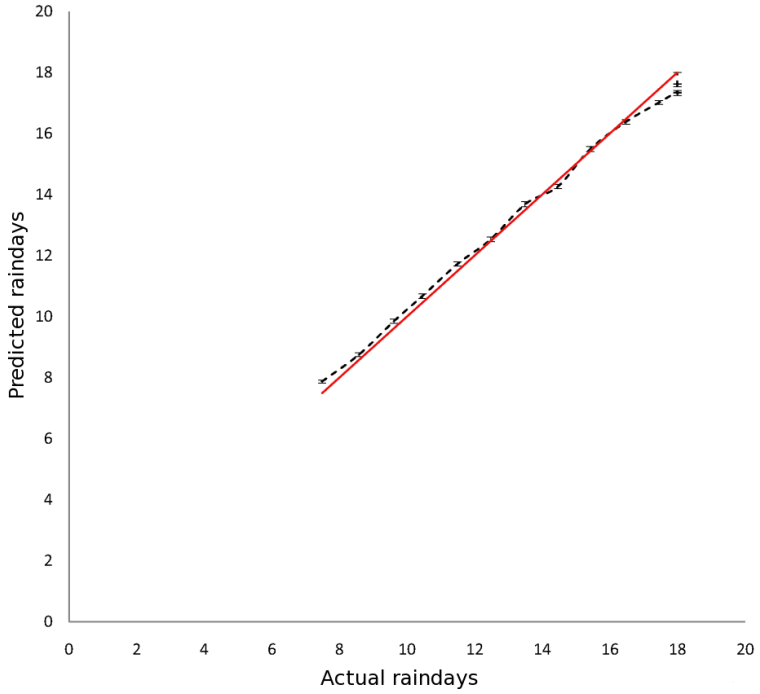


Figure 1. The number of rain days predicted using the GAM against the actual number of rain days (- - - - -) (± coefficient of variation). The line of perfect correlation is also shown (——).

This validation suggests that the model is accurate when extrapolating spatially, indicating the models reliability when applied to novel climatic conditions (Figure 1). To substantiate the accuracy when extrapolating temporally the model predictions were tested on the 1991-2000 monthly gridded data-sets (Met Office, 2010), with 10 year monthly averages for all parameters. Despite applying the model to data of a different temporal and spatial resolution to the training data-set, it still provides a reliable surrogate for rain days, with the model explaining 92% of the variation (R^2=0.92, df = 1210, mean predicted – mean actual = 0.6 rain days).

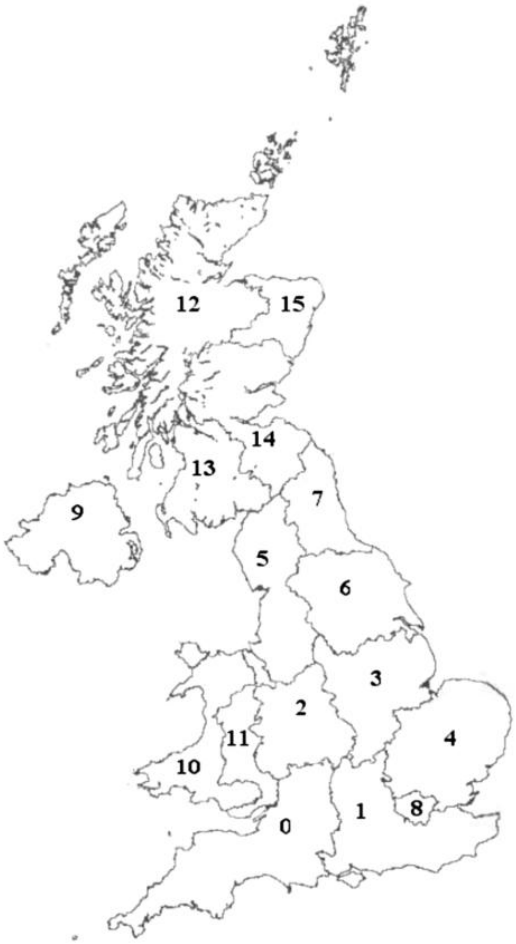
In a further validation of the model, using the 1961-1990 test dataset (n = 1054), the Mt values were first calculated using the original Ollerenshaw index, and then calculated using the modified Ollerenshaw index, with the GAM providing a surrogate value for rain days.

There was no significant difference in Mt calculated using the original and modified approach (Paired t-test, t=1.42, df = 1052, p-value > 0.1) for the historic period.

The modified Ollerenshaw index was therefore used to calculate future fasciolosis risk.

2.4.4 Spatial analysis

Fine scale risk maps for past and future Mt were generated using ArcGIS (Figures 3 and 5). However, comparisons between past and future risk were made at the scale of the regions shown in figure 2. These follow administrative boundaries with GIS layers downloaded and merged from EDINA (EDINA. http://edina.ac.uk/ukborders).



Code	Region
0	South West
1	South East
2	West Midlands
3	East Midlands
4	East of England
5	North West
6	Yorkshire and The Humber
7	North East
8	London
9	Northern Ireland
10	West Wales and The Valleys
11	East Wales
12	Highlands and Islands
13	South Western Scotland
14	Eastern Scotland
15	North Eastern Scotland

Figure 2. The 15 regions of the UK used in comparing past and future risk. England = 0-8, Northern Ireland = 9, Wales = 10-11, Scotland = 12-15.

2.5 Results

2.5.1 Reconstructing past risk

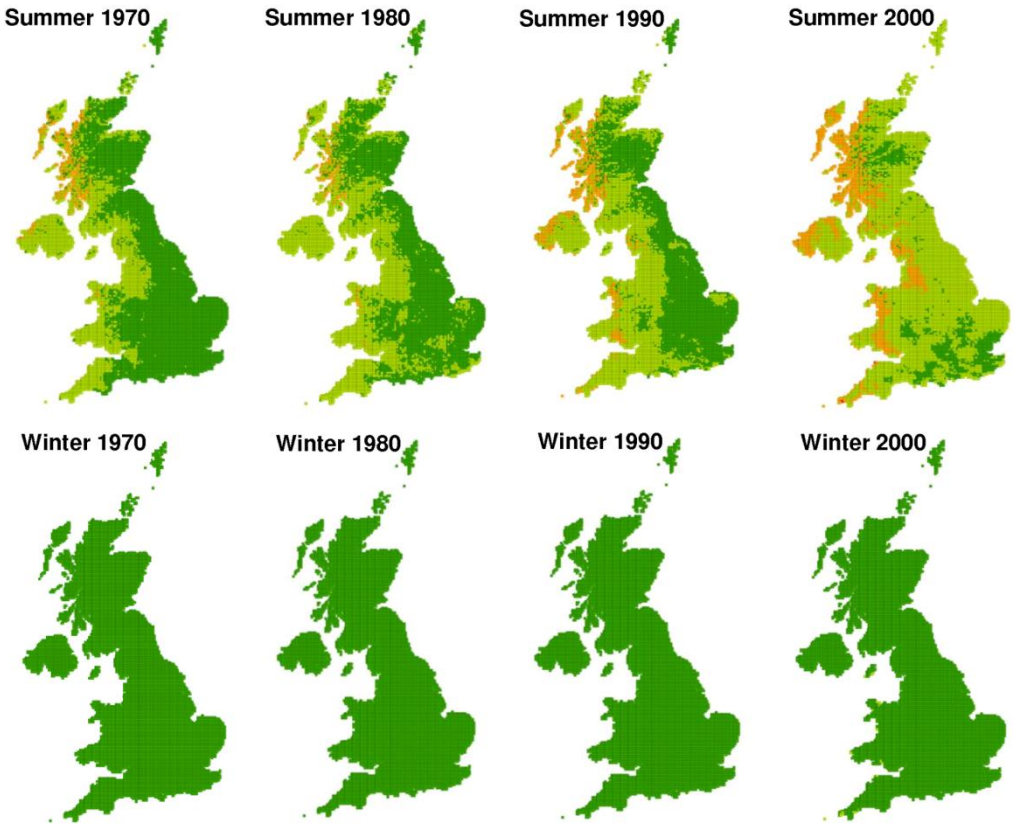


Figure 3. Past change in fasciolosis risk. Decade averages of summer and winter *F.hepatica* risk across the UK at a resolution of 5km squares, 1970-2006. Risk categories of monthly fasciolosis risk value (Mt) are based on those used by Ollerenshaw & Rowlands (1959): Little or no disease: Mt < 300 (■), occasional losses: 300 < Mt ≤ 400 (■), disease prevalent: 400 < Mt ≤ 474 (■), serious epidemic: Mt > 474 (■).

The average fasciolosis risk from summer infection has increased across the past four decades. The maps indicate that in the 1970s a majority of the UK was fasciolosis free, however by 2000 most of the UK was suffering occasional losses, with disease being prevalent in large sections of west Wales and Scotland (figure 3). This pattern of increase across the UK echoes the trends reported from passive surveillance records (Kenyon *et al.*, 2009b; McCann *et al*., 2010; Van Dijk *et al*., 2008; VLA, 2008). There has been little change in risk from overwintering larvae, however by 2000 there are areas of Cornwall and the

Welsh west coast showing occasional losses, as minimum development threshold temperatures have been exceeded in recent years.

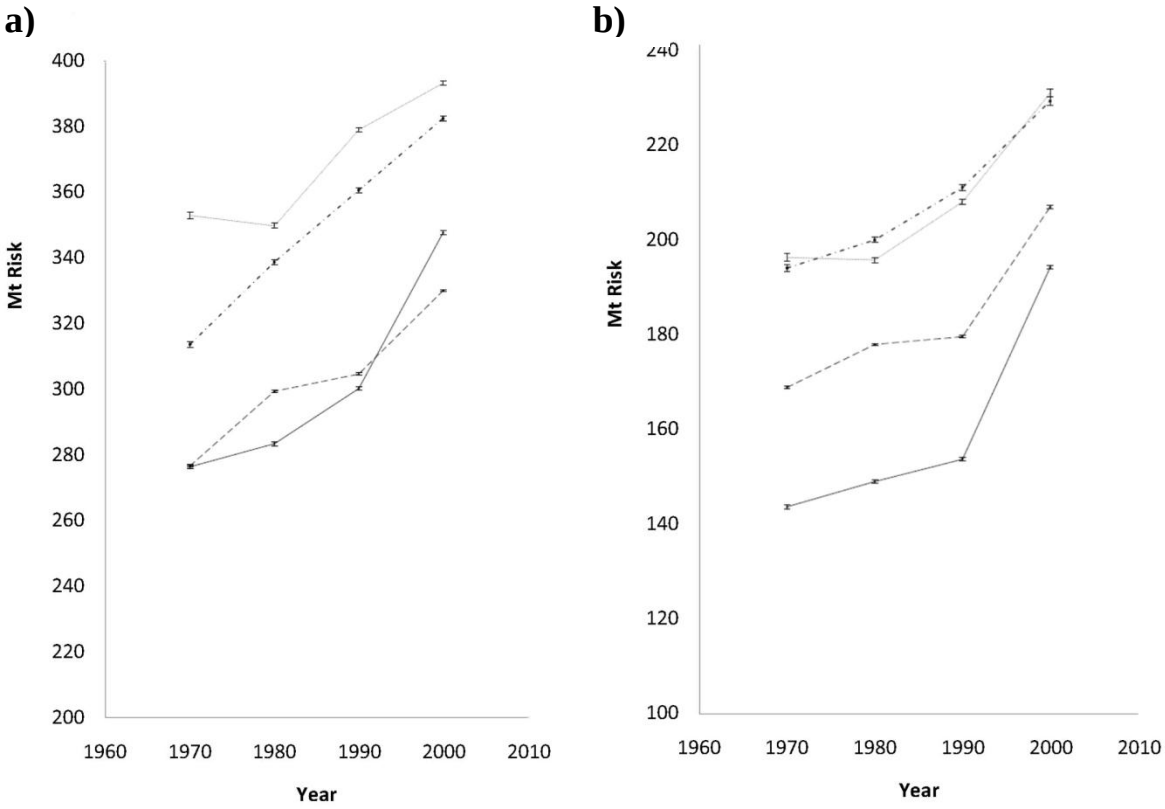


Figure 4. Past trends in fasciolosis risk. Change in *F. hepatica* risk for England (— — —), Scotland (———), Wales (· - · - ·) and Northern Ireland (·····), 1970-2006 (± SE) for a) summer and b) winter. (Mt = monthly fasciolosis risk value). The standard error values show the variation in Mt level across all grid squares within each region.

There has been a steady rise in *F. hepatica* risk in all parts of the UK (figure 4). Northern Ireland and Wales have so far experienced the highest levels of fasciolosis risk, with Scotland showing higher summer levels than England since the 1990s. The mean risk from overwintering larvae has increased in all parts of the UK (figure 4b). This matches reported changes in timing of fasciolosis infection, with outbreaks occurring earlier in the year due to the ingestion of overwintering larvae (De Waal *et al*., 2007). Despite the steady increase in winter risk index, a majority of the UK remains in the lowest risk category.

2.5.2 Predicting future risk

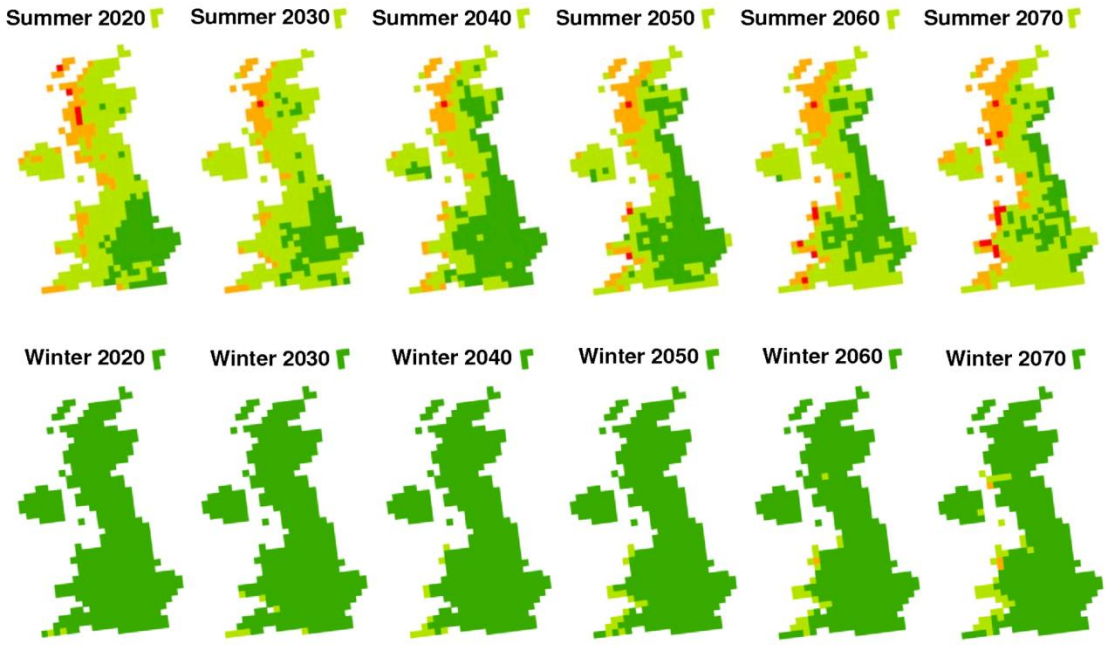


Figure 5. Projected change in fasciolosis risk. Summer and winter *F. hepatica* risk across the UK at a resolution of 25km squares, 2020 – 2070. Risk categories are based on those used by Ollerenshaw & Rowlands (1959): Little or no disease: Mt < 300 (■), occasional losses: 300 < Mt ≤ 400 (■), disease prevalent: 400 < Mt ≤ 474 (■), serious epidemic: Mt > 474(■). (Mt = monthly fasciolosis risk value)

The future risk maps show the projected change in fasciolosis risk from both winter and summer outbreaks (figure 5). The summer maps illustrate that predicted risk increases in certain areas, with serious epidemics predicted in Wales by 2050. However due to the complexity of future climate change and the long term variation in the system, risk will reduce in some areas and fluctuate greatly over time in others. A steady increase in risk from overwintering larvae is depicted along the West Coast as mean monthly temperatures exceeding 10^{o}C become commonplace, with Wales again being most at risk.

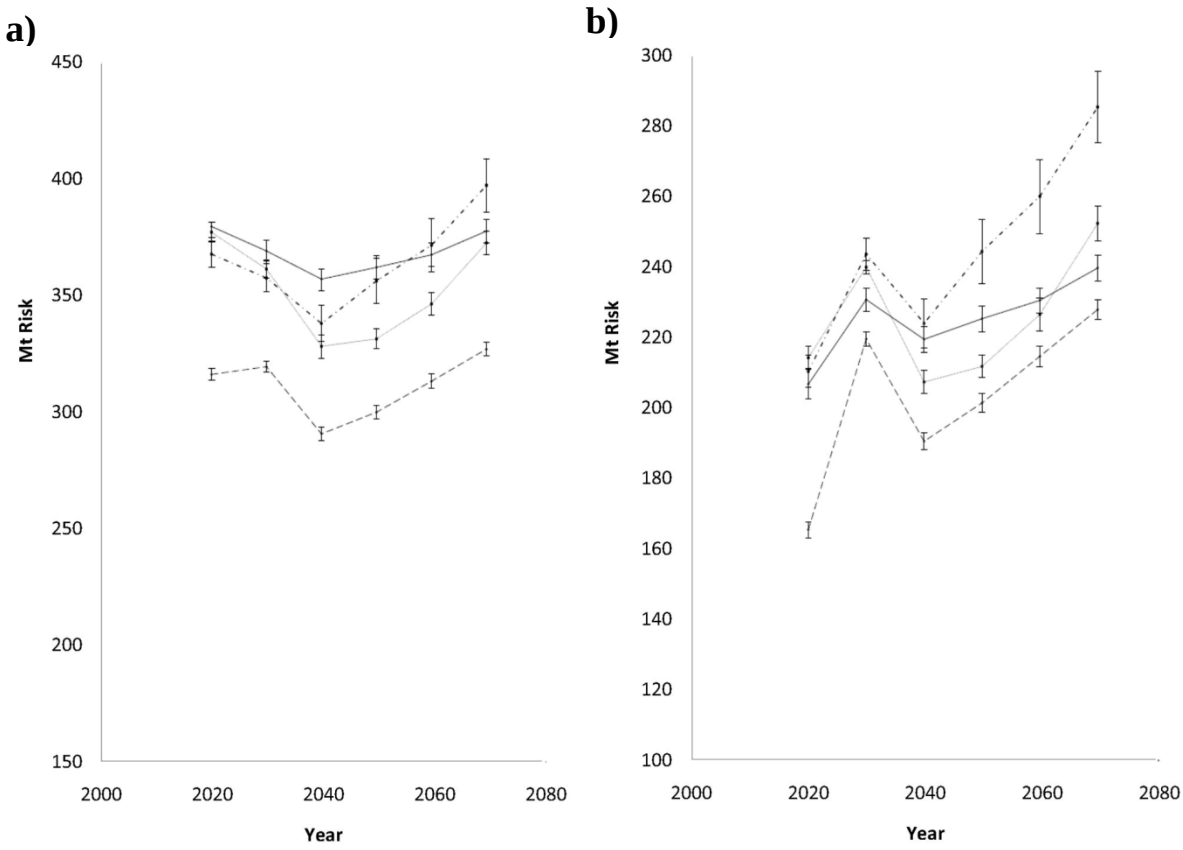


Figure 6. Future trends in fasciolosis risk. Predicted change in *F. hepatica* risk for England, (·····), Scotland (— — —), Wales (———) and Northern Ireland (- · - · - ·), 2020-2070 (± SE) for a) summer and b) winter. (Mt = monthly fasciolosis risk value). The standard error values show the variation in Mt level across all grid squares within each region.

In terms of the overall trend in summer risk by country, Wales shows the greatest rise (figure 6a). The non-linear increase in all regions due to the fall in 2040 echoes a decline in predicted summer rainfall during this time period. There is a projected rise in risk from overwintering larvae across the UK, with the greatest rise being in Wales (figure 6b). The steep rise in 2030 is due to high levels of predicted rainfall.

2.5.3 Comparing past and future risk

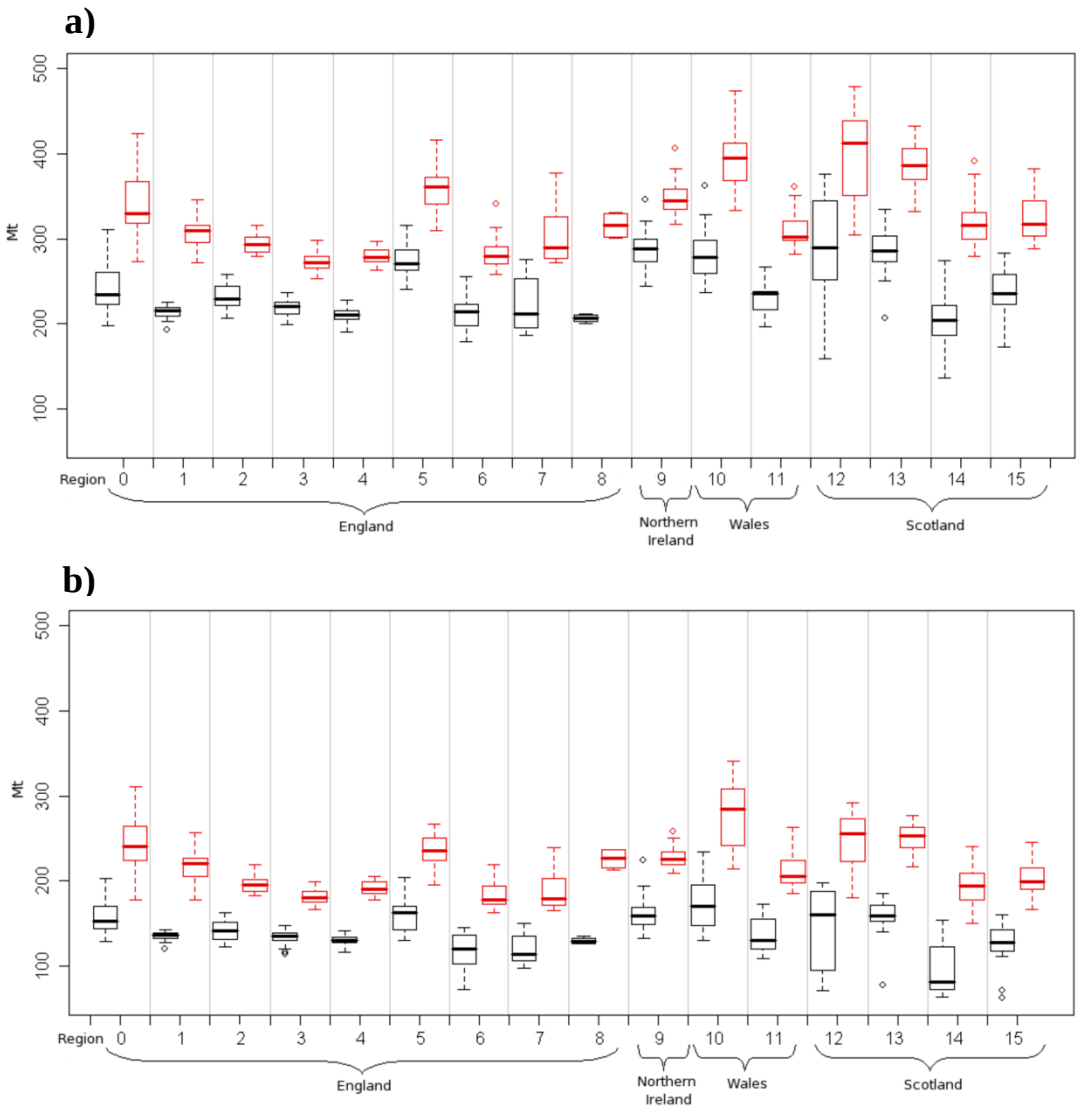


Figure 7. Comparing past and future risk. *F. hepatica* risk for each region for both 1961-1990 (———) and 2030-2070 (———) long term averages, for a) summer and b) winter. For region codes see figure 2. (Mt = monthly fasciolosis risk value)

The mean fasciolosis risk in each season will be higher in the future than the past for all regions of the UK (figure 7), with the highest overall risk being in West Wales (region 10). There is intra-region variability predicted, with the Highlands of Scotland (region 12) showing the greatest range in risk.

2.6 Discussion

Over the past four decades fasciolosis risk has spread across the UK from a restricted distribution in 1970, with only occasional cases seen in the west, to the current levels where large swathes of the UK are seeing regular outbreaks. The increase that is evident in the 1970-2006 risk maps is consistent with empirical data (Kenyon *et al.*, 2009b; Pritchard *et al*., 2005; VLA, 2008) and provides further evidence that the changes in fasciolosis in the UK are indeed climate-driven. The reliability of the Ollerenshaw index is further substantiated by the agreement between the map of current risk levels and the latest fasciolosis prevalence data (McCann *et al*., 2010). However the lack of long term, fine scale prevalence data makes quantitative validation of the model impossible.

Although liver fluke has been having a big impact on farms in recent years, according to the Ollerenshaw index we are yet to experience extended large scale epidemics. It is predicted here that the UK may experience unprecedented levels over the next 60 years, with the overall future risk from fasciolosis set to be higher than the past risk for all regions of the UK. The future maps show that serious epidemics are expected to be the norm by 2020 in parts of Scotland, and by 2050 in parts of Wales. Due to the coarser scale of the future risk maps, localised areas of serious epidemic could be more easily obscured; for a serious epidemic risk to show on the map a high increase in the average risk index is required throughout a 25km square over a 30 year period.

The model drivers are rainfall, temperature, and the interactions between them. Temperature has the major impact in areas where the mean temperature is raised above the 10^{o}C threshold and rain is not restrictive. This is especially pertinent in the Scottish Highlands in the summer months. The rise in temperature also accounts for the change in risk from overwintering larvae with the increased temperature in the winter months permitting their survival and development, resulting in a spread of risk heading north along the West Coast. Where temperatures are already above the development threshold of 10^{o}C the primary driver becomes changing rainfall patterns. Risk is highest in areas with extended high annual rainfall, high soil moisture and surplus water. Where high temperatures are combined with decreased rainfall the resulting soil moisture deficits will threaten the intermediate hydrophilic stages of the parasites life cycle. This accounts for the trend seen along the East Coast of the UK where future risk decreases from a current level of ‘occasional losses’ to a state of little or no disease by 2040.

Interactions between rainfall and temperature account for the fine scale spatial variation within each region with some locations set to experience diminishing infection levels. For example there is a predicted decrease in the warmer and drier parts of the South West, although this decrease is not enough to drive an overall decline at the regional level. The highest within region variation is seen in the Scottish Highlands, where the levels of spatial climatic variability are highest. The lowest variation is in the East Midlands and East of England, where rainfall and temperature levels are more consistent across each region. Although intra-region variation is of interest, caution must be exercised when applying the Ollerenshaw index at too fine a spatial resolution. At the local level a myriad of non climatic factors begin to exert the dominating influence over *F. hepatica* survival and development (Asrat *et al*., 2007; Malone & Zukowski, 1992).

In addition to spatial variation, there will be temporal variation in infection risk across the UK. Overall summer infection risk is expected to decrease below current levels in 2040. This is a consequence of the projected decrease in summer rainfall levels at this time, antagonised by ever increasing summer temperatures, resulting in decreased moisture availability.

To date there has been little increase in risk from overwintering larvae, as the minimum development threshold is still not consistently reached across a majority of the UK. However the maps show a few pockets in the South West and along the Welsh coast where risk from occasional losses has begun to appear. This phenomenon is already being realised on the ground with reports of changing timing of infection (De Waal *et al*., 2007). Winters are predicted to become even milder and more months will have a mean temperature of above the 10^{o}C development threshold. As a consequence, outbreaks in late spring/early autumn can be expected. These will be restricted initially to the far south, but will spread slowly north over time. With some parts of the UK experiencing longer development windows, fasciolosis infection could extend from being a seasonal to a year-round threat. Active disease surveillance should be focused in the South and West to capture changes in timing of infection, as this will impact on control strategies such as timing of anthelmintic administration. Surveillance should also be targeted in the areas of Scotland and Wales where serious epidemics are predicted.

Due to the limited scope of current climate projection scenarios, it is not possible to determine the impacts of short term weather fluctuations on infection levels. Increases in extreme events have been forecast (UKCP09, 2009a) and extreme fluctuations could be inimical to

fluke survival. If the predicted combination of high temperatures and droughts are realised, the larvae and intermediate hosts could succumb to desiccation. Conversely, drought years can result in increased fasciolosis risk. Following the dry summers of 1959 (Ollerenshaw, 1966) and 2003 (Kenyon *et al.*, 2009b), there were exceptionally high levels of fasciolosis in livestock. The losses following dry periods are a consequence of stock being forced to graze verdant flukey areas as water levels recede and metacercariae-free herbage becomes sparse (Ollerenshaw, 1966). In contrast, extensive rainfall can be detrimental to transmission as snails and fluke larvae can be washed away by large quantities of rain (Rapsch *et al*., 2008). A sensitivity analysis of the model could highlight its robustness under extreme parameter combinations, and elucidate the conditions where qualitative shifts in the predicted probability of fasciolosis outbreaks could occur.

A changing climate is also likely to have wider impacts, affecting farming behaviour (Mader & Davis, 2004; Rivington *et al*., 2007) and land suitability for different farming practices. There will also be direct impacts of climate on the hosts of infection (Harle *et al.*, 2007; Nardone *et al.*, 2006) combined with increased anthelmintic resistance (Wolstenholme et al., 2004) exacerbating infection risk. Due to these other factors, together with the gap between the spatial and temporal scales of climate modelling and the real scales at which transmission dynamics exist, the forecasts presented here can only be considered indicative. Nevertheless, the climate-driven risk maps closely match past changes in infection, suggesting that climate is the dominant driver of these changes.

Regular reviews of the fasciolosis risk predictions should be carried out as long-term climate projections become ever more refined. However, modifications to the broad risk patterns are likely to be relatively minor. It is clear that *F. hepatica* infection in the UK is likely to expand both geographically and in terms of severity, with regions such as West Wales set to experience unprecedented levels of disease outbreaks. Due to the complexities of climate change and its impacts on *F. hepatica* transmission there will be spatio-temporal variation in parasite risk, with some areas experiencing diminishing disease levels. The projections show where limited resources should be focussed and surveillance should be targeted. Ultimately, data from such surveillance will improve our understanding of the impacts of climate change on parasite levels, and provide information which can help us to develop effective mitigation or adaptation strategies.

Chapter 3

Modelling parasite transmission in a grazing system: The importance of host behaviour and immunity

3.1 Preface

As demonstrated in the previous chapter, predictions based on correlative models can provide broad indications of future risk for parasites whose complex life-cycles are governed by fundamental climatic factors. This approach can indicate the role of climate change in parasite distribution, and inform targeted surveillance and long-term control strategies. However, the lack of fine-scale surveillance data for a majority of helminths impedes the creation of similar models for a wider species range. There are also further limitations to this approach, as detailed in chapter one.

To overcome these limitations and address more complex questions surrounding helminth transmission in a changing climate, a different approach is required. A process-based mechanistic model is developed in the next two chapters, which incorporates the pivotal elements of the transmission process: survival and development of the parasite both within the host and on pasture, the host's immunological response and grazing behaviour, and spatial heterogeneity of both pathogens and resources. This model allows the key elements of macro-parasite transmission in a grazing system to be explored in a spatial context for the first time (chapter three). The model is then used to explore potential impacts of climate change on parasite outbreaks (chapter four).

This chapter formed the basis of the publication: Fox NJ, Marion G, Davidson RS, White PCL, Hutchings MR. (2013) Modelling Parasite Transmission in a Grazing system: The Importance of Host Behaviour and Immunity. PLoS ONE: Article In Press. doi: 10.1371/journal.pone.0077996

3.2 Summary

Parasitic helminths present one of the most pervasive challenges to grazing herbivores. Many macro-parasite transmission models focus on host physiological defence strategies, omitting more complex interactions between hosts and their environment. This chapter explores how both host behaviours and immunity influence macro-parasite transmission in a spatially and temporally heterogeneous environment. This chapter concentrates on gastrointestinal nematodes transmitted via the faecal oral route, within a controlled grazing system.

A spatially explicit, individual-based, stochastic model is developed, that incorporates both the host's immunological response to parasitism, and key grazing behaviours including faecal avoidance. The results demonstrate that grazing behaviour affects both the timing and intensity of parasite outbreaks, through generating spatial heterogeneity in parasite risk and nutritional resources, and changing the timing of exposure to the parasite's free-living stages.

The influence of grazing behaviour varies with the host-parasite combination. Faecal avoidance can limit transmission for parasites that have fast on-pasture development times, and when hosts have a limited ability to mount an immune response. However, for parasites with prolonged development times on pasture, faecal avoidance can increase parasite burdens.

Through incorporating the two-way interaction between infection dynamics and grazing behaviour, the potential benefits of parasite-induced anorexia are also demonstrated. Hosts with phenotypic plasticity in grazing behaviour that make grazing decisions dependent on current parasite burden, can control infection with minimal loss of intake over the grazing season.

This work represents the first model that integrates both the behavioural and physiological elements of helminth parasite transmission dynamics in managed grazing systems. The magnitude and timing of parasite outbreaks is influenced by host immunity and behaviour, and the interactions between them; the incorporation of both regulatory processes is required to fully understand transmission dynamics. Understanding of both physiological and behavioural defence strategies could aid the development of novel approaches for control.

3.3. Introduction

Parasitic helminths present one of the most pervasive challenges to grazing herbivores (Burgess *et al*., 2012). The prevalence and intensity of parasite outbreaks is determined by a multitude of factors. These include the influence of host immunity on parasite establishment and fecundity, and the timing and frequency of contacts with parasites' free-living infective stages. There is a propensity for macro-parasite transmission models to focus on host immunological defence strategies, omitting more complex interactions between hosts and their environment (Churcher *et al.*, 2006; Cornell, 2005; Dobson *et al*., 1990; Gaba & Gourbière, 2008; Leathwick *et al*., 1992; Louie *et al.*, 2005; Roberts & Grenfell, 1991, 1992). This chapter explores how host behaviours influence macro-parasite transmission in a spatially and temporally heterogeneous environment. The focus is on monoxenous macro-parasites, transmitted via the faecal oral route, within a controlled grazing system.

A pivotal regulator of parasite transmission is host immune response. Prolonged exposure to the infective stages of gastro-intestinal nematodes (GINs) leads to a decrease in the establishment, fecundity and survival of parasites in the host (Adams & Beh, 1981; Anderson, 1987; Barger *et al.*, 1985; Coyne *et al*., 1991; Leathwick *et al.*, 1992; Mckellar, 1993; Ploeger *et al.*, 1995; Ractliffe *et al.*, 1971; Vercruysse & Claerebout, 1997). The incorporation of host immunity as a regulatory constraint of parasite populations within transmission models can explain key features of the dynamics (Anderson, 1987), and its influence has been investigated previously, in the absence of host behaviour. Roberts & Grenfell (1991) proposed a mechanistic model encapsulating the dynamics of directly transmitted GIN infections in managed ruminant populations. Their model captured key aspects of the parasite's infrapopulation (the parasites within a specific host), suprapopulation (all parasites of a given species, at all stages of development within an ecosystem) (Esch *et al.*, 1975), and the regulation of transmission through the host's acquired immune response (Roberts & Grenfell, 1991). This deterministic model represented the average host (adult worm burden and immune response) and the infectious stage larval population on an average sward. In an extension of this work, Marion *et al* (1998) developed a stochastic formulation of the model and argued that a stochastic approach needs to be adopted to account for dynamics at low population levels, and to incorporate variability and extinctions.

Infective larvae are unevenly distributed in both space and time (Boag *et al.*, 1989). Host grazing behaviours contribute to the generation of this heterogeneity, and are crucial in determining exposure to disease risk in a grazing system (Marion *et al*., 2008). Spatial

heterogeneity is created through selective grazing by the host population. Through faecal avoidance it is believed that herbivores can limit contact with pathogens in the environment, consequently lowering infection risk (Cooper *et al.,* 2000)(Bao *et al*., 1998; Forbes & Hodgson, 1985; Gunn & Irvine, 2003; Hutchings *et al.,* 1998). This selective grazing results in a heterogeneous resource distribution, with mosaics of tussocks (tall contaminated patches), and gaps (short, uncontaminated patches) (Hutching *et al.,* 2001). This uneven resource distribution is reinforced by leaching of nutrients from the faeces resulting in relatively high nutrient concentrations in the contaminated tussocks (Haynes & Williams, 1993). As the contaminated tussocks harbour increased concentrations of both parasites and nutritional resources, the mosaic represents a parasitism versus nutrition trade-off (Hutchings *et al.,* 2001a; Hutchings *et al.,* 2001b; Hutchings *et al*. 2000). The grazing behaviours of herbivorous hosts have been extensively studied (Arnold, 1987; Black & Kenney, 1984; Hutchings *et al*., 1998; Wallisdevries *et al.,* 1998), allowing mathematical models to be meaningfully parameterised to encapsulate the grazing processes. In the model developed by Marion *et al.,* (2005) and Swain *et al.,* (2006) the behaviour of grazing herbivores in response to local environmental cues has been described using a spatially explicit model incorporating stochastic rules representing primary behavioural responses. Within this framework, contacts with faecally-contaminated swards have previously been employed as a measure of potential infection events (Smith *et al.,* 2010; Smith *et al.,* 2009) and parasite transmission was not explicitly incorporated.

However, there is a two-way interaction between host grazing behaviour and parasite populations. In grazing herbivores, parasitism can induce inappetance, reduction in grazing time and changes in grazing behaviour (Forbes *et al.,* 2000; Forbes *et al.,* 2007; Hutchings *et al.,* 1999; Johnson, 1998). The extent of this parasite induced anorexia will vary with the degree of pathological changes and the parasites' sites of predilection within the host (Forbes *et al*., 2000). This anorexia has been observed to lead to intake reductions of between 30 and 60%, compared with uninfected animals (Coop *et al.,* 1982; Fox *et al.,* 2002; Kyriazakis *et al.,* 1998). Parasitised hosts also exhibit higher levels of faecal avoidance compared to uninfected grazers (Hutchings *et al.,* 2001a; Hutchings *et al*., 1998; Hutchings *et al.,* 2001b; Hutchings *et al*., 1999; Hutchings *et al*., 2000). As resistance to infection is acquired, anorexia ceases and intake and faecal avoidance levels return to normality; this also happens following anthelmintic induced parasite expulsion (Coop & Kyriazakis, 1999; Hutchings *et al.,* 2001a; Hutchings *et al.,* 2001b; Kyriazakis *et al*., 1998). It has been suggested that parasite-induced anorexia evolved to either facilitate host recovery or benefit the parasite, rather than merely being a maladaptive response of no benefit to either party (Exton, 1997;

Johnson, 1998). However, there is much debate over the function of anorexia (Ayres & Schneider, 2009; Kyriazakis *et al*., 1998).

This chapter develops a framework which integrates a stochastic version of the parasite transmission model of Roberts & Grenfell, (1991), with the grazing model of Marion *et al*., (2005) to create a spatially-explicit, individual-based model that incorporates both the host's immunological response to parasitism and key grazing behaviours. This integrated approach also incorporates the other pivotal elements of the transmission process: survival and development of the parasite both within the host and on pasture; spatial heterogeneity of both pathogens and resources; and the interactions between host grazing behaviour and parasitised state.

This framework is subsequently applied to explore how host behaviours influence macro-parasite transmission in a spatially and temporally heterogeneous environment, with the following objectives: 1) Determine the impact of spatial aggregation on pasture, of both nutritional resources and infective larvae, on host parasite burden; 2) Determine the impact of host faecal avoidance behaviour on the timing and intensity of parasite outbreaks, for parasites with different on-pasture development times; 3) Determine the influence of faecal avoidance on parasite dynamics, for hosts with differing abilities to mount an immune response; and finally 4) Explore the interactions between host grazing behaviour and parasitised state, to elucidate potential benefits that anorexia can provide the host.

3.4 Methods

3.4.1 Model structure

Individual grazing is modelled as in Marion *et al.*, (2005), which incorporates the key elements of grazing behaviour and resource use in response to local environmental cues. The current study builds on this grazing model to incorporate pathogen population dynamics, both on pasture and within the host. A cohort of D animals (labelled $k = 1 \ldots D$) move around a lattice of N patches (labelled $i = 1 \ldots N$), making grazing decisions based on the sward height h_i at that patch and the level of faecal contamination f_i. The patch and animal state variables are outlined in table 1. All state variables within the model are assumed to be integers.

Patch states	**Notation**
co-ordinates of patch *i*	(x_i, y_i)
Sward height at patch *i*	h_i
Faecal contamination at patch *i*	f_i
Pre-infective larvae at patch *i*	l_i
Infective L3 larvae at patch *i*	L_i
Animal states	**Notation**
Location of animal *k*	i_k
Immune response of animal *k*	r_k
Immature parasites in animal *k*	a_k
Mature parasites in animal *k*	A_k
Parasite eggs in animal *k*	e_k
Stomach contents of animal *k*	s_k
Faecal deposit size	s_0

Table 1. State variables.

Swain *et al*., (2007) further developed the grazing model of Marion *et al*., (2005) to explore the influence of search rate and search distance on host grazing. Following Swain *et al.*, (2007), the rate of movement from patch *i* to patch *j* is modelled as:

$$\frac{v}{z(i)} F(i, j) h_j$$

where v is the intrinsic movement rate and h_j is the sward height at patch j, using the normalisation factor:

$$z(i) = \sum_{j \in N_i} F(i, j)$$

The search kernel $F(i,j)$ follows the power-law $F(i, j) = |i - j|^{-\alpha}$ in which $|i - j|$ is the Euclidean distance between patch i and j. The normalisation prevents animals accumulating near the boundaries by virtue of having a lower movement rate. If the search coefficient, α, is large, animals are restricted to nearest neighbour movement, while if $\alpha = 0$ animals will search the whole lattice uniformly. In addition the total movement rates remain constant as α changes.

Sward growth is modelled logistically with the rate of increase at patch i given by:

$$\gamma h_i \left(1 - \frac{h_i}{h_{\max}} \right)$$

where γ is the intrinsic growth rate of the sward and h_{max} is the maximum sward height attainable. The sward height of a given patch is reduced by B when an animal grazes at that location, while the stomach content s_k of the corresponding animal is increased by one unit of size B. An individual takes a bite on its current patch at a rate:

$$\beta(h_i - h_0) e^{-\mu_k f_i (a_k + A_k)^{\Lambda}}$$

where f_i represents the level of faecal contamination at patch i, μ is the level of faecal avoidance, a_k+A_k is the total number of parasites in host k, Λ is the anorexia coefficient, and h_o is the minimum grazable portion in each patch. Thus the bite rate is monotonically decreasing with the amount of faecal contamination and level of avoidance, and non-zero values of Λ allow for the avoidance to be amplified with increased parasite burden. The model also includes a daily intake requirement R_k for each animal (as introduced by Smith *et al.*, (2008). The intake of each animal accumulates until its requirement R_k is reached, but is reset at the end of each day.

Grazing behaviour affects the timing of host contact with the parasite's free living stages. In order to understand the interactions between grazing behaviours and parasite transmission, it is important to consider the multiple delays in the development of monoxenous nematodes. After release from the host the non infective free living parasites (termed l_i here) develop through multiple larval stages before reaching their infective third stage (L3) (termed L_i here).

After ingestion by an herbivorous host, they moult and develop onto fourth stage larvae (L4) (termed a_k here), before maturing into fecund adults (L5) (termed A_k here) (Gunn & Irvine, 2003). The Roberts and Grenfell (1991) model makes the implicit assumptions that larvae are instantaneously infective upon release onto pasture and parasites in the host are immediately fecund upon establishment. It is straightforward to relax these assumptions within the stochastic framework adopted here. Thus each patch (labelled $i = 1 \ldots \mathrm{N}$) is assigned a number l_i of non-infective larvae as well as a number L_i of infective L3 stage larvae. Similarly, within each host (labelled $k = 1 \ldots \mathrm{D}$) separate variables a_k, A_k and e_k are introduced for the number of immature parasites, mature parasites and eggs respectively. Incorporating these developmental delays allows us to investigate the influence of grazing behaviour on parasite risk and the timings of outbreaks.

When an animal takes a bite of size B, the number of non-infective (l_i) and infective larvae (L_i) on its current patch, decreases by

$$\left(\frac{B}{h_i}\right) \times l_i \text{ and } \left(\frac{B}{h_i}\right) \times L_i$$

When an animal takes a bite of size B, the number of immature parasites in host k, a_k, increases by

$$\theta(r_k) \times \left(\frac{B}{h_i}\right) \times L_i$$

where θ is the probability of ingested L3 larvae establishing and becoming immature larvae in the host, and is a monotonic non-increasing function of r, representing the detrimental effect of resistance on parasite establishment.

Roberts and Grenfell (1991) modelled a host resistance mechanism in which the level of resistance of host k, here denoted r_k, was a function only of the number of L3 ingested. In reality, helminth populations are regulated by multiple density-dependent mechanisms (Basáñez & Ricárdez-Esquinca, 2001; Churcher *et al*., 2006). The acquisition of resistance is partially dependent on cumulative larval intake (Barger & Le Jambre, 1988; Cattadori *et al.*, 2005). However, adult burden also plays a role in density-dependent regulation (Claerebout *et al.,* 1998). If resistance acquisition in the model were solely dependent on ingested L3, then the true impact of host grazing behaviours that delay the ingestion of L3 could not be explored. Consequently the model has scope for mounted resistance to be dependent on the history of both L3 ingested and the number of established parasites.

When infective larvae are ingested, the resistance r_k of host k increases by

$$\left(\frac{L_i}{h_i}\right)\times B\times\psi$$

where ψ is a resistance gain coefficient. r_k, also increases as a function of the current parasite burden, at rate $(a_k+A_k)\eta$, where η is a second resistance gain coefficient. Death of immature parasites in the host occurs at a rate ζa_k. Immature parasites develop into mature, egg producing adult parasites at a rate χa_k. Death of adults in host k occurs at rate $\tau(r_k)A_k$, where $\tau(r_k) > 0$ is a monotonic non-decreasing function which models the influence of acquired immunity on parasite mortality in the host. The loss of resistance in host k occurs at rate σr_k.

e_k represents the number of eggs in host k. Egg production from the dioecious parasites within host k occurs at a rate of

$$\frac{\lambda(r_k)A_k}{2}$$

where $\lambda(r_k)$, the rate of egg production of adult parasites, is a monotonic non increasing function of r_k.

The rate of defecation for an individual in its current patch is $fdep(s_k - s_0)\Theta(s_k - s_0)$ where the Heaviside function $\Theta(s_k - s_0)$ is unity if the stomach contents, s_k, are greater than the faecal deposit size, s_0, and is otherwise zero. When a defecation event occurs, e_k decreases by $\frac{s_0}{s_k}e_k$ and the number of pre-infective larvae in patch i, l_i, increases by the same quantity. The non-infective l_i larvae develop into infective L_i larvae at a rate of εl_i. The decay rate for faecal contamination at patch i is φf_i , and the death rates of non-infective and infective larvae are ωl_i and ρL_i respectively.

The stochastic model is simulated on the state-space variables (table 1) using the events and associated rates described above (see table 2) following the Gillespie algorithm (Keeling & Rohani, 2008). The model is simulated where an event e with associated rate r_e occurs with a probability $r_e\delta t$ during a small time interval from t to $t + \delta t$. r_{ei} represents the rate of events of type e happening in patch i, including faecal decay, sward growth, larval development and L1 and L3 larval death rates. r_{ek} represents the rate of event

type *e* happening to animal *k* including bite, movement, faecal deposition, resistance loss, adult larvae death, egg production and egg death rates. The total event rate is, $R = \Sigma_e \Sigma_i r_{ei} + \Sigma_e \Sigma_k r_{ek}$, where the chosen time step ensures that $R\delta t$ is less than one, so all rates can be interpreted as probabilities. The model was developed in C++ and run on a linux platform. All events are summarised in figure 1, and model parameters are listed in table 3.

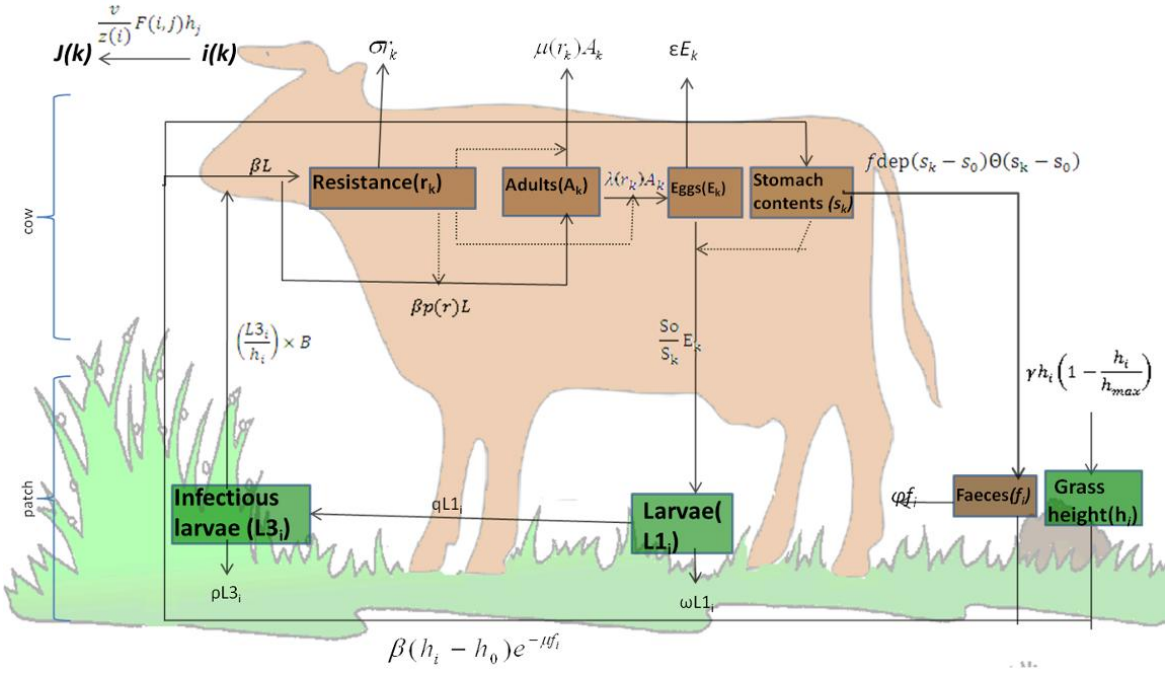


Figure 1. Summary of all model events

Patch Event	**Rate r_{ei}**	**Change in state variables**
Growth of sward at patch *i*	$\gamma h_i\left(1-\frac{h_i}{h_{\max}}\right)$	$h_i \rightarrow h_i + 1$
Development of larvae at patch *i*:	εl_i	$l_i \rightarrow l_i - 1$ $L_i \rightarrow L_i + 1$
Death of pre-infective larvae at patch *i*:	ωl_i	$l_i \rightarrow l_i - 1$
Death of infective L3 at patch *i*:	ρL_i	$L_i \rightarrow L_i - 1$
Decay of faeces at patch *i*:	φf_i	$f_i \rightarrow f_i - 1$

Animal Event	**Rate r_{ek}**	**Change in state variables**
Bite at current patch *i*, potential ingestion of infective and non-infective larvae, potential establishment of infective larvae and gain in immunity	$\beta(h_i - h_0)e^{-\mu_k f_i(a_k+A_k)^{\Lambda}}$	$h_i \rightarrow h_i - 1$ $L_i \rightarrow L_i - \left(\frac{B}{h_i}\right) \times L_i$ $l_i \rightarrow l_i - \left(\frac{B}{h_i}\right) \times l_i$ $s_k \rightarrow s_k + 1$ $r_k \rightarrow r_k + \left(\frac{B}{h_i}\right) \times L_i$ $a_k \rightarrow a_k + \theta(r_k)\left(\frac{B}{h_i}\right) \times L_i$
Death of immature adults in host *k*	ζa_k	$a_k \rightarrow a_k - 1$
Maturity of adults in host *k*	χa_k	$a_k \rightarrow a_k - 1$ $A_k \rightarrow A_k + 1$
Death of adults in host *k*	$\tau(r_k)A_k$	$A_k \rightarrow A_k - 1$
Gain of immunity in host *k* due to parasite burden	$(a_k+A_k)\eta$	$r_k \rightarrow r_k + 1$
Loss of immunity in host *k*	σr_k	$r_k \rightarrow r_k - 1$
Egg production in host *k*	$\frac{\lambda(r_k)A_k}{2}$	$e_k \rightarrow e_k + 1$
Defecation by host *k*	$f_{dep}(s_k - s_0)\Theta(s_k - s_0)$	$e_k \rightarrow e_k - \left(\frac{s_o}{s_k} e_k\right)$ $e_i \rightarrow e_i + \left(\frac{s_o}{s_k} e_k\right)$ $s_k \rightarrow s_k - s_o$ $f_i \rightarrow f_i + s_o$
Movement of animal *k*	$\frac{v}{z(i)}F(i,j)h_j$	$i_k = i \rightarrow i_k = j$

Table 2. Summary of events.

Parameter	
Patch	
Intrinsic growth rate of sward	γ
Development rate non-infective to infective larvae	ε
Death rate of non-infective larvae	ω
Death rate of infective larvae	ρ
Decay of faeces	φ
Animal	
Bite rate	β
Faecal avoidance coefficient	μ
Death of immature larvae in host	ζ
Maturity of larvae in host	χ
Rate of resistance loss	σ
Resistance gain coefficient 1	ψ
Resistance gain coefficient 2	η
Death rate of adult larvae in host	τ
Rate of egg production of adult parasite	$\lambda(r_k)$
Anorexia coefficient	Λ
Intrinsic movement rate	ν
Probability of ingested L3 larvae establishing as adults	$\theta(r_k)$

Table 3. Summary of parameters, with all parameters expressed in units of minute^{-1}, with the exception of μ, ψ, η, Λ, r and θ, which are dimension free.

3.4.2 Parameterisation

Where parameter values are not stated for specific simulations, parameter values detailed in this section are used. The model was parameterised to simulate five hosts over one grazing season, in a set-stocked temperate grassland system, as described by Smith *et al* (2010). All simulations were run for 365 days and replicate the spatial scale of such agricultural systems, using a field represented by a lattice consisting of 78 x 78 patches with each patch representing $0.5m^2$. This patch area corresponds with the area of one faecal pat and the refusal zone around it (Phillips, 1993). Hosts move around the lattice with a search rate representative of a cattle step rate of approximately three steps per second (Lazo & Soriguer, 1993) (v = 0.015), and a bite rate representing approximately 20,000 bites per day (Phillips, 1993) (β =0.1). When a bite event occurs, one unit of forage is removed. Each $0.5m^2$ patch contains 50 bite areas of forage, as each cattle bite is approximately $0.01m^2$ (Phillips, 1993). Each patch is initialised with a sward height that provides 200 units of forage, and has a maximum sward height providing 400 units of forage. Each patch has an ungrazeable portion of 50 units of forage, and grass grows over time at rate γ =0.00004 (Marion *et al*., 2008). These parameter values give rise to a set stocking scenario where intake approximately matches sward growth (Marion *et al*., 2008). Cattle deposit faeces approximately 10-15 times per day (Phillips, 1993) (f_{dep}=1.0, S_0=2000.0), and the field is initialised with no faecal contamination ($f_i = 0 \ \forall \ i = 1, \ldots, N$). Faeces decays at a rate where 10% of the faecal deposit remains 3 months post deposition (Haynes & Williams, 1993) (φ = 0.00001776). Faecal avoidance for animal k varies from no avoidance (μ_k = 0) to effectively complete avoidance (μ_k = 10) (Hutchings & Gordon, 2002; Smith *et al*., 2010), where almost complete avoidance of fresh faeces (μ_k = 5) results in a bite rate from freshly-contaminated patches <1% of the bite rate from non-contaminated patches (Hutchings & Gordon, 2002; Smith *et al*., 2010).

The parasite's lifecycle is representative of a typical gastrointestinal helminth of grazing herbivores in a temperate climate. Death rate of pre-infective stages (ω = 0.0001) results in approximately 1% of larvae remaining after 1 month (Kao *et al*., 2000; Leathwick *et al*., 1992). Approximately 50% of surviving pre-infective larvae develop to the infective L3 stage after 2 weeks on pasture (Kao *et al*., 2000; Leathwick *et al*., 1992; Pandey, 1972; Smith *et al*.,1986) (ε = 0.00005). The death rate of infective L3 results in approximately 10% remaining after 3 months (Kao *et al*., 2000; Pandey *et al.,* 1993) (ρ = 0.000015).

Following ingestion of the infective stages approximately 40% of L3 larvae establish within a naïve host (Kao *et al.,* 2000) (θ = 0.4). The proportion that establish is monotonically non-

increasing with increased levels of acquired resistance. Increase in resistance is dependent upon ingestion of L3 (ψ = 0.25) and the size of the host's parasite population (η = 0.025). In the absence of parasitism, immunity wanes over time (σ = $1.9x10^{-8}$) (Roberts & Grenfell, 1991). Ingested larvae develop into fecund adult parasites in approximately 3 weeks (Kao *et al*., 2000) (χ = 0.00003). Fecund adult parasites produce eggs at a rate which is monotonically decreasing as host resistance increases (Kao *et al*., 2000) (λ = 2). The life expectancy of the adult parasites in the host is approximately 5 weeks (Kao *et al*., 2000) (τ = 0.00002).

The starting condition of each simulation was representative of naïve hosts being released onto contaminated pasture. Each simulation was initialised with uninfected hosts (a_k =0, A_k =0, $\forall$ k = 1…D) on a pasture with 24000 infective L3, distributed over 20 randomly selected patches to reflect the aggregated distribution of larvae on pasture (Boag *et al*., 1989). Each scenario was repeated over 10 realisations to account for the stochastic nature of the model.

3.4.3 Model runs performed

Aggregation of risk on pasture

Pre-infective larvae are released with the hosts' faeces, so the aggregation of faeces on pasture results in an uneven distribution of parasitic larvae on the field. Cattle normally deposit faeces approximately 10-15 times per day (Phillips, 1993) (f_{dep}=1.0, s_0=2000.0). To investigate the impact of aggregation of faeces and infective larvae on pasture, simulations were run with varying sizes of faecal deposit (s_0). Simulations were run with the number of faecal deposits ranging from 200 to 5 per day (s_0 = 100, …, 4000, in increments of 100). Faecal avoidance was set at μ_k = 3.

Influence of faecal avoidance across parasites with different development rates

There is substantial inter-species variation in observed larvae development rates (Kao *et al*., 2000; Smith *et al*., 1986). For GINs of herbivores in temperate climates, development times vary from less than one week to over 5 months (Kao *et al*., 2000; Leathwick *et al*., 1992; Pandey, 1972; Smith *et al*., 1986). The influence of faecal avoidance behaviour on parasite transmission will vary with larval development time due to the changes in the number and timing of infective larvae ingested. To investigate how faecal avoidance influences host parasite burdens for parasites with different on-pasture development times, simulations were

run with varying development rates, ε = 0.00003 (development time of 3 weeks), ε = 0.00005 (development time of 2 weeks) and ε = 0.0001 (development time of 1 week), over differing faecal avoidance levels ranging from no avoidance (μ_k = 0), to effectively complete avoidance (μ_k = 10).

Influence of faecal avoidance across hosts with different rates of resistance acquisition

A host's ability to mount an effective immune response varies with a number of factors including the parasite species, host age, genotype, nutritional and hormonal status (Vercruysse & Claerebout, 1997). Simulations were run to determine how faecal avoidance influences parasite burden for parasite-host combinations where hosts have varying abilities to mount an immune response interpreted here in terms of the rates of acquisition of immune resistance. Four sets of simulations were run for cohorts of hosts with: very low resistance (ψ= 0.01, η = 0.0075), low resistance (ψ = 0.125, η = 0.0125), medium resistance (ψ = 0.25, η = 0.025), and high resistance (ψ = 0.5, η = 0.05). For each resistance level, simulations were run over differing faecal avoidance levels ranging from no avoidance (μ_k = 0), to effectively complete avoidance (μ_k = 10).

Parasite-host interactions (parasite induced anorexia)

To elucidate the fundamental dynamics of the system, initial runs were performed with no interaction between the host's parasitised state and its behavioural response (Λ = 0). However hosts can have phenotypic plasticity, with parasitised animals exhibiting heightened faecal avoidance compared to non-parasitised animals (Hutchings & Gordon, 2002; Hutchings *et al.*, 2001a; Hutchings *et al.*, 2001b; Hutchings *et al.*, 1999; Hutchings *et al*., 2000; Smith *et al*., 2010). A set of simulations were run for a cohort of hosts with parasite-induced anorexia, where faecal avoidance $e^{-\mu_k f_i (a_k + A_k)^{\Lambda}}$ ranged from low to high depending on parasite burden (with μ_k = 3, Λ = 0.0006, such that min μ_k = 3, max μ_k = 8, and mean μ_k = 4). When parasite burden was highest, these hosts exhibited realistic levels of reduction in intake of approximately 40% compared to control hosts (Λ = 0) with low faecal avoidance (μ_k = 3) (Coop *et al*., 1982; Fox *et al*., 2002; Kyriazakis *et al*., 1998). For comparison, three further sets of simulations were run for cohorts of hosts with faecal avoidance levels constant across the grazing season, at levels equivalent to the minimum, mean and maximum faecal avoidance levels exhibited by anorexic hosts; low faecal avoidance (μ_k = 3, Λ = 0), high faecal avoidance (μ_k = 8, Λ = 0), and average faecal avoidance (μ_k = 4, Λ = 0).

3.4.4 Quantities observed in the simulations

The mean, averaged over 10 simulations, and the standard deviation, were reported for each output variable including peak parasite intensity, day of peak parasite intensity, and mean daily intake. Peak parasite intensity was used as a measure of infection as host morbidity and mortality are directly proportional to parasite intensity (Grenfell & Dobson, 1995). However, a host can be affected by both parasite intensity and the duration of infection. To determine the usefulness of this measure as a reliable indication of disease levels, both the peak parasite intensity and the cumulative exposure over the grazing season (not shown), measured by integrating the infection curve, were calculated for the scenarios detailed above. Over the range of simulations, both measures provided qualitatively similar results. Peak parasite intensity is used as a measure of infection as it is a more intuitive measure than the area under the curve, and can be compared to empirical data. If the use of cumulative burden had instead been chosen as a measure of parasitism, the trends shown in the results, and the conclusions, would remain the same.

3.5. Results

Using values outlined in the main parameterisation section, the model successfully reproduces the parasite dynamics empirically observed in livestock grazing systems (Callinan *et al*., 1982; Claerebout *et al*., 1998; Cornell *et al.*, 2003; Hilderson *et al*., 1993; Roberts & Grenfell, 1991; Smith & Grenfell, 1985; Smith & Guerrero, 1993; Williams *et al.*, 1993). The introduction of susceptible hosts onto contaminated pasture accounts for the rapid increase in ingested larvae and adult parasites in the host, and the subsequent acquisition of immunity accounts for the consequent decline in parasites (figure 2).

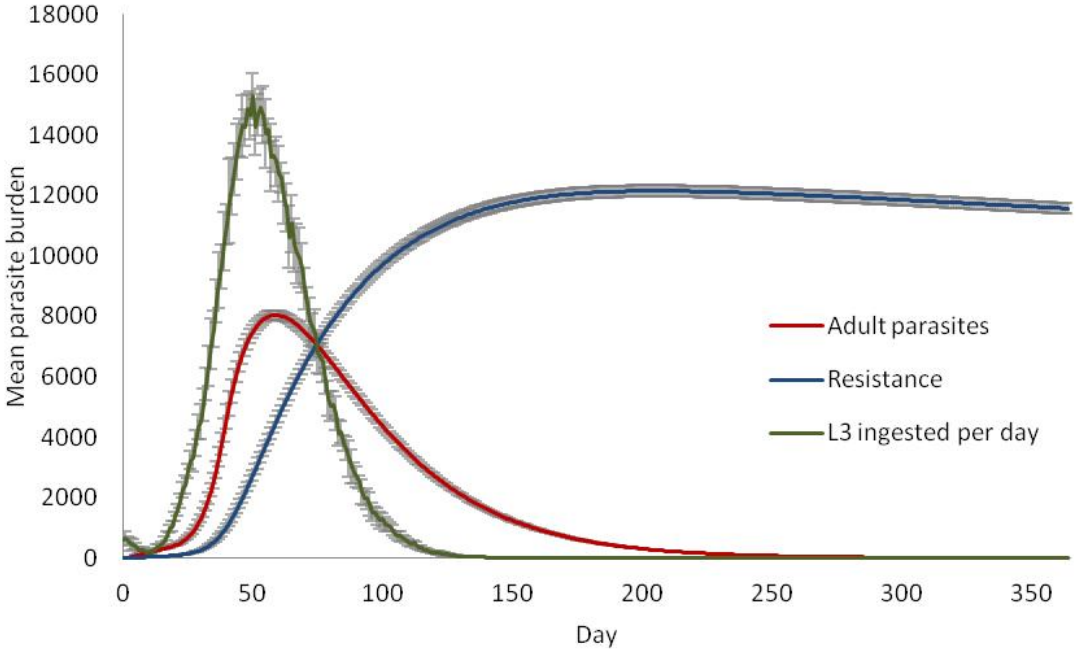


Figure 2. Host parasite burden, L3 ingested per day and host resistance level (±SD) over one grazing season, using the standard parameter values detailed above (μ_k = 3).

Aggregation of risk on pasture

As the size of faecal deposits increases the level of clustering of larvae increases, leading to a rise in the severity of outbreaks (figure 3). At higher levels of clustering, the peak parasite burden steadily declines.

In runs with realistic levels of clustering (one faecal deposit per 2,000 bites (Phillips, 1993)) spatial heterogeneity in infection risk is consistent with field observations (Boag *et al*., 1989) with larvae having a skewed distribution on pasture (figure 4).

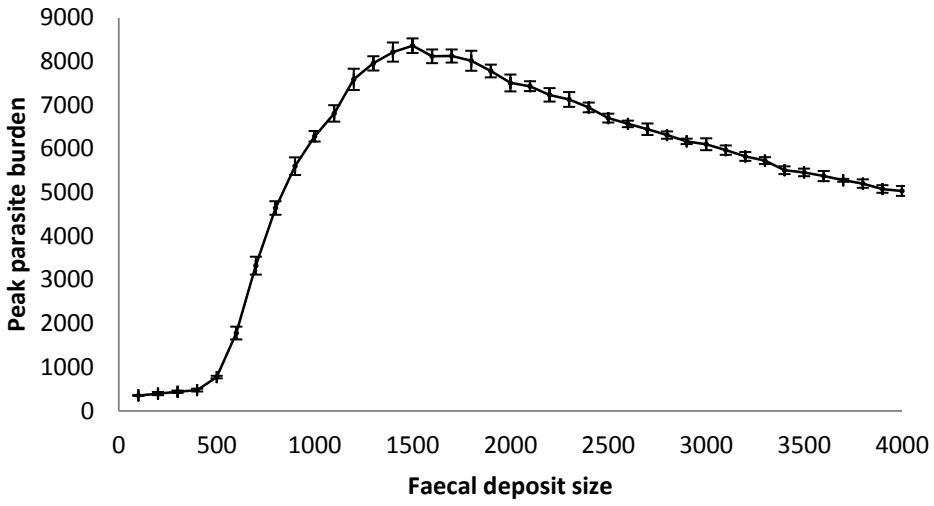


Figure 3. Influence of spatial clustering of both free-living larvae and faecal contamination on peak parasite burden. (f_{dep}=1.0, s_0=100,….., 4000, in increments of 100).

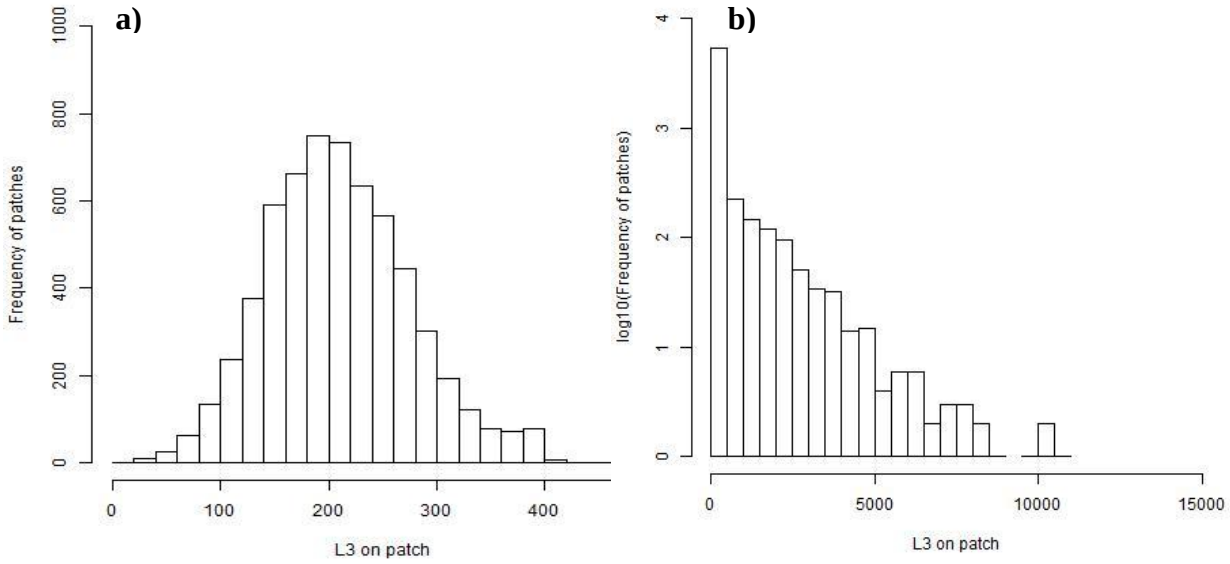


Figure 4. Distribution of L3 larvae on pasture at day 70, for a) low (f_{dep}=1.0, s_0=100; 1 faecal deposit per 100 bites) and b) realistic (f_{dep}=1.0, s_0=2000; 1 faecal deposits per 2000 bites) clumping scenarios. In figure b log10 of frequency of patches is used.

Influence of faecal avoidance across parasites with different development rates

Grazing behaviour also has a great influence on parasite transmission affecting both the timing and level of exposure to the parasite's free living stages. For directly-transmitted pathogens that are infective immediately or develop quickly on pasture, faecal avoidance can decrease risk (figure 5). However, for parasites with delayed development on pasture, higher levels of faecal avoidance can lead to increased levels of parasitism (figure 5a). For levels of faecal avoidance observed on pasture (μ_k = 3 to 8) (Hutchings & Gordon, 2002; Smith *et al*., 2010); this behaviour can lead to higher levels of risk from parasites which take over two weeks to reach their infective stage. In addition to influencing the magnitude of parasite burdens, faecal avoidance behaviour also affects the timing of outbreaks. As figure 5b shows, the higher the level of faecal avoidance the later the peak in burden.

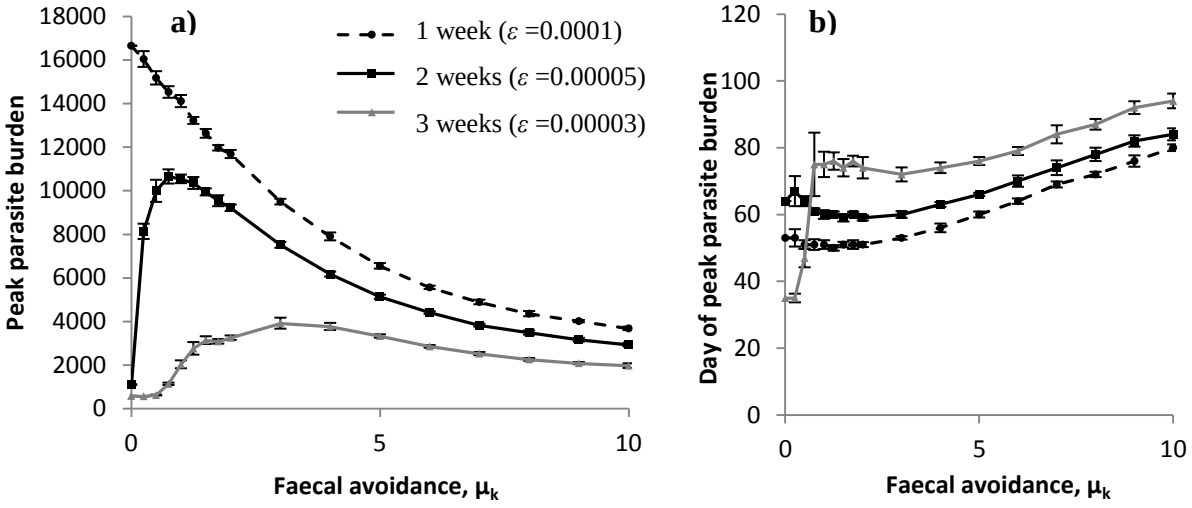


Figure 5. a) Intensity and b) timing of peak parasite burdens over varying levels of faecal avoidance, for parasites with different development times on pasture. simulations were run with varying development rates (q = 0.00003 (development time of 3 weeks), ε = 0.00005 (development time of 2 weeks) and q = 0.0001 (development time of 1 week), over differing faecal avoidance levels ranging from no avoidance (μ_k = 0), to complete avoidance (μ_k = 10)

Influence of faecal avoidance across hosts with different rates of resistance acquisition

The efficacy of faecal avoidance in minimising parasite risk varies with the host's ability to mount an immune response. For hosts with a very limited ability to gain resistance, a range of faecal avoidance levels are advantageous (figure 6).

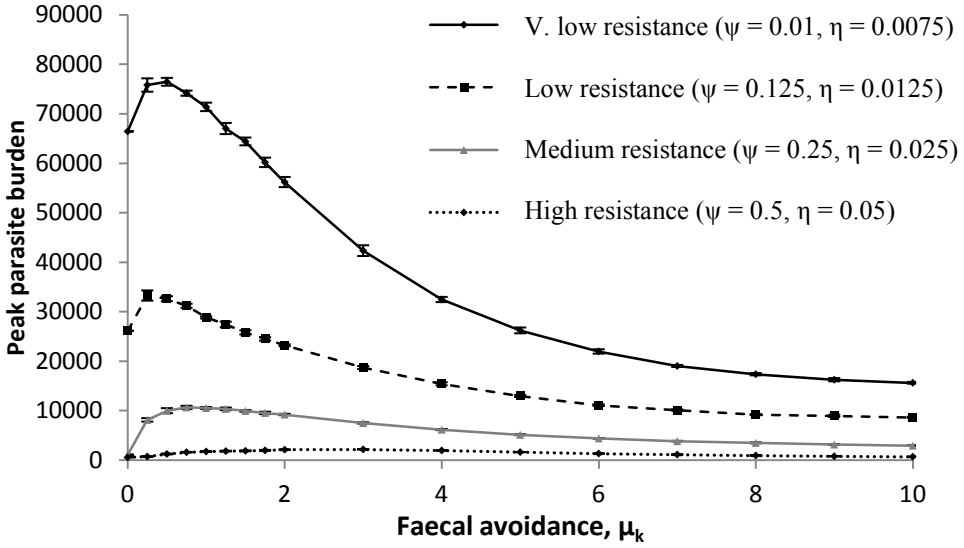


Figure 6. Peak parasite burden across varying faecal avoidance levels, for hosts with differing abilities to acquire resistance, for a parasite that takes two weeks to develop on pasture. for cohorts of hosts with: very low resistance (ψ= 0.01, η = 0.0075), low resistance (ψ = 0.125, η = 0.0125), medium resistance (ψ = 0.25, η = 0.025), high resistance (ψ = 0.5, η = 0.05). For each resistance level, simulations were run over differing faecal avoidance levels ranging from no avoidance (μ_k = 0), to complete avoidance (μ_k = 10).

Showing no faecal avoidance is a preferable strategy for parasite-host combinations where the host has an effective immune response and for pathogens with long on-pasture development times. In contrast, faecal avoidance is an effective defence strategy for parasite-host combinations where the host has limited ability to mount an immune response and for parasites with quick development times on pasture (figures 6 and 5a). However, increases in faecal avoidance lead to a decrease in daily herbage intake; this presents the hosts with a parasitism versus nutrition trade off.

Parasite-host interactions (parasite induced anorexia)

To explore the fundamental interactions between grazing behaviour and parasite dynamics, in the previous simulations grazing behaviour was independent of parasite burden (figures 2-6). In reality, individuals exhibit anorexia (increasing faecal avoidance and reduced daily intake) as parasite burdens rise, with grazing behaviour returning to normality once parasites are purged.

Figure 7 shows mean daily intake and peak parasite burden over one grazing season for hosts with phenotypic plasticity whose faecal avoidance is dependent on their parasite burden, and hosts with constant levels of faecal avoidance. Hosts which undergo an anorexic episode in response to parasite burden can benefit most from the nutrition versus parasitism trade-off (figure 7), minimising both parasite infection intensity and intake losses over the grazing season.

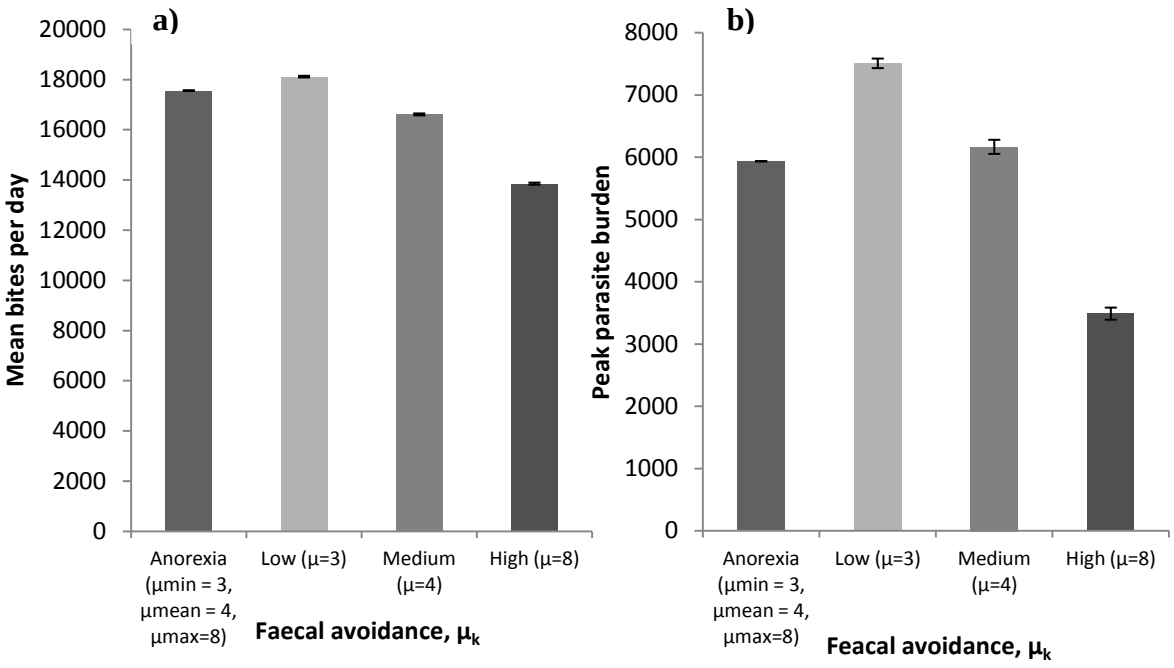


Figure 7. Mean daily intake over one grazing season (a), and peak parasite burden (b), for different faecal avoidance strategies. Hosts with phenotypic variation in faecal avoidance leading to parasite-induced anorexia (with $\mu_k = 3$, $\Lambda = 0.0006$, such that min $\mu_k = 3$, max $\mu_k = 8$, and mean $\mu_k = 4$), and hosts with constant levels of faecal avoidance: low faecal avoidance ($\mu_k = 3$, $\Lambda = 0$), average faecal avoidance ($\mu_k = 4$, $\Lambda = 0$).), and high faecal avoidance ($\mu_k = 8$, $\Lambda = 0$).

3.6. Discussion

The infection dynamics shown in figure 2 match the findings of Roberts and Grenfell (1991), and the trends echo empirical data (Callinan *et al*., 1982; Claerebout *et al*., 1998; Cornell *et al*, 2003; Hilderson *et al*., 1993; Smith & Grenfell, 1985; Smith & Guerrero, 1993; Williams *et al*., 1993), with peak parasite burdens within realistic bounds (Hilderson *et al*., 1993; Love & Hutchinson, 2003; Ractliffe *et al*., 1971). At the start of the grazing season, infection is initiated through ingestion of infective larvae that have over-wintered on pasture. There is then a delay where burdens stay at a low level as parasites in the host mature into fecund adults and the free-living stages develop into their infective state. Infections and pasture contamination then rise rapidly to a peak. This is followed by a precipitous decline as acquisition of resistance both reduces post exposure parasite establishment in individual hosts, and also reduces parasite fecundity thus regulating burdens at the supra-population level.

Transmission dynamics is influenced by processes which regulate infection (maintaining parasite population density within certain bounds), and those which control infection (perturbatory processes) (Smith & Galligan, 1988). For helminth-ruminant interactions host immune response is an important regulator of seasonal transmission dynamics within managed systems. Additionally, host grazing behaviour can control the timing and intensity of outbreaks.

Aggregation of risk on pasture

Transmission dynamics are influenced by the spatial heterogeneity that is created and maintained in the system; the clumped release of host faeces and parasite progeny, and the host's selective grazing, create an uneven distribution of resources, risk (infective larvae) and perceived risk (faecal contamination) on pasture.

For simulations parameterised with realistically-sized faecal deposits, spatial heterogeneity in infection risk is qualitatively consistent with field observations (figure 4b) (Boag *et al*., 1989). High levels of aggregation increase the likelihood of high intensity parasite outbreaks (figure 3). With low clumping (a relatively even distribution of larvae on pasture), there are many exposure events, but at each event only a small number of larvae are ingested. This low-level trickle infection is enough to engender an immune response, but not to lead to high parasite

burdens. As the level of clumping increases the skewness of the distribution of infective larvae on pasture increases, and the number of larvae ingested at each exposure event rises. This allows a significant number of larvae to establish, resulting in high intensity outbreaks. It is worth noting that, although not incorporated in the model, aggregation also increases the parasite's mating probability within the host. For dioecious helminths there is a 'breakpoint' below which transmission is not maintained due to the mating frequency being too low (Anderson, 1987). As levels of clustering increase, the peak parasite burden steadily declines. This is due to the presence of a decreasing number of more highly-contaminated patches. The severity of the faecal contamination cue in these patches, combined with the abundance of uncontaminated sward elsewhere on the field, results in hosts grazing these patches once the number of infective larvae in them has begun to recede.

Influence of faecal avoidance across parasites with different development rates

In addition to influencing the spatial distribution of parasites, grazing behaviour also alters timing of ingestion of the parasites' free living stages. Hosts with no faecal avoidance encounter parasites when they are fresh on pasture, whilst increasing levels of faecal avoidance delay contact. For parasites that are immediately infective, or have quick development times on pasture, faecal avoidance decreases infection risk, as the host is less likely to graze contaminated patches when the population of infective larvae is at its highest.

However, for parasites with delayed development on pasture (2 to 3 weeks), hosts with no faecal avoidance have the lowest parasite burdens (figure 5a). This is because hosts with no aversion to highly contaminated sward ingest a proportion of non-infective larvae soon after release onto pasture, decreasing the future potential population of infective larvae. This supports findings that suggest parasite transmission can be reduced by co-grazing cattle with a second non-susceptible herbivore species, exploiting the parasite's host specificity and enabling potentially infective larvae to be removed from the system (Waller, 2006a).

For hosts with higher levels of faecal avoidance, individuals are more likely to take a bite from a verdant patch once faeces has had time to decay, grass has grown tall and larvae have developed into their infective stage. This illustrates how faecal avoidance can increase parasite risk, and that faecal contamination level alone is not a reliable proxy for infection potential. This has previously been demonstrated by Van Der Wal *et al.*, (2000) who found that reindeer have a preference for grazing wetter habitats where forage quality and quantity

were greatest, but also where parasite infection risk is highest, and avoided drier sites which had higher levels of dung deposition but lower numbers of infective larvae (Van Der Wal *et al*., 2000).

The increased parasite risk incurred through faecal avoidance demonstrated here could be amplified by environmental factors not currently included in the model. For example, contaminated patches that have been left ungrazed for an extended period would enable greater survival of L3 due to increased protection from heat and desiccation. A corollary to this has been demonstrated with a decrease in parasite intensity in cattle co-grazed with sows; the sows' rooting behaviour breaks up the cattle faeces, reducing survival and availability of infective larvae (Fernández *et al.*, 2001).

Influence of faecal avoidance across hosts with different rates of resistance acquisition

The extent to which grazing behaviour influences parasite transmission varies with the host's ability to mount an immune response (figure 6). Development of immunity is affected by multiple factors including host age, nutritional and hormonal status, genotype and the influence of intercurrent diseases (Vercruysse & Claerebout, 1997). For hosts with limited ability to gain resistance, faecal avoidance can be advantageous (hosts with low levels of resistance acquisition, and faecal avoidance above $\mu_k=2$, have lower burdens than those with no avoidance, see figure 6). For hosts with impaired immunity and low faecal avoidance, low-level trickle infection from patches where some larvae have developed is enough to allow parasites to establish, but not for an effective immune response to be mounted, leading to high parasite burdens. For hosts with a greater ability to mount an immune response, the low-level trickle infection received by hosts with no faecal avoidance is enough to engender an immune response, but not enough to lead to high levels of parasite establishment. If these hosts had high levels of faecal avoidance and delayed their encounters with infected patches until all larvae on that patch had matured, they would ingest large numbers of fully-developed larvae in one go, which could allow significant numbers of parasites to complete their lifecycle. This effect of faecal avoidance on parasite risk will vary across parasites species with different development times (see figure 5a).

High levels of faecal avoidance can reduce parasite intensity for parasite-host combinations where the host has low levels of resistance acquisition (figure 6). However, high levels of faecal avoidance are potentially detrimental as the host's ability to ingest enough nutrients

would be greatly impaired in a set stocking scenario. Weight loss and inappetance have been observed in cows grazed on pasture with high levels of faecal contamination (Reid *et al.*, 1972). This highlights the trade-off between forage intake and parasite risk.

In addition to changing the intensity of parasite outbreaks, grazing behaviour also affects the timing of peak parasite burdens (figure 5b). Faecal avoidance changes the timing of when hosts come into contact with parasites on pasture; this delay in L3 ingestions can delay the acquisition of immunity resulting in the parasite burden peaking later in the grazing season. This could have substantial consequences for production, as delaying the acquisition of immunity can lead to pathogenic parasitism shifting towards the time when livestock are older and normally productive (Ploeger *et al*., 1995). The timings of heavy infections (with regard to the age of the host) have also been shown to influence how the host is affected (Callinan *et al*., 1982). As host susceptibility varies over the year with age and physiological status (Callinan *et al*., 1982; Coop & Kyriazakis, 1999; Williams *et al*., 1993), changes in the timing of infection could further alter transmission dynamics.

Parasite-host interactions (parasite induced anorexia)

In the initial simulations (figures 2 - 6), host grazing behaviour was independent of parasite burden. In reality there is a two-way interaction between infection dynamics and grazing behaviour, with increased parasite intensity leading to reduced intake, due to increased faecal avoidance and a reduced bite rate. It has previously been suggested that anorexic behaviour can be of benefit to the host (Exton, 1997; Kyriazakis *et al*., 1998; Langhans, 2000), however this benefit had not previously been demonstrated or quantified. Figure 7 shows the potential benefits that phenotypic plasticity in grazing behaviour can provide the host. Over the grazing season hosts that undergo an anorexic period can control their parasite burden with minimal loss of intake compared to hosts with fixed levels of avoidance.

Our findings qualitatively demonstrate the influence of anorexia on transmission dynamics. However anorexia is part of the generic acute phase response common to most infections (Exton, 1997; Langhans, 2000) and the potential costs and benefits are likely to vary across different pathogens and hosts. Specific parameterisation will be required to quantify the effects of anorexia in different systems. The inclusion of anorexia in the model does not allow for potential interactions between nutritional intake and the immune response. Associations between poor nutrition and infection levels have been demonstrated (Coop & Kyriazakis, 1999; Stear *et al*., 1997; Thomas, 1982; Vlassoff *et al*., 2001). Therefore, the

benefits of anorexia shown here could be overestimated. However, parasitised hosts are more selective grazers, and have been shown to select herbage with higher nutrient contents (Coop & Kyriazakis, 1999), so the decline in bulk herbage intake may not be mirrored by an equal decline in nutrient intake**.**

Conclusions

In conclusion, grazing behaviour affects the timing and intensity of parasite outbreaks, by generating spatial heterogeneity and changing the timing of exposure to the parasites' free living stages. The influence of grazing behaviour varies with the host-parasite combination, with faecal avoidance behaviour being most beneficial when hosts have a limited ability to mount an immune response, and against parasites with fast on pasture development times. For parasites with prolonged development times on pasture, faecal avoidance behaviour can increase risk. Further development of the model to incorporate co-infection with parasite species which exhibit varying development times could reveal an optimal grazing strategy. The results also demonstrate that parasite-induced anorexia can be beneficial for the host through minimising both intake losses and parasite burdens over a grazing season. Many transmission models focus on the role of host immunity in regulating parasite dynamics. This chapter illustrates that timing and magnitude of parasite outbreaks is driven by a combination of both grazing behaviour and host immunity, and the interactions between these regulatory processes. This integrated approach will also allow more informed predictions to be made of how outbreaks will be affected by future changes in the system, including the impacts of climate change.

Chapter 4

The impacts of climate change on nematode transmission in a grazing system

4.1 Preface

In the previous chapter a transmission model was developed which included the pivotal elements of macro-parasite dynamics. Known patterns of infection were reproduced, and the importance of incorporating spatial aggregation and host grazing decisions into transmission models was highlighted.

As detailed in chapter one many elements of the transmission process are sensitive to climate change, including larval survival and development. There is a need for predictive models which incorporate both the impacts of climate change on parasite transmission, and the wider elements of livestock management (Morgan & van Dijk, 2012). The architecture of the model developed in chapter three enables the exploration of how changes in climate sensitive parameters influence parasite outbreaks, within a managed grazing system.

4.2 Summary

Changing patterns of livestock parasite outbreaks in temperate regions have been attributed to climate change. There is an urgent need to understand the potential impacts of climate change on macro-parasite transmission, to foresee changes in risk and develop control strategies. Through developing a mechanistic model that incorporates the key elements of the transmission process, this chapter explores how changes in climate sensitive parameters will influence parasite outbreaks. The focus is on a monoxenous parasite in a managed grazing system.

Many stages of the macro-parasite transmission process are sensitive to abiotic conditions and climate change will impact on the frequency and intensity of outbreaks. A rise in temperatures is projected; survival and development of a parasite's free living stages are particularly temperature sensitive. The results demonstrate that changes in larval development and survival can result in non-linear responses in transmission dynamics, leading to a rapid increase in parasite burdens. Consequently small changes in climatic conditions around a critical threshold could results in dramatic changes in outbreak patterns. The position of the tipping point is influenced by the initial level of larval contamination on pasture at the start of the grazing season, and once the tipping point has been surpassed, the magnitude of outbreaks will be determined by the host's immune response. In addition to a rise in the mean annual temperature, an increase in amplitude of temperature fluctuations is expected. It is demonstrated that the amplitude of seasonal fluctuations in key parasite development and survival rates can affect the timing and magnitude of infections.

UK livestock have already experienced a shift in parasite species composition, with the emergence of tropically adapted species. Through simulating the impacts of rising temperatures on parasite dynamics, it is demonstrated that the increase in larval death rates of temperate species could result in a reduction in the number of high intensity outbreaks, and a shorter transmission window. Whilst for tropically adapted species, the temperature driven increase in larval development rate could lengthen the transmission window, and increase the frequency of high intensity outbreaks.

4.3. Introduction

There has been a rise in livestock helminth prevalence and intensity in temperate regions (Kenyon *et al.,* 2009b; Mitchell & Somerville, 2005; Pritchard *et al*., 2005), with climate change being implicated as one of the main drivers (Kenyon *et al*., 2009b; Van Dijk *et al*., 2008, 2010). Infections of these physically and economically damaging parasites are characterised by weight loss, lower milk yield, loss of condition, abortion and infertility, with heavy infections causing host mortality (Bisset, 1994; Mckellar, 1993). With potential for further climate driven increases in parasite prevalence and intensity, and the consequent welfare and economic implications, there is a need to understand the impacts of climate change on macro-parasite transmission.

The latest climate change projections indicate an expected rise in UK summer temperatures by 2.0^{o}C to 2.8^{o}C by 2050, for different regions of the UK (relative to 1961-1990 base-line, at 50% probability level, medium emissions scenario) (UKCP09, 2009a). Winter temperatures are projected to rise between 1.6^{o}C and 2.2^{o}C in the same period (UKCP09, 2009a). Climate change will impact on various stages of helminth transmission. Survival and development of a parasite's free-living stages are highly sensitive to abiotic conditions, and the influence of climate on these rates has been extensively studied (Kao *et al*., 2000; O'Connor *et al*., 2006).

Temperature has the predominant influence on the free-living stages with increased temperatures driving an increase in parasite development rate for a majority of livestock helminths (Fiel *et al.,* 2012; Pandey, 1972). However extreme temperatures are inimical to larval survival and the percentage of larvae recovered on pasture decreases at very low and high temperatures (Pandey, 1972), with thermal tolerance ranges varying with parasite species (O'Connor *et al*., 2006). Relative humidity has also been shown to influence larval survival and development (Krecek *et al.,* 1992; O'Connor *et al*., 2007; Pandey *et al*., 1993). However, humidity inside host faeces is sufficient to allow hatching, and shelter the larvae from desiccation; so temperature remains the most important climatic determinant of larval levels (Fiel *et al*., 2012; Krecek *et al*., 1992). In addition to influencing the survival and development of larvae within a grazing season, climate also affects over-winter survival and thus availability of infective larvae at the start of the following grazing season. It is these larvae that cause initial infections early in the year when naïve hosts are turned out to pasture (Waller & Thomas, 1978).

Long-term climatic trends influence the distribution of parasites at a coarse spatio-temporal scale, however the timing and intensity of outbreaks will be dependent on finer scale meteorological phenomena (Epstein, 2001). In addition to general warming trends, increased weather variability is predicted (Hansen *et al*., 2012; Planton *et al*., 2008), and temperatures are projected to rise faster in summer than winter (UKCP09, 2009a). Temperature fluctuations impact on population dynamics (Altizer *et al*., 2006; Roberts & Grenfell, 1992), with development times of the major parasites of livestock varying from one to two weeks in summer to four to six weeks in winter (Fiel *et al*., 2012). There are also seasonal patterns in livestock management processes. Spatio-temporal shifts in availability of resources are expected, due to predicted changes in climate and atmospheric CO_2 availability (Sutherst, 2001). This could result in timings of livestock reproduction and grazing being managed differently (Kenyon *et al*., 2009b; Rivington *et al*., 2007). Models that assume all rates remain constant across the year could lead to erroneous predictions of parasite dynamics.

In addition to affecting outbreak patterns of endemic species, climate change could also influence the spread of emerging parasites. Helminth prevalence and species composition has changed in the UK (Burgess *et al*., 2012; Kenyon *et al*., 2009b; Mitchell & Somerville, 2005). Historically, helminth infections of UK livestock were limited to species better adapted to colder climes e.g. *Ostertagia ostertagi*, *Teladorsagia circumcincta*, *Cooperia Spp*, *Trichostrongylus Spp*, and *Nematodirus Spp*. However there has been an increase in more tropically adapted species such as *Haemonchus contortus*, which typically dominates in regions with warm moist summers (O'Connor *et al*., 2006). In a recent survey *H. contortus* was found to be present on around 50% of UK farms with a high prevalence and widespread distribution, but a low outbreak intensity across its geographic range (Burgess *et al*., 2012). Its distribution extends to the north of the UK; with infections found on a majority of Scottish farms (Bartley *et al*., 2003). Throughout most of its range, parasite burdens are not high enough to lead to clinical cases, however heavy infections occur sporadically and pathological cases of heamonchosis are becoming an increasing problem for farmers (Burgess *et al*., 2012). It is not yet understood what is driving this pattern of infection, although changing climate is a possible culprit. The projected increase in UK temperatures will have differing effects on the survival and development of temperate and tropically adapted species. In addition to changing the intensity of parasite burdens, the periods of the year when transmission is possible (the transmission window) could also change.

A number of studies have aimed to link recent changes in the patterns of helminthiasis outbreaks with climate change (Kenyon *et al*., 2009b; Mas-Coma *et al*., 2008; Mitchell &

Somerville, 2005; Pritchard *et al*., 2005), yet projections of future risk for a majority of helminths remain elusive (Fox *et al.*, 2012). Of the existing predictions of future species distributions, most are based on correlative ecological niche models (Fox *et al*., 2011; Lawler *et al*., 2006; Pagel & Schurr, 2012; Thuiller *et al*., 2005). However, mechanistic process-based models are considered superior to correlative models in extrapolating beyond current conditions and forecasting the impacts of climate change (Mangal *et al*., 2008), and are less prone to breaking down when applied to novel scenarios (Fox *et al*., 2012).

This chapter aims to determine how changes in climate-sensitive elements of the transmission process influence macro-parasite risk. Specifically, it aims to explore the influence of 1. Changing development rates of the parasites' free living stages; 2. Changing death rates of the free-living stages; 3. Over-winter survival of the parasites free-living stages; 4. Host resistance under changing conditions; and 5. Changes in seasonal temperature fluctuations on the transmission windows of temperate and tropically adapted parasite species. Development of the mechanistic model in chapter three, that incorporates the key elements of the transmission process, allows us to explore how changes in climate sensitive parameters will influence parasite outbreaks.

4.4. Methods

4.4.1 Model structure

This chapter concentrates on monoxenous macro-parasites, transmitted via the faecal oral route, within a controlled grazing system. It is imperative to consider climate-sensitive elements of transmission within the context of a wider system of interacting processes. In the previous chapter (chapter three), the importance of incorporating spatial aggregation and host grazing behaviour in transmission models was demonstrated. It is particularly important to consider host grazing behaviour when exploring changes in survival and development of the parasites free-living stages. Although larval development determines the timing of availability of infective larvae on pasture, ultimately host grazing behaviour determines when hosts come into contact with such free-living stages.

The framework developed in chapter three is used here. This framework is a spatially-explicit, individual based model that incorporates the pivotal elements of the transmission process, including: survival and development of the parasites both on pasture and in the host, spatial heterogeneity of both resources and pathogens, the host's immunological response to parasitism and host grazing behaviour. The model is described in detail in chapter three. For completeness here the state variables are listed in table 1, model parameters are listed in table 2, and a summary of events is provided in table 3 below.

Patch states	**Notation**
co-ordinates of patch *i*	(x_i, y_i)
Sward height at patch *i*	h_i
Faecal contamination at patch *i*	f_i
Pre-infective larvae at patch *i*	l_i
Infective L3 larvae at patch *i*	L_i
Animal states	**Notation**
Location of animal *k*	i_k
Stomach contents of animal *k*	s_k
Immune response of animal *k*	r_k
Immature parasites in animal *k*	a_k
Mature parasites in animal *k*	A_k
Parasite eggs in animal *k*	e_k

Table 1. State variables.

Parameter	
Patch	
Intrinsic growth rate of sward	γ
Decay of faeces	φ
Development rate of L1 to L3 larvae	ε
Death rate of pre-infective larvae (L1)	ω
Death rate of infective larvae (L3)	ρ
Animal	
Bite rate	β
Faecal avoidance coefficient	μ
Death of immature larvae in host	ζ
Maturity of larvae in host	χ
Rate of resistance loss	σ
Resistance gain coefficient 1	ψ
Resistance gain coefficient 2	η
Death rate of adult larvae in host	τ
Rate of egg production of adult parasite	$\lambda(r_k)$
Anorexia coefficient	Λ
Intrinsic movement rate	ν
Probability of ingested L3 larvae establishing as adults	$\theta\,(r_k)$

Table 2. Summary of parameters, with all parameters expressed in units of minute^{-1}, with the exception of μ, ψ, η, Λ, r and θ, which are dimension free.

Patch Event	**Rate r_{ei}**	**Change in state variables**
Growth of sward at patch *i*	$\gamma h_i\left(1-\frac{h_i}{h_{\max}}\right)$	$h_i \rightarrow h_i + 1$
Development of larvae at patch *i*:	εl_i	$l_i \rightarrow l_i - 1$ $L_i \rightarrow L_i + 1$
Death of pre-infective larvae at patch *i*:	ωl_i	$l_i \rightarrow l_i - 1$
Death of infective L3 at patch *i*:	ρL_i	$L_i \rightarrow L_i - 1$
Decay of faeces at patch *i*:	φf_i	$f_i \rightarrow f_i - 1$

Animal Event	**Rate r_{ek}**	**Change in state variables**
Bite at current patch *i*, potential ingestion of infective and non-infective larvae, potential establishment of infective larvae and gain in immunity	$\beta(h_i - h_0)e^{-\mu_k f_i(a_k+A_k)^{\Lambda}}$	$h_i \rightarrow h_i - 1$ $L_i \rightarrow L_i - \left(\frac{B}{h_i}\right) \times L_i$ $l_i \rightarrow l_i - \left(\frac{B}{h_i}\right) \times l_i$ $s_k \rightarrow s_k + 1$ $r_k \rightarrow r_k + \left(\frac{B}{h_i}\right) \times L_i$ $a_k \rightarrow a_k + \theta(r_k)\left(\frac{B}{h_i}\right) \times L_i$
Death of immature adults in host *k*	ζa_k	$a_k \rightarrow a_k - 1$
Maturity of adults in host *k*	χa_k	$a_k \rightarrow a_k - 1$ $A_k \rightarrow A_k + 1$
Death of adults in host *k*	$\tau(r_k)A_k$	$A_k \rightarrow A_k - 1$
Gain of immunity in host *k* due to parasite burden	$(a_k+A_k)\eta$	$r_k \rightarrow r_k + 1$
Loss of immunity in host *k*	σr_k	$r_k \rightarrow r_k - 1$
Egg production in host *k*	$\frac{\lambda(r_k)A_k}{2}$	$e_k \rightarrow e_k + 1$
Defecation by host *k*	$f_{dep}(s_k - s_0)\Theta(s_k - s_0)$	$e_k \rightarrow e_k - \left(\frac{So}{S_k}e_k\right)$ $e_i \rightarrow e_i + \left(\frac{So}{S_k}e_k\right)$ $s_k \rightarrow s_k - s_o$ $f_i \rightarrow f_i + s_o$
Movement of animal *k*	$\frac{v}{z(i)}F(i,j)h_j$	$i_k = i \rightarrow i_k = j$

Table 3. Summary of events.

4.4.2 Parameterisation

Where parameter values are not stated for individual simulations they are set as outlined in this section. The model was parameterised to simulate five hosts over one grazing season, in a set-stocked temperate grassland system, as described by Smith *et al* (2010). All simulations were run for 365 days and replicate the spatial scale of such agricultural systems, using a field represented by a lattice consisting of 78 x 78 patches with each patch representing $0.5m^2$. This patch area corresponds with the area of one faecal pat and the refusal zone around it (Phillips, 1993). Hosts move around the lattice with a search rate representative of a cattle step rate of approximately three steps per second (Lazo & Soriguer, 1993) ($v = 0.015$), and a bite rate representing approximately 20,000 bites per day (Phillips, 1993) ($\beta = 0.1$). When a bite event occurs, one unit of forage is removed. Each $0.5m^2$ patch contains 50 bite areas of forage, as each cattle bite is approximately $0.01m^2$ (Phillips, 1993). Each patch is initialised with a sward height that provides 200 units of forage, and has a maximum sward height providing 400 units of forage. Each patch has an ungrazeable portion of 50 units of forage, and grass grows over time at rate $\gamma = 4x10^{-5}$ **(**Marion *et al*., 2008). These parameter values give rise to a set stocking scenario where intake approximately matches sward growth (Marion *et al*., 2008). Cattle deposit faeces approximately 10-15 times per day (Phillips, 1993) (f_{dep}=1.0, S_0=2000.0), and the field is initialised with no faecal contamination ($f_i = 0 \ \forall \ i = 1, \ldots, N$). Faeces decays at a rate where 10% of the faecal deposit remains 3 months post deposition (Haynes and Williams, 1993) ($\varphi = 1.776 \text{ x} 10^{-5}$). Faecal avoidance for animal *k* varies from no avoidance ($\mu_k = 0$) to effectively complete avoidance ($\mu_k = 10$) (Hutchings *et al* 2002, Smith *et al*., 2010), where almost complete avoidance of fresh faeces ($\mu_k = 5$) results in a bite rate from freshly-contaminated patches <1% of the bite rate from non-contaminated patches (Hutchings *et al* 2002, Smith *et al.*, 2010).

The parasite's lifecycle is representative of a typical temperate gastrointestinal helminth of grazing herbivores in a temperate climate. Death rate of pre-infective stages ($\omega = 0.0001$) results in approximately 1% of larvae remaining after 1 month (Kao *et al*., 2000; Leathwick *et al*., 1992). Approximately 50% of surviving pre-infective larvae develop to the infective L3 stage after 2 weeks on pasture (Kao *et al*., 2000; Leathwick *et al*., 1992; Pandey, 1972; Smith *et al*., 1986) ($\varepsilon = 5 \text{ x} 10^{-5}$). The death rate of infective L3 results in approximately 10% remaining after 3 months (Kao *et al*., 2000; Pandey *et al*., 1993) ($\rho = 1.5 \text{ x} 10^{-5}$).

Following ingestion of the infective stages approximately 40% of L3 larvae establish within a naïve host (Kao *et al*., 2000) ($\theta = 0.4$). The proportion that establish is monotonically non-

increasing with increased levels of acquired resistance. Increase in resistance is dependent upon ingestion of L3 (ψ = 0.25) and the size of the host's parasite population (η = 0.025). In the absence of parasitism, immunity wanes over time (σ = $1.9x10^{-8}$) (Roberts and Grenfell, 1991). Ingested larvae develop into fecund adult parasites in approximately 3 weeks (Kao *et al*., 2000) (χ = $3x10^{-5}$). Fecund adult parasites produce eggs at a rate which is monotonically decreasing as host resistance increases (Kao *et al*., 2000) (λ = 2). The life expectancy of the adult parasites in the host is approximately 5 weeks (Kao et al., 2000) (τ = 2 x 10^{-5}).

The starting condition of each simulation was representative of naïve hosts being released onto contaminated pasture. Each simulation was initialised with uninfected hosts (a_k =0, A_k =0, $\forall$ k = 1…D) on a pasture with 24000 infective L3 larvae, distributed over 20 randomly selected patches to reflect the aggregated distribution of larvae on pasture (Boag *et al*., 1989). Each scenario was repeated over 10 realisations to account for the stochastic nature of the model.

4.4.3 Model runs performed

Larval development rate

Climate change projections indicate a rise in temperatures across all regions of the UK (UKCP09, 2009a). The development rate of parasites on pasture, from non-infective to infective stages, is temperature dependent, with development rate increasing as temperatures rise (Chaparro & Canziani, 2010; Fiel *et al*., 2012; Le Jambre & Whitlock, 1973). For gastro-intestinal nematodes of herbivores, development times vary from less than one week to over 5 months (Kao *et al*., 2000; Leathwick *et al*., 1992; Pandey, 1972; Smith *et al*., 1986). To investigate how temperature driven changes in development rate of the free-living stages influences host parasite burdens, simulations were run with varying development rates from pre-infective to infective larval stages, ε = 10^{-5} to 10^{-4} in increments of 10^{-5}, (development time of 10 to 1 weeks). For simplicity, L1 refers to all pre-infective larval stages, whilst L3 refers to the infective larval stage. Larval death rates remained constant: L3 death rate, ρ = 3 x 10^{-5} (5% remaining after 3 months), and pre-infective L1 death rate, ω = 10^{-4} (approximately 1% of larvae remaining after 1 month) (Kao *et al*., 2000; Leathwick *et al*., 1992).

Larval death rate

Rising temperature under climate change will also affect death rate of the free-living stages. Increased summer temperatures can increase the death rate of temperate species; simulations were run to explore how temperature driven changes in larval death rate influence parasite levels. 3D larval development and death rate plots were generated to explore the relationship between these parameters. Climate will have differing impacts on the various free-living stages, with the pre-infective stages most sensitive to adverse abiotic conditions (O'Connor *et al*., 2006). Death rate of pre-infective stages were varied from $\omega = 2x10^{-5}$ to $2x10^{-4}$ in increments of $2x10^{-5}$, across the larval development range used above ($\varepsilon = 10^{-5}$ to 10^{-4} in increments of 10^{-5}). Infective L3 are more resilient to changing conditions as their protective sheath shields them from desiccation. However, the protective sheath prevents feeding, so an increase in temperatures could diminish L3 survival through raising metabolic rate and depleting energy reserves (O'Connor *et al*., 2006). Death rate of infective L3 larvae were varied from $\rho = 10^{-5}$ to 10^{-4} in increments of 10^{-5}, across the aforementioned developmental range.

Changes in over-wintering larvae

Climate change will influence over-winter larval survival, and thus the concentration of infective L3 at the start of the grazing season. To explore the influence of over-winter survival on transmission dynamics, runs were initiated with low (12000), medium (24000) , and high (48000) numbers of L3, distributed over 20 randomly selected patches to reflect the aggregated distribution of larvae on pasture (Boag *et al*., 1989). The influence of initial contamination levels was explored over the full range of L3 death rates (ρ) and larval development rates (ε) ($\rho = 10^{-5}$ to 10^{-4} in increments of 10^{-5}, $\varepsilon = 10^{-5}$ to 10^{-4} in increments of 10^{-5}).

Influence of host resistance

The importance of the host's immune response in transmission dynamics was demonstrated in chapter three. A host's ability to mount an effective immune response could be affected by climate change due to heat stress (Kelley, 1980), and the introduction of heat tolerant breeds with different immune responses. Additionally, climate change may lead to the introduction of novel pathogens, for which the host's ability to mount an immune response may be limited. Simulations were run to determine how changes in parasite development rate influence parasite burden for hosts with varying abilities to mount an immune response. Four sets of simulations were run for cohorts of hosts with: very low resistance (ψ= 0.01, η = 0.0075), low resistance (ψ = 0.125, η = 0.0125), medium resistance (ψ = 0.25, η = 0.025), and high

resistance (ψ = 0.5, η = 0.05). For each resistance level, simulations were run over differing larval development rates; $\varepsilon = 10^{-5}$ to 10^{-4} in increments of 10^{-5}, (development time of 10 to 1 weeks).

Amplitude of seasonal fluctuations

The impact of annual variation in key rates is also examined. In previous runs all rates remain constant over the year, in reality there are temperature driven periodic oscillations in larval development and death rates (Fiel *et al*., 2012). Variation in the amplitude of seasonal fluctuations around annual averages were explored for larval development rate (ε), L1 death rate (ω) and L3 death rate (ρ). As a general rule, larval death rates are highest in winter and summer as they are vulnerable to extreme temperatures, whilst larval development is accelerated by increasing temperature so is highest in summer, and lowest in winter. Fluctuations between minimum and maximum rates over the year, for larval development and death rates, are shown in figure 1. To explore the impact of seasonal variation, the amplitude of fluctuations were varied from 0% (rates remained constant at the annual average) to 100% (rates varied between the minimum and maximum rates as illustrated in figure 1), in 25% increments (figure 1.).

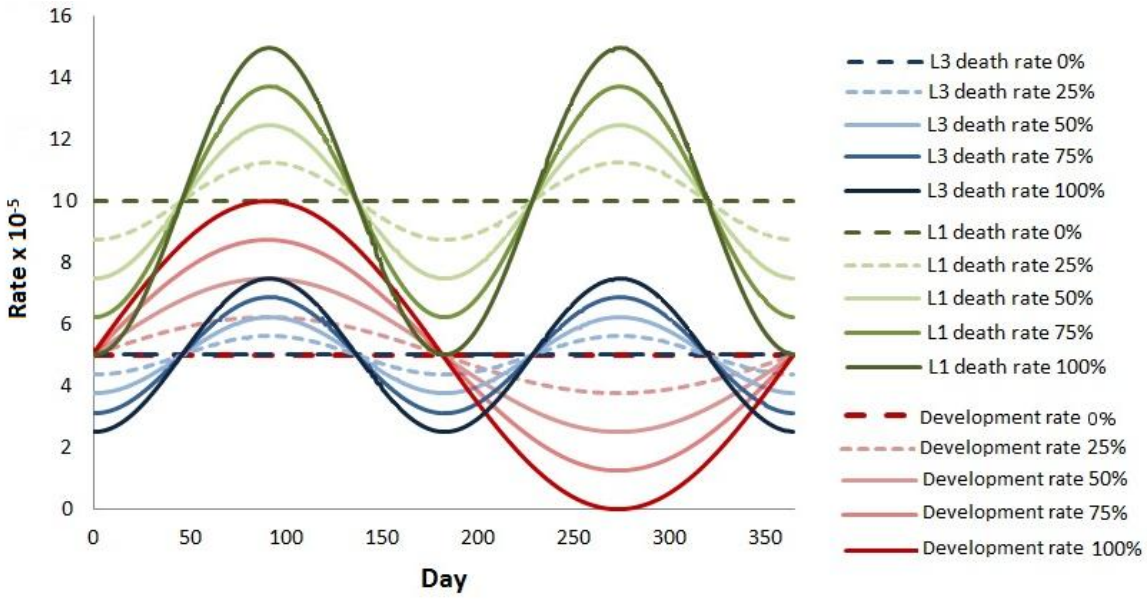


Figure 1. Seasonal variation in larval death and development rates

Impacts of climate change on temperate and tropically adapted species: current and future climate scenarios

The projected increase in UK temperatures will have differing effects on the relationship between development and death rates for temperate and tropically adapted species. For temperate species, increased temperatures will increase the death rates of the parasites free-living stages faster than it increases the development rate. In contrast, increased temperatures will increase the development rate of tropically adapted species, more than it influences the death rates, since such species are adapted to higher temperature regions. The impacts of climate change on the intensity of parasite outbreaks, and the periods of the year when outbreaks are possible (the transmission window), are explored by simulating development and death rates of a temperate and a tropically adapted species under current, and future climate scenarios. For all scenarios, it was assumed that the amplitude, but not the frequency, of annual climate cycles will change.

The following runs include seasonal variation in larval development and death rates. Climate change is expected to alter the timing of various management processes (Kenyon, Sargison, *et al*., 2009b; Rivington *et al*., 2007). With the incorporation of seasonality, there is temporal variation in the relationship between larval development and death rates, making timing of grazing important. For the runs of current and future climate scenarios for tropical and temperate species, the influence of timing of the grazing season and shifts in the transmission window are also explored; hosts are introduced onto contaminated pasture at different times of the year: 0%, 10%,20%,30%,40%,50%, 60% and 70% into the year.

Temperate parasite species - current climate scenario

To simulate transmission of a temperate species under current climatic conditions in a temperate region, the model was run with larval development rates representative of larvae developing from their pre-infective (L1) to infective (L3) stages in a minimum of 7 days ($min(\varepsilon) = 0$, $max(\varepsilon) = 10^{-4}x1$) . L1 and L3 death rates are representative of the average L1 and L3 larvae surviving on pasture for between 5 and 14 days, and between 9 and 28 days respectively ($min(\omega) = 10^{-5}x5$, $max(\omega) = 10^{-4}x1.5$; $min(\rho) = \omega = 10^{-5}x2.5$, $max(\rho) = 10^{-5}x7.5$).

Temperate parasite species - future climate scenario

To capture the influence of rising temperatures on temperate species, death rates of L1 and L3 larval stages were increased ($min(\omega) = 10^{-5}x5$, $max(\omega) = 10^{-4}x2$; $min(\rho) = 10^{-5}x2.5$, $max(\rho) = 10^{-4}x1.5$), These values are representative of the average L1 and L3 larvae surviving on

pasture for between 3 and 14 days, and between 5 and 28 days respectively. The development rates of larvae were no higher than in the current climate simulation ($min(\varepsilon) = 0$, $max(\varepsilon) = 10^{-4}x1$).

Tropical parasite species - current climate scenario

To simulate transmission of a tropical species under current climatic conditions in a temperate region, the model was run with larval development rates representative of larvae developing from their pre-infective (L1) to infective (L3) stages in a minimum of 14 days ($min(\varepsilon) = 0$, $max(\varepsilon) = 10^{-5}x7.5$). L1 and L3 death rates are representative of the average L1 and L3 larvae surviving on pasture for between 5 and 14 days, and between 9 and 28 days respectively ($min(\omega) = 10^{-5}x5$, $max(\omega) = 10^{-4}x1.5$; $min(\rho) = 10^{-5}x2.5$, $max(\rho) = 10^{-5}x7.5$).

Tropical parasite species - future climate scenario

To capture the influence of rising temperatures on tropically adapted species, the development rate of larvae increased compared to the 'current climate scenario', representative of larvae developing from their pre-infective (L1) to infective (L3) stages in a minimum of 3 days ($min(\varepsilon) = 0$, $max(\varepsilon) = 10^{-4}x\ 2$). Death rates of L1 and L3 larval stages were not increased from the 'current climate' scenario ($min(\omega)=10^{-5}x5$, $max(\omega) = 10^{-4}x1.5$; $min(\rho) = 10^{-5}x2.5$, $max(\rho) = 10^{-5}x7.5$).

4.4.4 Quantities observed in the simulations

The mean, averaged over 10 simulations, and the standard deviation, were reported for each output variable (parasite intensity, infective L3 ingested per host per day and host resistance). Peak parasite burden was used as a measure of infection, as host morbidity and mortality are directly proportional to parasite intensity (Grenfell & Dobson, 1995). However, a host can be affected by both parasite intensity and the duration of infection. To determine the usefulness of this measure as a reliable indication of disease levels, both the peak parasite intensity and the cumulative exposure over the grazing season, measured by integrating the infection curve, were calculated for the scenarios detailed above. Over the range of simulations, both measures provided qualitatively similar results. Peak parasite intensity is used as a measure of infection here as it is a more intuitive measure than the area under the curve, and can be compared to empirical data. If cumulative burden was chosen instead as a measure of parasitism, the trends shown in the results, and the conclusions, would remain the same.

4.5. Results

Our model successfully reproduces the parasite dynamics empirically observed in a livestock grazing system (Callinan *et al*., 1982; Claerebout *et al*., 1998; Cornell *et al*., 2003; Hilderson *et al*., 1993; Roberts & Grenfell, 1991; Smith & Grenfell, 1985;. Smith & Guerrero, 1993; Williams *et al*., 1993). The introduction of susceptible hosts onto contaminated pasture accounts for the rapid increase in ingested larvae and adult parasites in the host, and the subsequent acquisition of immunity accounts for the consequent decline in parasites (figure 2).

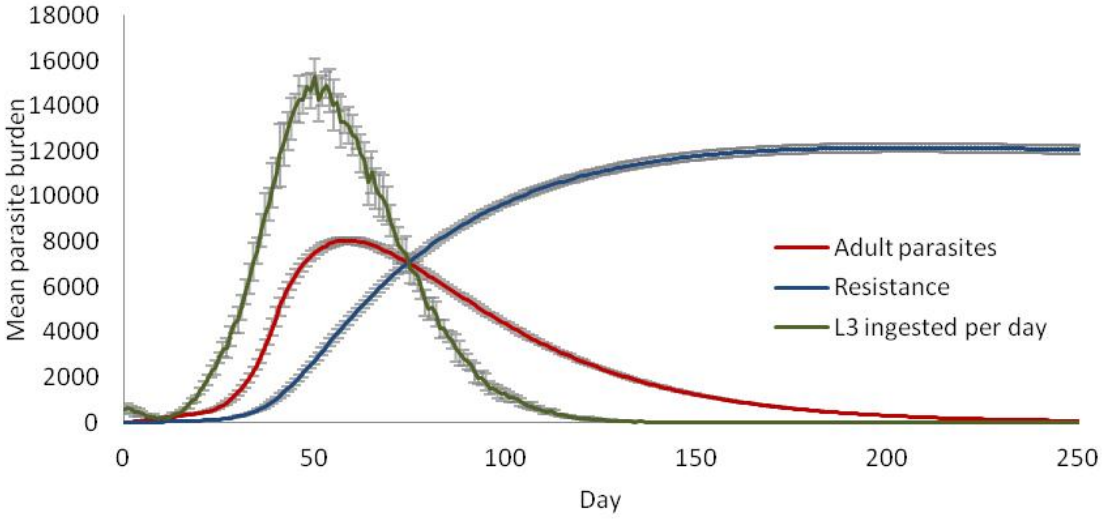


Figure 2. Host parasite burden, L3 ingested per day and host resistance level (±SD) over one grazing season, using the standard parameter values detailed above.

Larval development

Changing temperatures will alter the development rate of larvae on pasture, with development rate rising with increasing temperature. Simulations show that increasing development rates result in a non-linear increase in parasite burden, with a distinct 'tipping point' (figure 3).

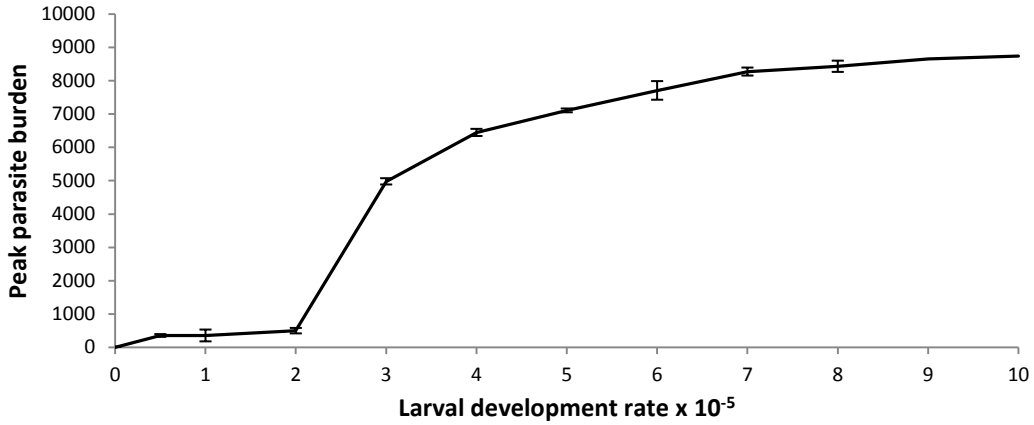


Figure 3. Peak parasite burden (±SD) over different larval development rates.

Larval death rate

Changes in abiotic conditions will also affect the death rate of the free-living stages. The position of the tipping point is primarily dependent on the development and death rates of both pre-infective (L1) and infective (L3) larvae (figure 4). Figure 4 illustrates the parameter space for which outbreaks occur, dependent on the relationship between larval development and death rates.

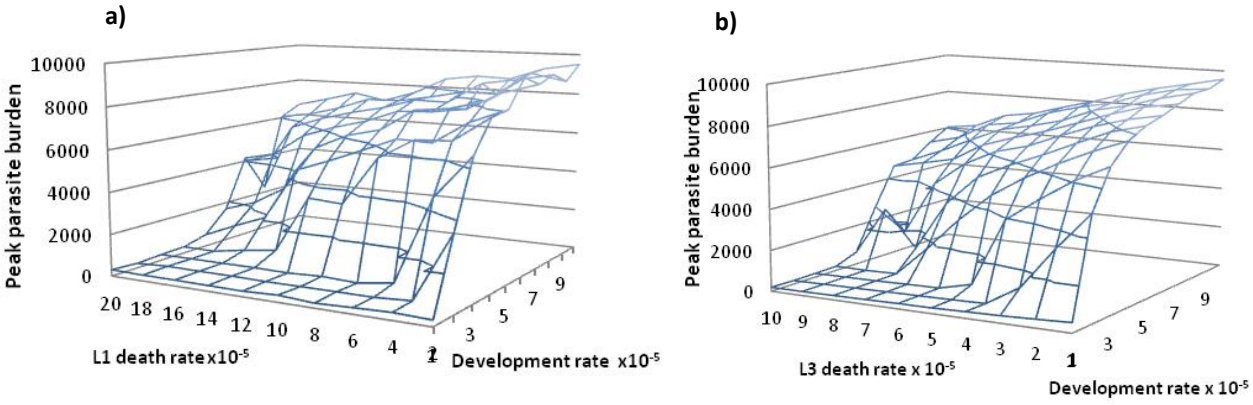


Figure 4. Influence of a) L1 death rate and larval development rate, and b) L3 death rate and larval development rate, on parasite burden.

Over-wintering larvae

Climate change will influence the overwinter survival of larvae, and hence the initial pasture contamination at the start of the grazing season. The position of the 'tipping point' (shown in figure 4) is influenced by the initial level of L3 contamination on pasture (figure 5).

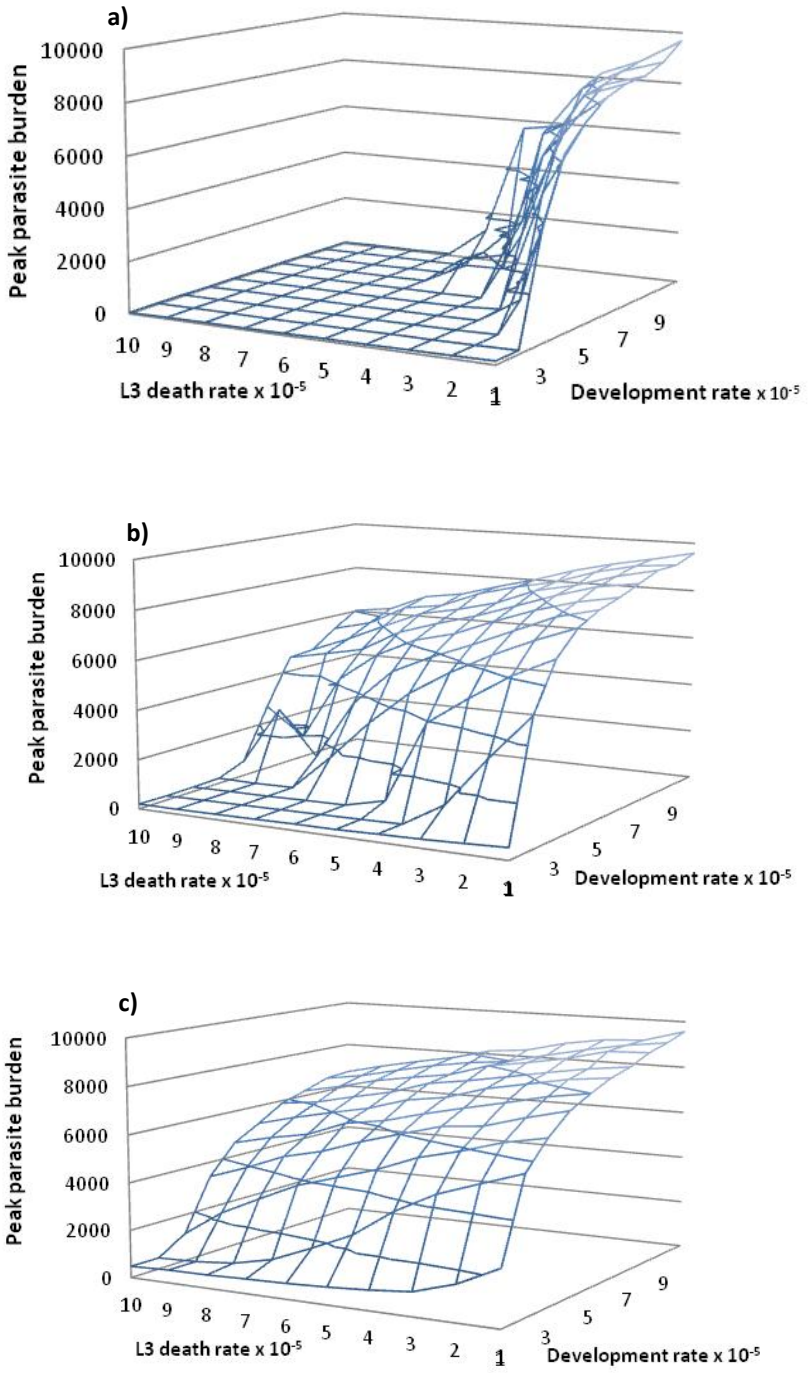


Figure 5. Influence of L3 development and death rates on parasite burden. Initial L3 concentration on pasture a) low (12000), b) medium (24000), and c) high (48000).

Host resistance

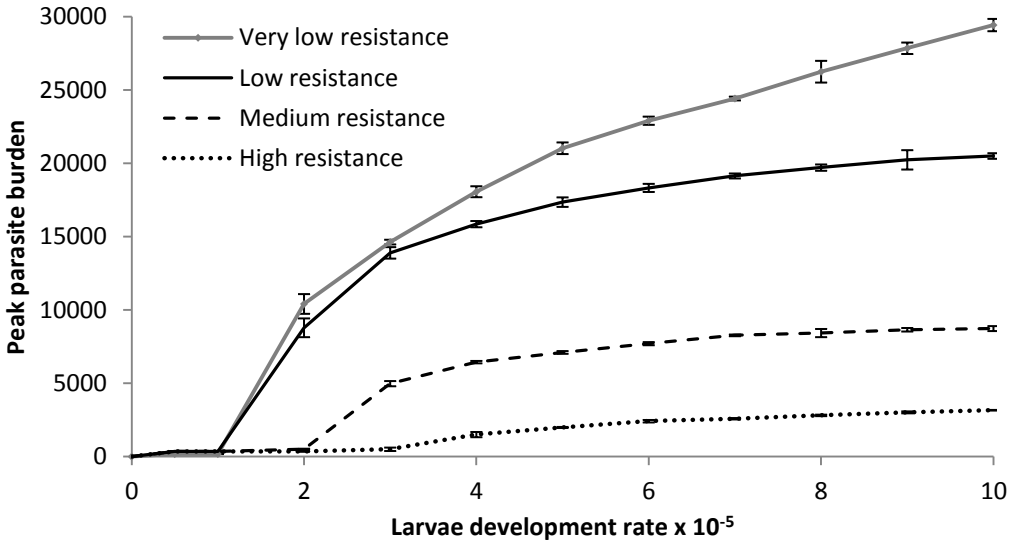


Figure 6. Influence of host resistance on peak parasite burden, across different larval development rates. Values shown for 'very low resistance' level are the actual values divided by two, to allow all values to be compared clearly on the same scale.

The position of the tipping point is also influenced by host resistance (figure 6). Additionally, once the tipping point has been reached, the magnitude of outbreaks is dependent on the host's ability to mount an effective immune response (figure 6)

Amplitude of seasonal fluctuations

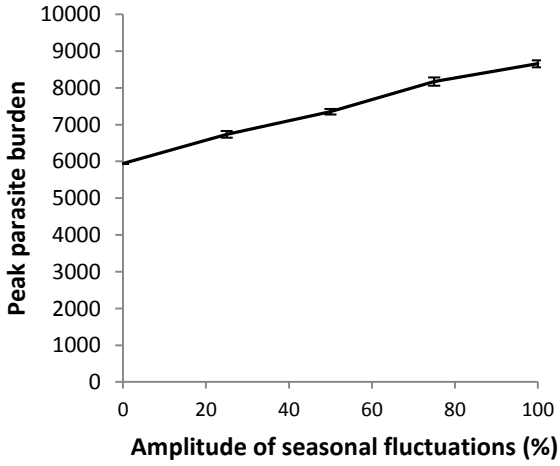


Fig 7. Peak parasite burden (±SD) under differing amplitudes of seasonal oscillation in larval development and death rates. Variation in amplitude of seasonal fluctuations around annual averages from 0 - 100%, with the grazing season starting in spring (25% into the year).

If seasonality is not incorporated the intensity of outbreaks can be underestimated (figure 7). This finding is consistent with the work of Roberts and Grenfell (1991), who demonstrated that temporal variation in environmental variables can influence outbreaks of parasites in managed livestock systems.

Changes in seasonal temperature fluctuations have differing influences on different parasite species. Increased temperatures accelerate the death rate of temperate species, resulting in a decrease in the transmission window between current (figure 8) and future climate scenarios (figure 9). The large error bars in the future climate scenario are due to outbreaks only occurring in some realisations of the stochastic model, illustrating the potential instability of the system under future conditions.

Under the current climate scenario, for a tropically adapted species, prolonged larval development times result in a short transmission window, with low levels of parasitism in some realisations and sporadic high intensity outbreaks in others (illustrated by the large error bars) (figure 9). High temperatures favour the development of tropical species, with little inimical influence on survival, enabling high intensity outbreaks of theses parasites to occur across a large proportion of the year in the future climate scenario (figure 10).

Temperate parasite species; current climate scenario

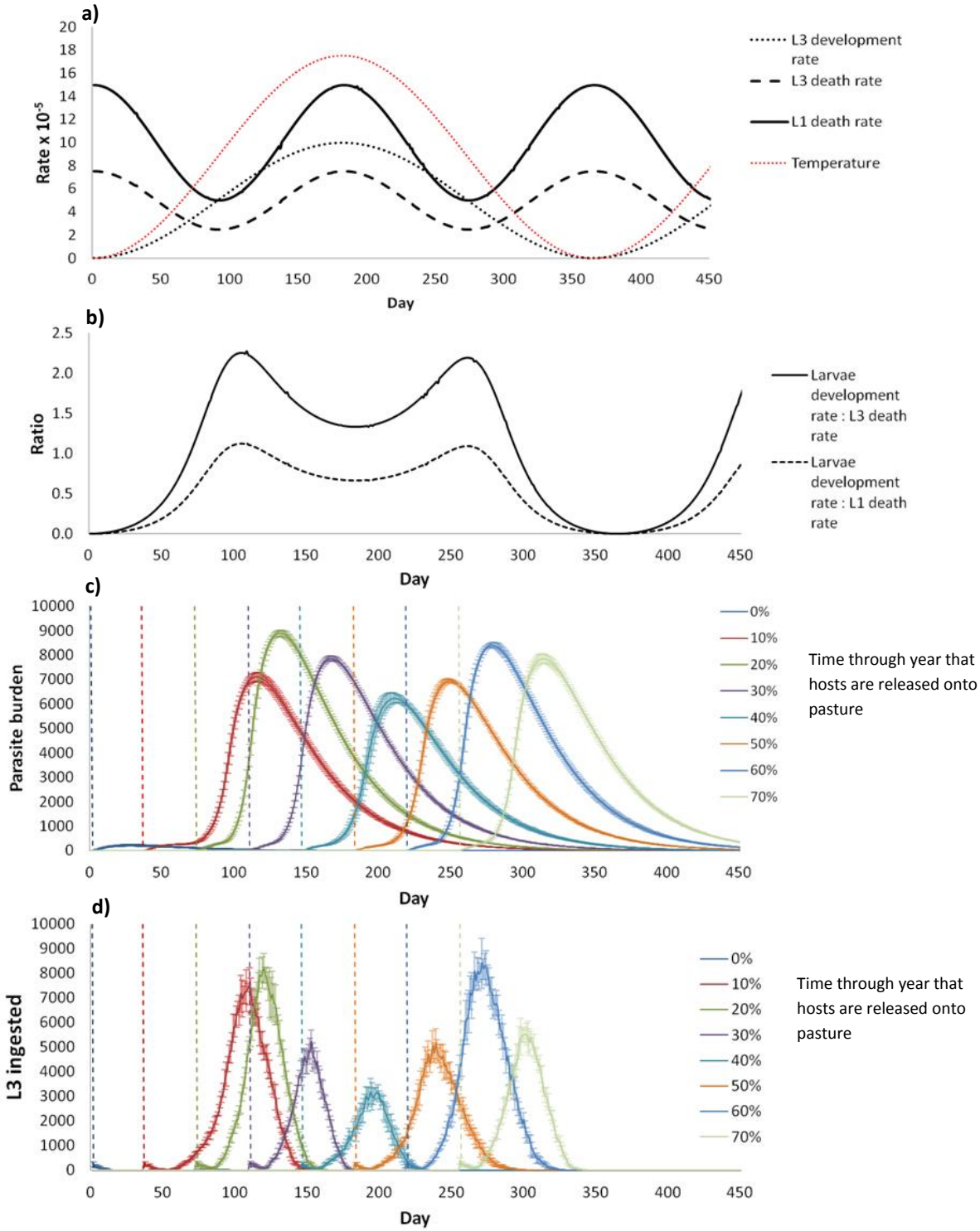


Fig 8. Temperate species, under current climatic conditions of a temperate region, for hosts released onto pasture at different times of year. a) Larval development rates, L1 and L3 death rates, temperature, b) ratio of larval development rate to L1 and L3 death rates over the year, c) parasite burden, ±SD, and times hosts are released onto pasture and d) L3 ingested per host per day, ±SD, and times hosts are released onto pasture.

Temperate parasite species; future climate scenario

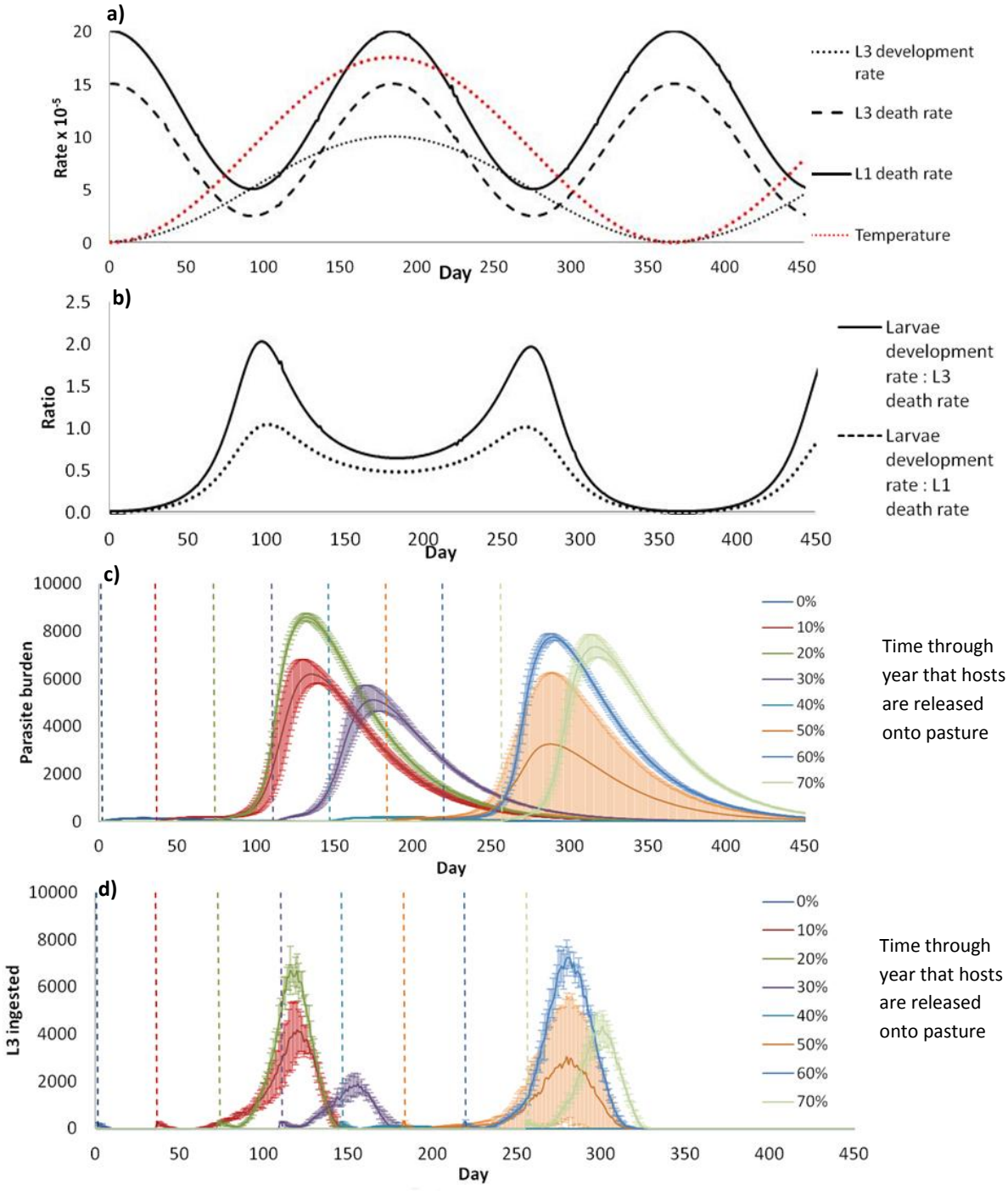


Fig 9. Temperate species, under increased temperatures (higher increase in larval death rate than development rate), for hosts released onto pasture at different times of year. a) Larval development rate, L1 and L3 death rates, temperature, b) ratio of larval development rate to L1 and L3 death rates over the year. c) parasite burden, ±SD, and times hosts are released onto pasture and d) L3 ingested per host per day, ±SD, and times hosts are released onto pasture.

Tropical parasite species; current climate

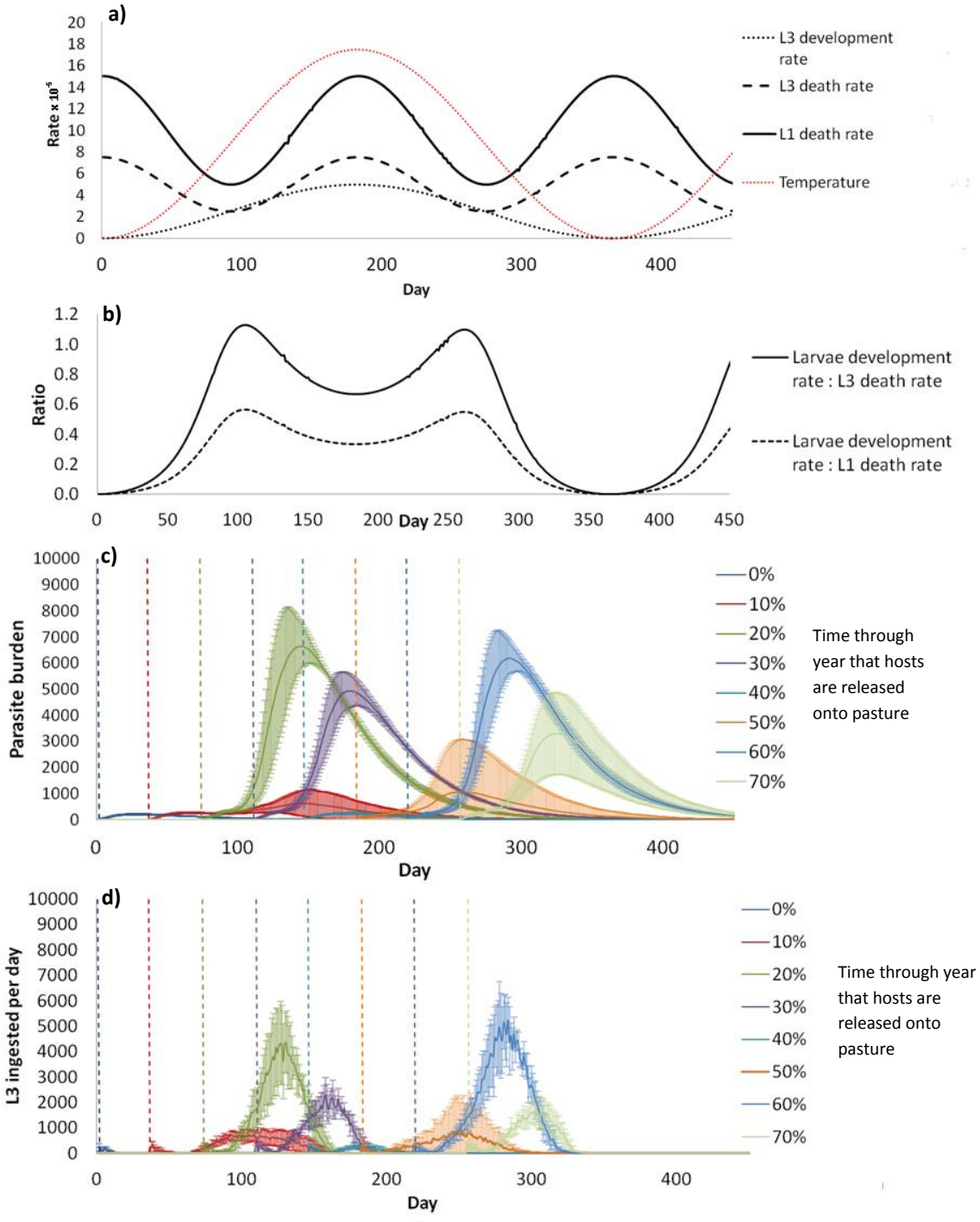


Fig 10. Tropically adapted species, under current climatic conditions of a temperate region, for hosts released onto pasture at different times of year. a) Larval development rate, L1 and L3 death rates, temperature, b) ratio of larval development rate to L1 and L3 death rates over the year. c) parasite burden, ±SD, and times hosts are released onto pasture and d) L3 ingested per host per day, ±SD, and times hosts are released onto pasture.

Tropical parasite species: future climate

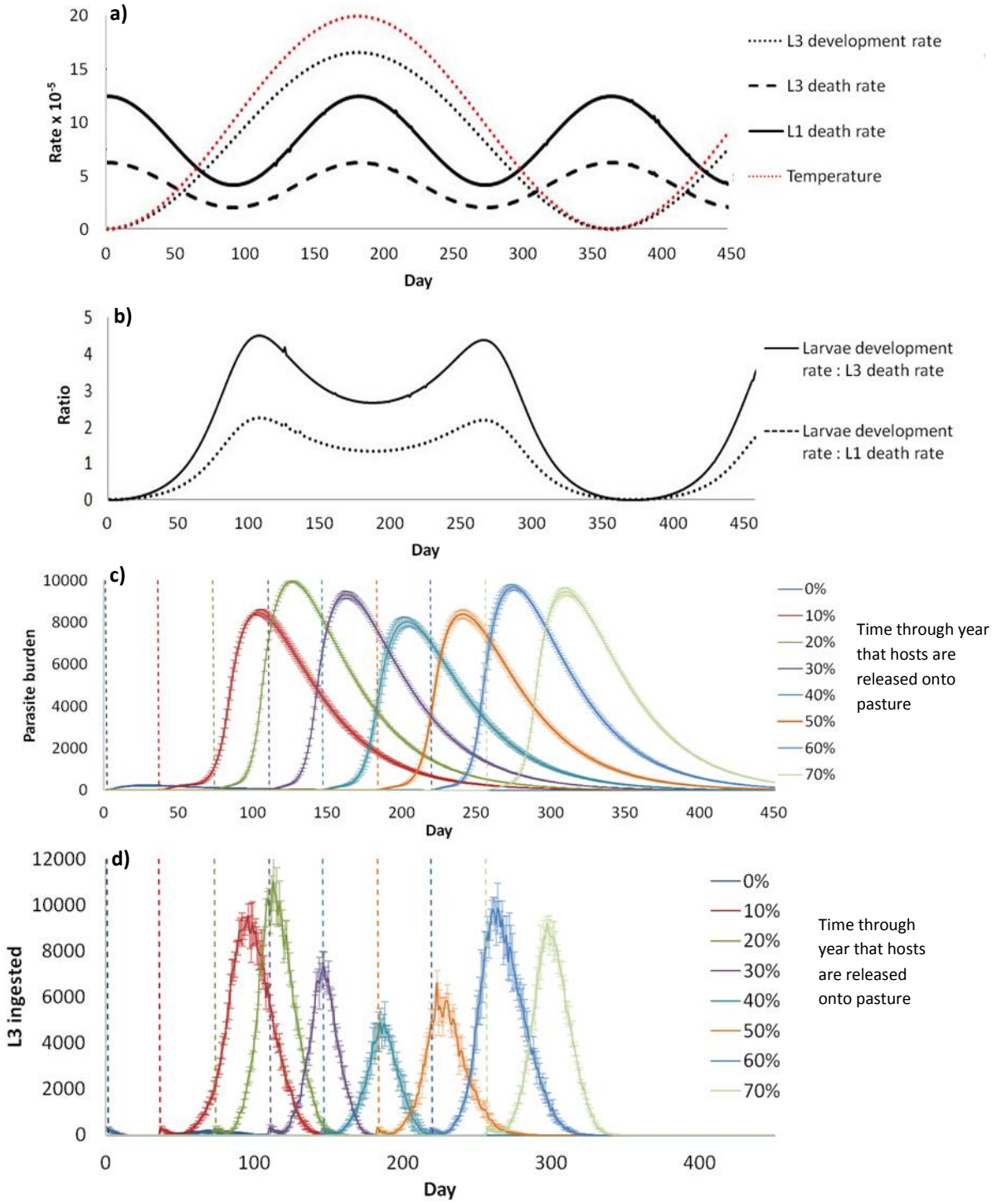


Fig 11. Tropically adapted species, under increased temperatures (higher increase in larval development rate than death rate), for hosts released onto pasture at different times of year. a) Larval development rate, L1 and L3 death rates, temperature, b) ratio of larval development rate to L1 and L3 death rates over the year. c) parasite burden, ±SD, and times hosts are released onto pasture and d) L3 ingested per host per day, ±SD, and times hosts are released onto pasture.

4.6. Discussion

Macro-parasite transmission is influenced by multiple factors; this chapter explores the impact of variations in climate sensitive elements of the transmission process. Prior to altering climate sensitive parameters, figure 2 confirms that the model successfully replicates trends observed in empirical studies (Callinan *et al*., 1982; Claerebout *et al*., 1998; Cornell *et al*., 2003; Hilderson *et al*., 1993; Smith & Grenfell, 1985; Smith & Guerrero, 1993; Williams *et al*., 1993). The properties of other aspects of the model including behavioural and immunological responses of the host are covered extensively in chapter three.

Larval development and survival

Climate change will influence transmission of parasitic nematodes through impacting on development of the parasites' free-living stages. An increase in larval development rate drives a non-linear increase in parasite intensity (figure 3). This sudden rise is due to decreased development times allowing multiple generations of larvae to build up on pasture over one season, causing high intensity outbreaks for parasites that pose minimal risk under current climatic conditions. Consequently, as temperatures gradually rise, a small change in abiotic conditions could result in a 'tipping point' being surpassed, leading to a sudden increase in parasite burdens with little warning. This could lead to a substantial increase in clinical outbreaks of parasites that are currently widespread but at low intensities. The identification of a tipping point provides a possible explanation for observed patterns of *H. contortus* infection in the UK (present at low levels across a wide thermal range, with occasional high intensity outbreaks (Burgess *et al*., 2012)). As summer temperatures continue to rise, high intensity pathological *H. contortus* outbreaks are likely to occur in more years and across a greater geographical range. The capacity for climate change to impact on different parasite populations is dependent on where on the response curve (figure 3) rates currently lie.

Survival of the parasites free-living stages will also be influenced by changing climatic conditions. Increased minimum temperatures are likely to decrease death rates of tropically adapted species, which are vulnerable to low temperatures (e.g. *H. contortus*). Conversely increased temperatures are likely to increase death rates of temperate species which are impervious to prolonged cold conditions but vulnerable to high temperatures and desiccation (e.g. *T. circumcincta*). Changes in larval death rates will impact on parasite transmission and lead to shifts in the position of the tipping point (figure 4); it is the balance between development and death rates that determines if a high enough infective larval population is

maintained for infections to perpetuate. Increased temperatures will sway the balance in opposing directions for different parasite species.

Over-wintering larvae

Climate change will also affect over-winter survival of larvae on pasture, influencing their availability at the start of the grazing season. Increased levels of initial contamination facilitate high intensity outbreaks of parasites across a broader range of development and death rates (figure 5). Consequently, the position of the tipping point (the relationship between larval death and development required for an outbreak) will be influenced by initial pasture contamination levels (figure 5). There is also potential for feedback between climate driven changes in transmission within a grazing season and the size of the overwintering larval population.

Climate change will have contrasting effects on the over-wintering potential of different parasite species. For temperate species that can survive cold winters, warmer temperatures could decrease over-winter larval survival (Kenyon *et al*., 2009b). This is due to temperatures accelerating the metabolic rate of the L3 larvae, depleting their finite energy reserves as their protective sheaths prevent them from feeding. The decreased survival on pasture could be counteracted by lengthening of the grazing season; parasites may not have to survive as long in a host free environment. For tropical species the decrease in frosts, combined with an extended grazing season, could enable the survival of parasites on pasture over winter.

Host resistance

Peak parasite burden, after the tipping point has been surpassed, will be regulated through the host's ability to mount an immune response (figure 6). This supports the empirical work of (Hudson *et al.,* 2006) who suggested that climate driven increases in parasite transmission will have the greatest impact on populations with limited ability to acquire an immune response.

Climate change will affect the host's ability to mount an effective immune response. In the short term, heat stress caused by extreme weather events will alter host susceptibility to infection (Kelley, 1980). In the longer term, climate change could alter breed structure, due to the introduction of heat tolerant breeds. This may impact on peak parasite burdens as different breeds have varying levels of disease susceptibility and immunity acquisition (Albers *et al*., 1987; Eguale *et al.,* 2009; Good *et al.,* 2006; Harle *et al*., 2007; Wilson &

Mellor, 2008; Yadav *et al.,* 1993). The results highlight that changes in immunity need to be considered when predicting the intensity of parasite outbreaks.

Climate change may also facilitate the introduction of tropical pathogens which have not co-evolved with the hosts. These novel parasite-host combinations are likely to lead to high intensity outbreaks, as the host's capacity to acquire resistance is likely to be more limited than for historically endemic pathogens. The ability of a host to mount an effective immune response against endemic parasites can also be impaired during extreme weather events, as the hosts experience heat stress (Kelley, 1980). Heat stress could have confounding impacts on transmission dynamics for a pathogen transmitted via the faecal-oral route Feed intake in cows decreases with temperature and rumen activity can even be shut down when cattle are exposed to prolonged periods of heat stress (Beatty *et al.,* 2008). This could lead to a decrease in the number of infective larvae ingested, although the true impact of inappetance on transmission is likely to be complex due to interactions between nutrition and immunity (discussed in chapter three).

Changes in the transmission window

Larval development and death rates differ across the year, driven by temperature oscillations. The amplitudes of temperature oscillations are likely to be affected by climate change with projections indicating that summer temperatures will increase faster than winter temperatures (UKCP09, 2009). It is important to incorporate seasonal variation in key rates in climate sensitive transmission models. If within year variations in larval development and death rates are not considered, the potential intensity of parasite outbreaks can be underestimated (figure 7). The influence of seasonality is dependent on the timing when naïve hosts are first exposed to infective L3 (figures 8-11), as the relationships between larval death rate and development rates oscillate over the year (figures 8b-11b). Expected changes in timing of livestock management processes (Kenyon *et al.,* 2009b; Rivington *et al*., 2007) could therefore alter parasite risk (figures 8c and 8d).

The consequences of changing the magnitude of seasonal weather fluctuations will vary with parasite species. For temperate species with high transmission levels under current conditions (figure 8), increased summer temperatures would have a disproportionately deleterious impact on the survival of free-living stages, as they are susceptible to desiccation (figure 9a). As a consequence the transmission window of these parasites would be reduced under future climatic conditions (figure 9c). In contrast, for tropically adapted species transmission is currently limited by slow development rates, resulting in only occasional outbreaks at limited

times of the year (figure 10). Rising temperatures would increase larval development rate, with little impact on death rate (figure 11a). This would amplify the availability of infective larvae on pasture (figure 11d) and parasite outbreaks could become the norm across a lengthened transmission window (figure 11c).

Quantitative predictions

Climate driven changes in parasite transmission could lead to sudden changes in the frequency and intensity of outbreaks. The timing and magnitude of these changes will vary across host-parasite combinations. Thermal tolerance ranges vary with parasite species, and if quantitative predictions are to be made for specific pathogens, response curves to extrinsic drivers need to be fully determined. However, the responses of a particular species to abiotic conditions can vary with location (Chaparro *et al*., 2011; Van Dijk & Morgan, 2010). To further complicate parameterisation of predictive models, parasite populations within the same location have been found to have multiple phenotypes with different developmental temperature thresholds (Le Jambre & Whitlock, 1973; Van Dijk & Morgan, 2010). This polymorphic bet-hedging provides populations with a wide thermal tolerance range, potentially enabling a given population to have multiple tipping points, facilitating outbreaks under a variety of climatic scenarios. The probabilistic nature of climate change projections further complicates quantitative predictions, with substantial variation in predictions of future temperatures, depending on region, emissions scenario, and probability level (UKCP09, 2009).

Implications for control

The efficacy of different parasite management strategies will vary depending on where on the curve of figures two and three infection levels lie. If the tipping point is only just exceeded, the influence of temperate on development could be negated through grazing management, decreasing the concentration of infective larvae at the start of the grazing season, or by applying larvicides to reduce larval survival on pasture. If rising temperatures push the parasites development rate far beyond the tipping point, and complete alleviation of outbreaks is unfeasible, increasing the ability of hosts to acquire resistance (e.g. though genetic selection or improved nutrition) will dampen outbreak intensity. Through the incorporation of seasonal fluctuations in larval development and death rates, the model can also indicate when concentrations of infective larvae are highest, and introduction of naive hosts onto pasture should be avoided.

Conclusions

Our results indicate that climate change can lead to non-linear responses in infection dynamics, and minor alterations in climatic conditions could cause dramatic shifts in outbreak patterns. This could lead to an increase in the frequency and geographic range of pathological cases for pathogens that are currently widespread but at low incidence levels. The relationship between survival and development of the parasites' free-living stages is a pivotal determinant of outbreak intensity; rising temperatures will push this balance in opposing directions for different parasite species. This precarious balance will also be influenced by over-winter larval survival, seasonal weather fluctuations, and host resistance.

Chapter 5

General Discussion

5.1. Summary

Climate change has been implicated as a driving force for recent parasite range expansions, and efforts have been made to model the relationship between pathogen levels and climate. The most economically important parasitic helminths in temperate climates include the nematodes *Ostertagia ostertagi*, *Cooperia oncophora*, *Trichostrongylus spp*, *Haemonchus contortus*, *Teladorsagia circumcincta* and *Nematodirus battus*, and the trematode *Fasciola hepatica* (Kenyon *et al*., 2009b; Van Dijk *et al*., 2010). The increase in these helminths in recent years (De Waal *et al*., 2007; Kenyon *et al*., 2009b; Mitchell & Somerville, 2005; Pritchard *et al*., 2005; Van Dijk *et al*., 2008) has been attributed to climate change, since the survival of the free-living stages is chiefly affected by temperature and moisture, and larval development rate is highly temperature dependent (Armour, 1980; Barnes *et al*., 1988; Coyne & Smith, 1992; O'Connor *et al*., 2007).

The development of evidence-based risk assessments and targeted surveillance are pivotal when the welfare and economic costs of these pathogens are considered. Despite the deleterious impacts of helminths on the livestock industry and their dependence on climatic conditions, predictions of long-term threats to animal health from climate change have so far concentrated on heat stress (Beatty *et al*., 2008; García-Ispierto *et al*., 2007; Gregory, 2010; Harle *et al*., 2007; Kendall *et al*., 2006; Nardone *et al*., 2006) and viruses spread by volant vectors, such as BTV (Caligiuri *et al*., 2004; De Koeijer *et al*., 2007; Gubbins *et al*., 2008; Pili *et al*., 2006; Purse *et al*., 2004; Racloz *et al*., 2007). Although there have been a number of studies aiming to link the recent changes in helminthiasis abundance and distribution with environmental change (Abbott *et al*., 2007; Kenyon *et al*., 2009b; Mas-Coma *et al*., 2008; Mitchell & Somerville, 2005; O'Connor *et al*., 2006; Pritchard *et al*., 2005; Van Dijk *et al*., 2008), there is a lack of predictions for future helminth risk to livestock.

In this thesis, the long term impacts of climate change on livestock helminths in the UK are considered. Chapter two focused on long-term projections of fasciolosis risk in the UK, whilst chapters three and four explored how climate driven perturbations in different elements of the

transmission process could affect outbreaks of monoxenous nematodes. This chapter explores the implications of the key findings, identify limitations in the current study and potential for future model developments, and highlighting the need for a broader systems approach for understanding future risks to the livestock industry.

5.2. Future fasciolosis risk

The UK's National Animal Disease Information Service (NADIS) and the Department of Agriculture and Food in Ireland currently predict *F. hepatica* incidence using the Ollerenshaw index, which is a correlative model focusing on temperature and moisture availability (Ollerenshaw, 1966; Ollerenshaw & Rowlands, 1959). In chapter two the first long-term projections of future *F. hepatica* risk for 2020-2070 across the UK are developed, through applying a modified Ollerenshaw index to UKCP09 climate projections (Fox *et al*., 2011). The resultant risk maps predict unprecedented levels of fasciolosis outbreaks, and possible changes in the timing of disease outbreaks due to increased risk from overwintering larvae. Despite an overall long term increase in all regions of the UK, spatio-temporal variation in risk levels is expected, with infection risk due to reduce in some areas and fluctuate greatly in others. This forecast is the first approximation of the potential impacts of climate change on helminth risk in the UK. This work illustrates that fasciolosis is a problem that is not going to go away under climate change, and ongoing disease surveillance and control will be required. The projected risk maps indicate where limited resources should be targeted

Despite the complexity of the liver fluke life-cycle, fasciolosis is primarily governed by elementary climate variables - temperature and moisture availability. This work demonstrates that predictions based on correlative models can provide broad indications of future risk for parasites whose transmission is governed by fundamental climatic factors. The Ollerenshaw index has not been superseded by a more advanced model primarily due to the dearth of accurate prevalence data. Ollerenshaw (1966) acknowledged that the lack of information on disease incidence is the primary obstacle in meteoro-pathological forecasting, yet little has been done since to rectify this fundamental deficit. Fasciolosis is not a notifiable disease; the number of outbreaks that are recorded is small, and the number of outbreaks that are accurately recorded is a smaller subset still. Sporadic sheep deaths are often unreported, so there is no recorded difference between years of low outbreaks and years of no outbreaks (Ollerenshaw, 1966). The Veterinary Investigation Surveillance Report (VIDA) can hint at the trends in fasciolosis levels however VIDA is a passive surveillance system; hence results

are affected by disease awareness, farmer impetus, and changing laboratory methods. There has been little change in laboratory methods and awareness for macro-parasites such as liver fluke, adding some stability to the data, so an indication of changing disease patterns can be gleaned from the VIDA database, despite its imperfections (Van Dijk *et al*., 2008).

The power of the model used in chapter two is qualitatively demonstrated by the predicted distribution shown in the 2000-2006 risk map echoing the latest fluke distribution map (Claridge *et al*., 2012), which is based on 2006-2007 prevalence data in England and Wales. Although quantitative validation was not possible in this thesis due to limitations in the availability of longitudinal datasets, possible data sources for future validation include integration of liver condemnation data from abattoirs with cattle movement records, or bulk milk ELISA based prevalence data.

For long term projections, ongoing validation is required to ensure that the changing climate is not pushing the model beyond its limits. To predict future risk under the climate change scenarios considered, correlative models need to be able to predict risk outside the temporal range of the training data set (Fox *et al*., 2012). The Ollerenshaw risk index was originally developed in 1959, and is still used by NADIS to provide UK farmers with an indication of the following season's liver fluke risk, demonstrating the reliability of the model when applied outwith the range of the training dataset. However, we are entering a world of climate extremes. There is therefore a need for ongoing validation and refinement of correlative predictive models to ensure that correlations still stand under novel climate conditions.

5.3. Impacts of climate change on macro-parasites in a grazing system

Due to the limitations of the correlative approach (discussed in detail in chapter one) there is a drive towards mechanistic, process-based models, which can account for the consequences of subtle interactions between various components of a system under climate influence. Parasite transmission is critically dependent on the timing of processes, and these timings are often temperature dependent; the incorporation of host grazing behaviour is necessary for determining when hosts come into contact with parasites on pasture. In chapter three a transmission model was developed which incorporated the key elements of parasite dynamics within a managed grazing system. In addition to providing the framework for understanding how climate change will impact on the transmission process, interesting findings are also revealed on the importance of differing host defence strategies in parasite transmission. Hosts

are able to limit parasite burdens through selective grazing, however under certain conditions faecal avoidance behaviour can increase parasite risk. The model also demonstrates the possible consequences of maintaining livestock in conditions where their freedom to express natural behaviours is compromised.

Chapter four explores how parasite burdens are affected by changes in the values of climate sensitive parameters. The results indicate that changes in larvae development and survival result in non-linear responses in transmission. Consequently small changes in climatic conditions around critical thresholds could result in dramatic changes in outbreak patterns. In addition to driving variations in outbreak intensity, the length of the transmission window could also change under future climes. High summer temperatures and milder winters could result in the transmission window contracting for temperate species, and expanding for tropically adapted species. However, it is unlikely that this will result in no net-change in the impact of parasite outbreaks. The host's ability to mount an immune response against novel pathogens may be limited, leading to the increase in highly pathogenic parasites outweighing the decrease in parasite species to which systems are currently adapted.

The consequences of climate driven changes in parasite development and survival are determined, in part, by the initial levels of pasture contamination at the start of the grazing season and the host's ability to mount an effective immune response. This reveals potential opportunities for mitigation and control strategies.

5.3.1 Potential model application

Due to subtle interactions between components of the transmission cycle and abiotic conditions, a changing climate will alter the efficacy of different control strategies. The model developed in chapters three and four could be applied to determine which of the panoply of potential helminth control strategies will be effective under specific climate change scenarios, and also, due to the uncertain nature of climate projections, show which would be most effective over the widest range of potential climate change scenarios. Through identifying leverage points, where changing conditions could have substantial impacts on parasite outbreaks, this approach could potentially identify novel areas for manipulation and control.

There is currently a strong reliance on anthelmintics for controlling helminths in intensively grazed livestock (Wolstenholme *et al*., 2004), either through targeting the number of adult parasites in the host, or the number of infective larvae on pasture. However, drug effectiveness is diminishing and anthelmintic resistance is rife (Abbott *et al*., 2007; Le Jambre *et al.,* 1976; Pandey & Sivaraj, 1994; Yadav *et al*., 1993), with nematodes in up to 80% of sheep farms in the UK resistant to at least one anthelmintic class and reports of multi-resistance (Van Dijk *et al*., 2008). There is ongoing development of new drugs, however in a warming climate the rate of development of resistance to anthelmintics could be accelerated. The impressive rate at which helminths evolve defences against our greatest attempts at chemical attack is due, in part, to their short generation time and high fecundity. The shortening of lifecycles through temperature driven acceleration in development times could quicken the development of anthelmintic resistance. An increase in extreme weather events might also play a role in pathogen evolution by causing alternating periods of high transmission and population bottlenecks that simultaneously limit strain diversity and cause rapid genetic shifts, particularly given that even small amounts of seasonal forcing can generate oscillations in prevalence.

Evolution of anthelmintic resistance is also accelerated if the parasite population with anthelmintic susceptible genotypes surviving in refugia is small, (e.g. due to larvae on pasture succumbing to desiccation in hot, dry summers, or hosts being turned out onto completely clean pasture after dosing). The maintenance of anthelmintic efficacy can be prolonged through more strategic and targeted drug use, which maintains susceptible genes within the parasite population (Kenyon *et al.,* 2009a). Although evolution of resistance is not modelled, the model's ability to capture changing dynamics at the supra-population level, tracking all stages of the parasites lifecycle, could facilitate the development of drug-based control strategies which prolong anthelmintic lifespans. Integrated management strategies could be explored which ensure that when drug use is unavoidable, infections are at least diluted by anthelmintic-susceptible parasites maintained in refugia.

With the inevitable wane of anthelmintic efficacy, strategies to lower the dependence on chemicals and manage the spread of resistance need to be adopted (Barger, 1996; Ketzis *et al*., 2006; Torres-acosta & Hoste, 2008; Waller, 2006b; Waller *et al.,* 2006). The key to developing these sustainable control strategies is to incorporate changes in climate, host management, and availability of infective larvae (Morgan & van Dijk, 2012). One possible control approach is to implement grazing management strategies which limit the exposure of hosts to infective larvae (Stromberg & Averbeck, 1999). The results of chapter four illustrate

the importance of reducing the number of infective L3 on pasture at the start of the grazing season. For systems that are above, but close to, their 'tipping point', the removal of exogenous larvae could dramatically reduce parasite burdens. The free-living larvae population can be controlled through the application of larvicides, however the long term efficacy of any chemical control method is questionable. The outputs of the model (chapters three and four) show the timings when the concentration of infective larvae on pasture are at their highest. Introduction of naive hosts onto pasture should be managed to avoid the highest levels of L3 pasture contamination. Through incorporating rotational grazing across multiple fields, an optimal grazing strategy could be identified which ensures that hosts encounter sufficient levels of larvae for trickle infection to initiate an immune response, but avoids deleteriously high challenges, which may overwhelm individual hosts. In addition to developing grazing strategies focussed on parasite control, the model incorporates grass growth and resource use, enabling an assessment of the extent to which intake requirements are met under such strategies.

If climatic conditions are ideal for larval survival and development, and the tipping point has been far surpassed, eradication of clinical parasitism will be difficult. The results of chapter four illustrate that once the tipping point has been surpassed, the peak parasite burden is primarily governed by the host's ability to mount an effective immune response. Host immunity can be improved through selective breeding (Gicheha *et al.,* 2007; Windon, 1996; Woolaston *et al.,* 1990; Woolaston & Baker, 1996), and improved nutrition (Coop *et al.,* 1995), and the results suggest this could help alleviate cases of clinical parasitism.

Widespread parasite control is unlikely to be through a one-size fits all panacea; the model developed here provides the framework to inform control strategies at the farm level. The potential impact of different control strategies will vary, depending on the balance between larval development and death rates. In addition to varying with climate and target species, optimal control strategies will vary with farming systems: e.g. intensively or extensively managed, purpose for which livestock is kept (milk, meat, wool production), local topography, local practices and resource availability. The robustness of these systems needs to be explored, for a range of climate change scenarios.

5.3.2 Restrictions to generating species specific predictions

Optimal development conditions vary both within (Le Jambre & Whitlock, 1973; Van Dijk & Morgan, 2010) and between helminths species (O'Connor *et al*., 2006). If species specific predictions of future outbreaks are to be made, based on accurate parameterisation, the response of parasites to the range of future conditions needs to be fully determined. Much research has explored the influence of abiotic conditions on survival and development of the main livestock helminths; these studies have already been extensively reviewed (Chaparro *et al*., 2011; Kao *et al*., 2000; O'Connor *et al*., 2006; Smith & Grenfell, 1994). There are however limitations to these studies which impede the accurate parameterisation of mechanistic models.

The frequency of extreme events is predicted to increase under climate change (Hansen *et al*., 2012; Planton et al., 2008). Such aberrations are often not accounted for, with most laboratory studies maintaining constant conditions, however efforts have been made to address this issue. Studies have shown that the influence of extreme conditions on larval survival is dependent on the duration of exposure to extreme temperatures (Walker *et al*., 2007), and it has been demonstrated that the temporal distribution of rain can be more important than the long term average amount (O'Connor *et al*., 2007). Development of the free-living stages is also influenced by short term weather fluctuations, with hatching occurring faster under stochastic, compared with deterministic daily cycles (Saunders *et al*., 2002). These short term fluctuations may be of increasing importance as climate variability continues to intensify.

Increased understanding of the impacts of short term weather fluctuations on parasite transmission can only be utilised in predictive models if climate projections are available at a suitably fine temporal-scale. To further obfuscate the generation of reliable projections, there is also a disparity between the spatial scales of climate predictions and parasite transmission. Weather stations are often one to two meters above the ground (Krecek *et al*., 1992); the conditions measured, and those projected under climate change scenarios, will differ from those experienced by the parasites free-living stages. There are often discrepancies between the ambient temperature at the soil surface, and the conditions experienced by parasitic larvae. In high temperatures, the temperatures in faecal pellets can exceed those of the surrounding air by several degrees (Walker *et al*., 2007). The micro-climate will also be modified by interacting factors including faeces composition, vegetation, aspect and soil type (Bailey *et al*., 2009)

5.3.3 Potential model development

The model used in chapters three and four broadened our understanding of transmission dynamics, revealing the importance of host responses (behavioural and immunological), and consequences of changing climate sensitive parameters. However, there is scope for model development. Instead of using fixed parameter values, latin hypercube sampling could have been used to generate a plausible collection of parameter values from a multidimensional distribution. This approach to generating stochasticity, and the between realisation variations in model outputs, could indicate the levels of observed variation expected in the system.

There is also scope for the incorporation of additional elements of parasite dynamics.

5.3.3.1 Co-infection

Hosts generally experience concomitant infections with multiple parasites (Graham *et al.*, 2007; Poulin, 2007), which influence parasite infections at the individual host and population level (Cattadori *et al.*, 2008; Poulin, 2007). Within host interactions can be classed as direct, through competition for resources, or indirect though the host's immune response (Cattadori *et al*., 2008). Whether two parasite species are cleared by the same effector mechanisms, or if existing parasites induce immunosuppression, determines the outcome of indirect interactions (Graham *et al*., 2007). Parasite interactions have been shown for common helminths of livestock, for example Dobson & Barnes, (1995) found the presence of *T.circumcincta* in young sheep to be detrimental to *H. contortus* establishment due to physiological abomasal damage, and cross-protection from a common immune response. Understanding individual and population level transmission dynamics could be improved through understanding co-infection and its epidemiological consequences.

Changes in species ranges could lead to novel parasite assemblages, with unforeseen consequences for both parasites and hosts. The introduction of a novel species may be negated or facilitated by the abundance and distribution of endemic parasite species. Equally, transmission and pathogenicity of endemic parasites could be affected by the spread of novel species. There is a need to understand how component species interact if we are to understand how parasite communities will be influenced by changes in climate

It is important to consider co-infection when predicting future risk, and developing control strategies. However, multi-parasite dynamics are complex, and no general laws have yet been

found to explain parasite community structures and interactions (Poulin, 2007). Little is known about the mechanisms that underlie within-host interactions; most studies focus on one species, and the response of the immune system to co-infection cannot be deduced from knowledge gained through multiple single infection studies (Bordes & Morand, 2009; Thakar *et al.,* 2012). Studies which do focus on co-infection are often limited to describing species abundance patterns at the host population level (Pedersen & Fenton, 2007). Limited knowledge of the direct and indirect interactions between concomitant parasites impedes the incorporation of co-infection in predictive models, and this level of complexity is beyond the scope of the mechanistic model developed here.

5.3.3.2 Herds of homogenous hosts: a need for individuals.

The model framework developed explicitly represents individuals and allows for variation between hosts in terms of the parameters governing their grazing behaviour and immunity. In chapters three and four host populations are assumed to be homogenous in both behaviour and susceptibility, and the results presented only show infection patterns of the average host. In reality, hosts exhibit variations in behaviour and susceptibility; consequently aggregation of parasites in host populations is a ubiquitous pattern (Gregory & Woolhouse, 1993; Grenfell & Dobson, 1995). In an over-dispersed population aggregation results in an increase in the effective density experienced by each parasite, increasing the influence of regulatory processes. (Churcher *et al.,* 2005; Shaw & Dobson, 1995; Smith & Guerrero, 1993). These regulatory processes drive a parasite population towards equilibrium (Paton et al., 1984), hence aggregated populations reach an equilibrium more quickly and at a lower level. As a consequence, by not incorporating host variability and taking into account the overdispersed parasite distribution, parasite burdens may have been overestimated.

Variation in host worm burden within a herd has been generated artificially in infection models through assuming a fixed distribution of worms across hosts, and imposing a pre-defined degree of overdispersion (Barnes & Dobson, 1990; Churcher *et al*., 2005). Although this approach allows the effects of aggregation to be explored, it does not address the origins of this aggregation. They also generally assume aggregation to be constant over time, whilst in reality it will change through the course of infection. In contrast Leung, (1998) and Barbour & Kafetzaki (1991) both developed homogeneous frameworks that gave rise to heterogeneity in host burden. However, these models for directly transmitted micro-parasites

(Barbour & Kafetzaki, 1991) and host seeking ecto-parasites (Leung, 1998), did not incorporate the influence of density dependent aspects on transmission.

There is a need for models that subsume both the mechanisms that generate aggregation, and the impacts of the resultant aggregation on infection dynamics. The individual based approach can allow factors driving the distribution of parasites at the suprapopulation level, and the resultant impacts on disease dynamics, to be explored. It has been proposed that heterogeneities in host infection levels arise due to numerous factors including variations in host resistance and susceptibility due to behavioural or physiological differences and spatial heterogeneity in infection risk (Barbour & Kafetzaki, 1991; Cornell *et al*., 2003; Louie *et al*., 2005; Shaw & Dobson, 1995). The transmission model developed in chapter three generated aggregation of infective parasites on pasture. It has been suggested that this uneven distribution of risk is one possible driver of the over-dispersed parasite distribution in host populations. However, the distribution of parasites within hosts during the simulations did not reach the levels of aggregation observed empirically, indicating that host variability in behaviour and/or susceptibility are the principal drivers of this phenomena, at least in the relatively high density, managed grazing systems considered here. The transmission model could be further developed to determine the levels of host heterogeneity (in behaviour, immunity etc) required to generate observed parasite distributions. Aggregation in natural systems has been quantified through multiple approaches (Gregory & Woolhouse, 1993; (Poulin, 1993; Smith & Guerrero, 1993) and has been measured for multiple nematode species across different hosts (Shaw & Dobson, 1995).

In addition to exploring the drivers of parasite aggregation, there is potential to investigate the influence of host heterogeneities on additional elements of transmission dynamics. Immunity profiles and grazing behaviours vary within a cohort of hosts, depending on genotype, age, parasite burden, exposure history, physiological state and dominance (Grenfell & Dobson, 1995). It has been demonstrated that the grazing decisions of individuals influence foraging behaviour at the group level (Smith *et al*., 2010). It is likely that the co-grazing of heterogeneous hosts will also influence transmission dynamics at the group level. Incorporation of variation in parameterisation of individuals (in e.g. physiological state or historic exposure at initialisation), a number of realistic scenarios could be explored; for example, co-grazing of young with adults undergoing periparturient relaxation in immunity. Models that incorporate the changing distribution of the suprapopulation of parasites would also allow identification of scenarios where individuals within a herd are at risk from heavy infections, thus addressing economic and welfare concerns

5.4. Looking beyond direct impacts of climate on pathogens: the need for a panoptic view

Climate change will impact directly on parasite survival and development; however transmission at the farm level will also be influenced by changing husbandry and host physiology. Livestock health will be directly affected by climate change, with a consequent need to adopt mitigation and adaptation strategies. Mechanistic models encompassing changes to livestock management, in addition to parasite-centric elements, will ultimately be required to fully determine how climate change could influence future outbreaks, and identify farming systems which leave livestock vulnerable to changing disease risk.

5.4.1. Direct impacts of climate change on grazing livestock

Heat-stress has been identified as one of the main threats to livestock production under climate change; consequently many studies have been carried out into direct temperature effects on livestock health. The impacts of heat-stress are most extensively studied for cattle, (Kadzere *et al.,* 2002; Ravagnolo *et al.,* 2000; West, 2003) as sheep are considered the most heat tolerant of all livestock species (Sevi & Caroprese, 2012). However sheep are still vulnerable to extreme temperatures and the impacts of heat-stress on sheep have also been well reviewed (Harle *et al*., 2007; Marai *et al.,* 2007). High temperatures have been found to impact production efficiency through negatively affecting weight gain, carcass weight, fat thickness and milk production (Abdalla *et al.,* 1993; Nardone *et al*., 2006; Wheelock *et al.,* 2010). The decreased production efficiency is attributed to decreased feed intake (O'Brien *et al.,* 2010) with feed intake decreasing with temperature, and rumen activity even being shut down when cattle are exposed to prolonged periods of heat stress (Beatty *et al*., 2008). Impacts of reduced feed intake on production can be mitigated through providing high energy supplementary feed (Mader & Davis, 2004; Sevi & Caroprese, 2012; West, 2003). Resultant changes in host grazing are likely to affect parasite dynamics, as grazing behaviour has a great impact on macro-parasite transmission (explored in detail in chapter three).

Heat stress also directly affects the immune response of sheep and cattle, however the exact mechanisms and consequences remain unclear (Sevi & Caroprese, 2012; Tao *et al.,* 2012). As the intensity of parasite outbreaks can be dependent on the host's ability to mount an effective immune response (shown in chapters three and four), heat-stress driven changes in immunity could have substantial impacts on parasite burdens. Livestock are particularly susceptible to heat stress during lactation, as lactation results in an increase in internal heat

production (Wilson *et al.,* 1998). As lactating ewes experience periparturient relaxation in immunity, impacts of heat-stress on their grazing patterns and immunity, and ultimately on parasite transmission, could be accentuated.

5.4.2 Changes in husbandry

Due to the potential economic and welfare impacts of heat stress (García-Ispierto *et al.,* 2007; Wilson *et al.,*1998a,b; Wolfenson *et al.,* 2000), the adoption of mitigation and adaptation strategies will be necessary under climate change (Silanikove, 2000). There is potential for climate driven changes in husbandry to influence parasite risk, however adaptation and mitigation strategies have yet to be incorporated in parasite transmission models. There is a propensity for predictive models to incorporate ever refined climate projections; however these will not provide meaningful indications of future risk if they are parameterised for outdated management approaches and redundant host population structures. Predictive models need to have the architecture to allow adaptation and mitigation strategies to be incorporated.

A range of adaptation approaches have already been proposed; potential impacts on parasite risk can be surmised, and these approaches could potentially be included in future predictive models. Shade provision can reduce heat accumulation through blocking solar radiation, and attenuation of heat-stress through shade provision has been widely explored (Berman & Horovitz, 2012; Brown-Brandl *et al.,* 2005; Eigenberg *et al.,* 2005; Kendall *et al*., 2006; West, 2003). These studies indicate that shade is an effective way of mitigating the effects of increased temperatures on heat stress. However mortality of free-living larvae increases with UV exposure, with temperate species most inimically affected (Van Dijk *et al*., 2009). Hence the provision of shade could protect exogenous larvae from UV exposure and desiccation. As the results of chapter four illustrated, the frequency and magnitude of parasite outbreaks is partly governed by larval survival on pasture, so the trade off between heat-stress and parasite risk needs to be considered when increasing levels of shade.

The provision of sprinklers has also been shown to decrease both body temperature and respiration rates in livestock (Avendaño-Reyes *et al*., 2006; Darcan & Güney, 2008; Huynh *et al.,* 2006; Mader & Davis, 2004; Schütz *et al.,* 2011; Wolfenson *et al*., 2000), and could be useful in reducing hyperthermia susceptibility through evaporative cooling. Morrow *et al*., (2005) proposed that sprinkling could have a deleterious effect on the condition of cattle, with

a possible impact on the pathogenic bacteria population living on, and within, the cows. Their study investigated the impacts of sprinkling feedlot cattle on the levels of *Escherichia coli* O157:H7 and Salmonella, on both their faeces and hides, concluding that the incidence of zoonotic pathogens was not adversely affected by sprinkling cattle with water. However the effects on wider pathogen groups have yet to be explored. Survival of macro-parasites' free-living stages can be improved through increased water availability, so there is potential for use of evaporative cooling techniques to impact on helminth transmission. Use of sprinkler systems to cool livestock is currently restricted to inside barns, so larval survival on pasture is unlikely to be affected, however parasite risk should be considered if the use of sprinkler systems is to be extended.

In addition to the implementation of adaptation strategies, climate change will force other changes in livestock management which could influence disease risk. The NFU (National Farmers Union, UK) report on agriculture and climate change (NFU, 2005) states that rising temperatures and a decrease in ground frosts will lead to an increased growing season and an increase in grass for both grazing and winter forage. An increase in CO_2 levels may result in changes in grass growth, however the impacts of raised CO_2 levels on grass growth are complex (Makino & Mae, 1999). From 1961-2004, growing season length in Scotland increased by over four weeks (Barnett *et al*., 2006), by 2080 a further increase in growing season by between 20 and 60 days is projected (UKCP09, 2009a). The results of chapter four indicate that the transmission window of livestock helminths could shift under climate change, hence changes in the timing and length of the grazing season could impact on host's exposure to parasite risk. Long term changes and short term seasonal fluctuations in grass growth could also be incorporated in the model. However, it is difficult to incorporate changes in time and length of grazing seasons into predictive models, as grazing is influenced by a number of climatic factors. For example, extreme weather events such as high winds and hot summers could increase time spent sheltering, thus decreasing grazing time. Increased winter rainfall could also impact housing as livestock will have to be kept indoors to prevent poaching of land. For example the wet autumn of 2000 led to UK livestock being housed two to four weeks earlier than usual (NFU, 2005). This effect could however be counteracted under climate change by an increase in winter temperatures allowing livestock to be kept outside for longer periods (NFU, 2005). The timing of other management processes could also be affected, for example timing of livestock reproduction being managed differently (Rivington *et al*., 2007). This would effect when naïve young are first grazing on pasture.

5.4.3 Changes in breed structure

There are breed differences in susceptibility to heat stress (Johnson *et al.*, 2012), which has led to much research into the heat tolerance of different breeds (Brown-Brandl *et al*., 2006; Harle *et al*., 2007; McManus *et al*., 2009; Panagakis, 2011). Under climate change the breed structure of UK livestock may have to change to ensure production levels are maintained and animal welfare standards are met. Susceptibility of livestock to heat stress can be combated by the introduction of heat and drought tolerant breeds from arid areas including Australia, Africa and the Middle East (NFU, 2005). Changes in breed structure could influence disease levels as different breeds have different levels of susceptibility (Wilson & Mellor, 2008). However, susceptibility of different breeds to macro-parasites requires further study before transmission models could be parameterised for different breed structures.

Heritability for heat tolerance has been demonstrated in sheep (Finocchiaro *et al.*, 2005) and cattle (Aguilar *et al.*, 2010). With increased risk from the direct and indirect effects of climate change, priorities for genetic selection will need to be addressed. Selection for heat tolerance is possible (West, 2003), although this is usually antagonistic to selecting for productivity (Aguilar *et al*., 2010; Finocchiaro *et al*., 2005). However Ravagnolo & Misztal, (2000) demonstrated that selection for both heat tolerance and productivity is possible. The impacts of breeding for increased production and heat-tolerance on immune response have yet to be explored. Due to potential increases in disease risk, and the importance of host immunity on transmission dynamics, selection for disease resistance and/or resilience traits should also be considered in breeding programmes.

At a broader scale, livestock species choice can be influenced by local climate. To demonstrate this Seo *et al.*, (2010) have projected changes in livestock species composition under climate change in South America, with a shift from dairy and beef cattle to sheep as temperatures rise and weather variability increases. Ultimately, the distribution of pathogens will be constrained by the distribution of viable hosts.

5.5. Conclusions

This thesis has elucidated the potential impacts of climate change on livestock parasites in the UK. The first long term fasciolosis forecast for the UK illustrates which areas are set to experience unprecedented levels of liver fluke outbreaks in the future. Although correlative

modelling is a useful tool for establishing baseline predictions, a drive towards mechanistic, process-based models will ultimately be needed if we are to address more complex questions and foresee the consequences of subtle interactions between various components of a system under climate influence.

Through the development of a mechanistic transmission model, a non-linear relationship between climate change and parasite risk is revealed, with a distinct 'tipping point' in outbreaks when temperature driven processes exceed a critical rate. This indicates that climate change could lead to sudden and dramatic changes in parasite risk. Although laboratory studies have been done to aid the creation of mechanistic models, limitations to these studies currently impede quantitative, species-specific predictions.

Modelling approaches can be broadly stratified as correlative or mechanistic, but in practice it is difficult to draw an absolute distinction between these modelling techniques. Ultimately, an integration of both modelling approaches may be required. Future improvements in predictions should arise from the continued development of a hybrid approach that combines mechanistic processes with correlative bioclimatic modelling. Irrespective of modelling approach, the quality of predictions is critically dependent on the quality of available data. The continued collection of active surveillance data and empirical observations on physiological responses to climate variables will ultimately drive the development and validation of meaningful predictions.

The recent expansion of helminth ranges has been mirrored by our increased understanding of the role of climate in their transmission dynamics. However, climate is just one factor affecting disease ecology. The application of mitigation and adaptation strategies, combined with changing control options, needs to be considered when determining the overall impacts of climate change. The extent of future uncertainties may ultimately necessitate a move towards robust systems, which would function well under a range of climate and transmission scenarios; this could be facilitated by the development of models which incorporate the wider elements of managed livestock systems and parasite dynamics. By combining improved empirical data and refined models with a broader view of the livestock system, we can identify potential risks and highlight opportunities for control.

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