Economics of Robust Surveillance on Exotic Animal Diseases: the Case of Bluetongue

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Abstract

Control of emerging animal diseases critically depends on their early detection. However, designing surveillance programs for exotic and emerging diseases is very challenging because of knowledge gaps on the probability of incursion and mechanisms of spread.

Using the example of Bluetongue Virus, which is exotic to the UK, we develop a meta-population epidemic-economic modelling framework that considers the incursion, detection, spread and control of a disease in a livestock production system composed of heterogeneous subpopulations. The model is then embedded in an information gap (info-gap) framework to assess the robustness of surveillance and vaccination policies to unacceptable outbreaks losses and applied to the case of Bluetongue in the UK.

The results show that active reporting of suspect clinical signs by farmers is a very robust way to reduce unacceptable outcomes. Vaccination of animals in high risk regions led to robustly protective programs. If vaccines are not available, surveillance targeted to the high risk region is very robust even if the extent of the high risk region is not known and effectiveness of detection is very low. Surveillance programs focusing in all regions with the same intensity are in general not robust unless the dispersal of the vector connecting both regions is very high.

Key words: compartmental epidemic model, emergent animal disease, Knightian uncertainty, sentinel surveillance system

Introduction

Animal disease outbreaks cause significant costs to societies, through loss of productivity and death in livestock industries (Rich and Winter-Nelson 2007). It has been recently reported that endemic animal diseases may reduce productivity by around 17% in UK and up to 50% in developing countries (Flint & Woolliams, 2008). Still more concerning are zoonotic animal diseases as they can spread to humans, affecting public health and leading to considerable losses. Climate change, circulation of people and animals, and increasing trade flows may facilitate the spread of exotic diseases and emergence of new diseases (Racloz et al 2007). These present new challenges to agencies managing and controlling animal diseases. One of the main difficulties of managing exotic and new infectious diseases arises from uncertainty on how, when and where diseases may emerge and how they may spread through an animal population. Specifically, there may be lack of knowledge on how animals are infected; how are they affected; and on transmission of infectious agents. Animal health authorities must decide how to invest limited resources on systems firstly, to identify new or exotic infectious disease and secondly, to control them despite these uncertainties.

The longer it takes to detect a disease the larger is its potential impact on societies. Therefore, successful management of animal diseases critically depends on their quick and accurate detection (Souza Monteiro, Hoinville and Cook 2010). This activity is also known as disease surveillance, which can be defined as the systematic collection, analysis and interpretation of data on diseases occurring in a population, enabling the elaboration of measures to control their impact (Anonymous 2004). Of particular interest is scanning surveillance, which is defined as the monitoring of animal populations of concern to detect the undefined and unexpected (Lysons et al 2007).

A number of studies have focused on the economics of infectious animal diseases (Bicknell, et al., 1999, Chi, et al., 2002, Gramig and Wolf 2007, Hennessy 2007, Horan and Fenichel 2007). These studies focus mainly on prevention, control and the incentives for adoption of preventive disease management practices. Another recent study demonstrated the value of having flexibility over different options to manage crisis events, such as a Foot and Mouth Disease outbreak (Lan Ge 2008). Little attention has been given to the economics of disease surveillance. Kompas et al. (2006) estimated the optimal level of surveillance for Foot and Mouth disease in the USA using stochastic optimal control theory. A related literature is the

one on detection of new pests in vegetable production and management of invasive species (Moffitt, Stranlund, and Osteen (in press)). While surveillance of endemic animal diseases is well established, there is great interest in designing effective and efficient surveillance for exotic and emerging diseases. In the case of these diseases there is often a significant dearth of data and information, which increases uncertainty of detection and prevention of disease outbreaks. In such circumstances, and specially when there is important knowledge limitations on infection and spread rates, we face severe uncertainty and in this case we may be better off designing robust surveillance strategies. These strategies inform decisions when we face information gaps and need to achieve a certain threshold performance criteria.

In this paper we aim to identify a robust surveillance program for the case of Bluetongue virus, an exotic disease to the UK. Given a spatially structured population divided into a number of subpopulations with heterogeneous transmission rates and incursion risk of an exotic disease, our goal is to analyse a system that can guarantee a level of detection that prevents losses beyond a given threshold of acceptable impact of disease epidemics. We further explore how the availability of vaccines for the disease impacts decisions on the design of robust surveillance programs.

We deal with the problem by developing a modelling strategy that comprises two stages. First we develop an epidemic-economic model considering the emergence, spread and detection of an emergent disease in two coupled subpopulations. Spread is modelled as a meta-population risk-structured dynamic epidemic compartmental model (Anderson and May, 1992, Kermack and McKendrick, 1927, Rowthorn, et al., 2009). The epidemic model is linked to an economic module that aggregates and discounts the costs subject to the disease and its control. Second, the model is embedded in an information-gap (info-gap) (Ben-Haim, 2006) framework to assess the robustness of different surveillance-vaccination strategies. We illustrate our approach with the case of bluetongue virus (BTV) incursion and spread in England and Wales.

Bluetongue disease in the UK

Bluetongue is a vector-borne disease of high economic importance caused by the bluetongue virus (BTV) which is capable of infecting a wide range of ruminant species. BTV is spread by a vector, a biting midge (*Culicoides*) from local hosts (Wilson and Mellor, 2008). Among domestic

animals, sheep present a high mortality and morbidity although noticeable symptoms and death have also been documented in cattle, especially for the case of BTV serotype 8 in Europe (Elbers, et al., 2008).

While bluetongue is endemic in the North of Africa, it is still considered exotic in the North of Europe and the UK. In the Summer/Fall 2006 an outbreak of this disease started in Belgium, Luxemburg, Netherlands, Western Germany and North Eastern parts of France affecting approximately 2000 holdings by mid January 2007 and causing considerable production losses and raising mortality rates (Department for Environment, Food and Rural Affairs [DEFRA] 2009). In August 2007, the first BTV infected farm in the UK was identified near Ipswich and two more farms in Cambridgeshire, three in Kent and one in Sussex were subsequently infected (DEFRA 2008).. These infections were considered the result of new independent introductions from the continent (Szmaragd, et al., 2009). These outbreaks in Northern Europe represented an 500 miles north shift of BTV occurrence and have been associated with climate change. Climate change allows for better overwintering of the virus and an expansion in the range of *Culicoides imicola*, the main BTV vector (Purse, et al., 2005). Since this first outbreak farmers throughout the UK have been encouraged to adopt preventive measures, namely through vaccination, although the vaccination uptake rates by farmers in different regions has been variable (Szmaragd, et al., 2009).

The European Commission has established provisions for the control and eradication of bluetongue in Europe (European Commission, 2000). Upon detection of a confirmed bluetongue case, a protection zone of 62 miles radius and a surveillance zone of 31 miles radius around the infected farm are imposed. Animal movement is restricted and insecticide applications and carcase incineration are carried out in a radius of 15.5 miles from the infected farm (European Commission, 2000). These rules were later implemented by the Commission Regulation EC/1266/2007 (European Commission, 2007) by which BTV monitoring and surveillance programs were specified. Monitoring programs are composed of serological surveys with sentinel animals tested at least once a month and an entomological survey with at least one ultra-violet aspiration trap in geographical units of 772.2 miles^2 (European Commission, 2007). Surveillance programs should be implemented at national level focusing on sampling high risk populations (European Commission, 2007).

High risk areas for the occurrence of BTV outbreaks can be identified according to

pathways of entry of infected vectors, temperature, animal movements and the occurrence of previous outbreaks - which might lead to new outbreaks after BTV overwintering if eradication was not totally achieved. Based on this information, sentinel early warning systems targeting high risk areas have been suggested as an efficient way to allocate surveillance efforts in Switzerland (Racloz, et al., 2008), however new introductions beyond the risk areas can also occur. Currently, there is a need to evaluate the effectiveness of surveillance programs for BTV in Europe and to identify the characteristics that would make them robustly protective.

A meta-population epidemic-economic model of disease spread and detection

A dynamic discrete-time meta-population epidemic-economic model considering the entry, spread, detection and control of an unknown emergent disease that affects ruminants was developed in the R environment (R Development Core Team, 2005). For the application of the model to BTV in the UK, the time period considered was 20 years and within each year we only modelled the period from the end of the Spring to mid Autumn because in colder months the vector is not active and thus there is no transmission of BTV. Policy-makers must formulate a strategy to detect new BTV outbreaks, whether through new incursion of virus or through persistence within the affected sub-population and to control the epidemic potential. The objective is to guarantee that the costs derived from the vector-borne disease, its surveillance and control are robustly below an unacceptable threshold. For simplicity, for the case of BTV in England and Wales we consider two distinct regions or subpopulations. More regions or subpopulations could be considered to increase the spatial resolution of the analysis without requiring model structural changes. For our model, we assume that the surveillance strategy recommended by the European Commission (2007) will be followed. We define a "high risk region" as a radius of 62 miles around the observed outbreaks in 2007 (protection zone); and a "low risk region" comprising the rest of England and Wales. Detection and vaccination efforts are allocated among the low risk region (proportion of farms with sentinel animals that are inspected: $\chi^{j=0}$; proportion of vaccinated animals: $\theta^{j=0}{}_{vac}$) and the high risk region ($\chi^{j=1}$; $\theta^{j=1}{}_{vac}$), where the superscript j indicates the region and $j = 0$ (1) indicate the high (low risk) regions respectively. The allocation of detection and vaccination resources is complex because there is severe uncertainty the probability of BTV emergence in each region and on the rate of transmission of the disease within and between regions. This severe uncertainty is due to the multiple factors that jointly

play in the emergence of BTV, such as weather conditions, existence of reservoir and presence of infected vectors.

Emergence of the disease

The initial infection in the population occurs because of the introduction of infected hosts or vectors exogenous to the system and is modelled with a Poisson stochastic process. The Poisson process implies that there is a constant probability per unit of modelled time of a first animal becoming infected and every initial infection is independent of every other (Vose, 1997). The daily probability of a successful incursion:

$$\text{Probability}\left(\text{incursion today in region j = 1 }\right) = \left(p_{incursion}^{j} e^{-p_{incursion}^{j}}\right) \qquad [1]$$

Where: $p_{incursion}^{j}$ is the daily probability of an incursion into the system. Given our distinction between high and low risk regions, we have the following relation $p_{incursion}^{j=1} > p_{incursion}^{j=0}$.

Disease spread

Disease spread among a population of susceptible individuals can be well approximated using epidemic compartmental models that assume homogeneous individuals and perfect mixing among them (Anderson and May, 1992, Diekmann and Heesterbeek, 2000 , Kermack and McKendrick, 1927). For the modelling of BTV it is necessary to consider the forces of infection between the host and the vector *Culicoides* spp., the fact that only some individuals become symptomatic and the existence of heterogeneous subpopulations. Our modelling strategy follows the epidemic model builds up from Gubbins, et al. (2008) and Szmaragd, et al. (2009). We employ a susceptible (S)-latent (L) (infected individuals that are not yet infectious) -infected (asymptomatic (A) and symptomatic (I))- and recovered (R) (SLAIR) compartmental epidemic model to represent the epidemics in the hosts. The SLAIR model is coupled with a susceptible (S^{vec})-exposed (E^{vec})-infected (I^{vec})-dead (D^{vec}) (SEID) model of the vectors. The model for the host is expressed by the following system of differential equations:

$$
\begin{aligned}
\frac{dS^{jk}}{dt} &= -\left(\lambda^{jk} + \lambda^{\neq jk}\right) S_t^{jk} \\
\frac{dL^{jk}}{dt} &= \left(\lambda^{jk} + \lambda^{\neq jk}\right) S_t^{jk} - \frac{1}{\mu^k} L_t^{jk} - \varphi\chi^{jk} n_{farm}^k p_{dE} L_t^{jk} \\
\frac{dA^{jk}}{dt} &= \theta_{asym}^k \frac{1}{\mu^k} L_t^{jk} - \frac{1}{\varepsilon_A^k} A_t^{jk} - \varphi\chi^{jk} n_{farm}^k p_{dA} A_t^{jk} \\
\frac{dI^{jk}}{dt} &= \left(1 - \theta_{asym}^k\right) \frac{1}{\mu^k} L_t^{jk} - \frac{1}{\varepsilon^k} I_t^{jk} - \eta^k I_t^{jk} - \varphi\chi^{jk} n_{farm}^k p_{dI} I_t^{jk} \\
\frac{dR^{jk}}{dt} &= \frac{1}{\varepsilon^k} I_t^{jk} + \frac{1}{\varepsilon_A^k} A_t^{jk} + \varphi\chi^{jk} n_{farm}^k p_{dE} L_t^{jk} + \varphi\chi^{jk} n_{farm}^k p_{dA} A_t^{jk} + \varphi\chi^{jk} n_{farm}^k p_{dI} I_t^{jk} \\
\frac{dD^{jk}}{dt} &= \eta^k I_t^{jk}
\end{aligned}
\qquad [2]
$$

Where the first equation expresses how the number of susceptible individuals decreases because of contact with infected vectors within the same region *j*. The process of susceptible animals becoming infected is governed by λ^j. This is the force of infection, i.e. the rate at which susceptible animals become infected and $\lambda^j = \min(\lambda^j, 1)$. The infection of susceptibles by contact with infected vectors between regions is represented by $\lambda^{\neq j}$. The second equation describes how those hosts newly infected become latent (first element of the equation) and how, after an incubation period, they become infected symptomatic or asymptomatic (second and third elements). The third and fourth equations represent how the number of infected animals increases by latent animals becoming infected and how they decrease due to their recovery, death and quarantine if detected. The fifth equation accounts for those animals that recovered naturally and infected animals that are detected, since it is assumed that quarantine measures would be imposed that prevent them from infecting other animals, thus epidemiologically behaving as recovered. The sixth equation accounts for the individuals that die due to the disease.

The parameters of the model are: the incubation period of the disease in the host (μ); the proportion of latent individuals becoming asymptomatic (θ_{asym}); the infectious period of infected symptomatic (ε) and asymptomatic (ε_A); the rate of fatal casualties due to the disease (η); probability of correctly detecting and quarantining exposed (p_{dE}), asymptotic (p_{dA}) and symptomatic (p_{dI}) infected individuals; the average number of host *k* per farm (n^k_{farm}); and $\varphi = 0$ when the epidemic has not been yet detected and $\varphi = 1$ when detected. The superscript *k* denotes the type of host with $k = 0$ for cattle and $k = 1$ for sheep.

The force of infection for the *k* host species has two forms depending on whether the infections occur within the region (λ^{j}) or between regions ($\lambda^{\neq j}$):

$$\lambda^{jk} = \rho_{mix} b a^{jk} \xi^{jk} \frac{N^{vec\_jk}}{N^{jk}} \frac{I^{vec\_jk}}{N^{vec\_jk}}; \qquad \lambda^{\neq jk} = \rho_{mix} \gamma b \xi^{\neq jk} a^{\neq jk} \frac{N^{vec\_\neq jk}}{N^{\neq jk}} \frac{I^{vec\_\neq jk}}{N^{vec\_\neq jk}} \qquad [3]$$

where N^{jk} is the population size in region *j* of host *k.* Recall that I is the number of infected vectors; *b* is the probability of transmission from an infected midge to a host; *a* is the biting rate, the reciprocal of the time interval between blood meals (Gubbins, et al., 2008); N^{vec_j} is the total number of vectors in region *j*; γ is the probability of a vector dispersing to other regions; and ρ_{mix} is a factor accounting for mixing imperfections between individuals such that $\rho_{mix} = 1$ indicates perfect mixing and $\rho_{mix} = 0$ would indicate a landscape where the distance between farms is beyond any range of movement of the vector. For the purpose of the model this is as if distance is infinite, making the transmission of the disease impossible. ξ^{kj} is the proportion of bites that are given to host *k* in region *j*:

$$\xi^{jk=0} = \left(\frac{\sigma N^{jk=0}}{\sigma N^{jk=0} + N^{jk=1}} \right); \qquad \xi^{jk=1} = 1 - \xi^{jk=0} \qquad [4]$$

where σ is the biting preference of the vector for cattle ($k = 0$) instead of sheep.

The infection of susceptibles between regions is modelled as a stochastic process by which $\lambda^{\neq j}$ equals zero if a random drawn from a uniform distribution (0, 1) is greater than $\lambda^{\neq j}$ and $\lambda^{\neq j}$ retains its value if the random drawn is lower.

As mentioned before the population dynamics of the vector are represented by a SEID model. The main difference with the SLAIR host model is that it does not present a recovered compartment (because the vectors do not recover once infected with BTV) nor an asymptomatic compartment:

$$\frac{dS^{vec\_j}}{dt} = rN_{vec}^{j} - \left(\lambda_{vec} + \lambda_{vec}^{j\neq}\right)S_t^{vec\_j} - \omega S_t^{vec\_j}$$
$$\frac{dE^{vec\_j}}{dt} = \left(\lambda_{vec} + \lambda_{vec}^{j\neq}\right)S_t^{vec\_j} - \frac{1}{\mu^{vec}}E_t^{vec\_j} - \omega E_t^{vec\_j}$$
$$\frac{dI^{vec\_j}}{dt} = \frac{1}{\mu}E_t^{vec\_j} - \omega I_t^{vec\_j}$$
$$\frac{dD^{vec\_j}}{dt} = \omega S_t^{vec\_j} + \omega E_t^{vec\_j} + \omega I_t^{vec\_j} \qquad [5]$$

where r is the rate of recruitment of the adult female midge; μ is the incubation period of the midge; and ω is the mortality of the midge. λ_{vec}^{j} and $\lambda_{vec}^{j\neq}$ are the force of infection experienced by the vectors within and between regions respectively:

$$\lambda_{vec}^{jk} = \rho_{mix} a\beta \sum_{k=0}^{1} \xi^{k}\left(\frac{I_t^{jk} + A_t^{jk}}{N^{jk}}\right); \quad \lambda_{vec}^{\neq jk} = \psi a\beta \sum_{k=0}^{1} \xi^{\neq jk}\left(\frac{I_t^{\neq jk} + A_t^{\neq jk}}{N^{\neq jk}}\right) \qquad [6]$$

where β is the probability of infection of a vector when biting an infected host; and Ψ is the proportion of animals that are moved within regions.

The differential equations of the host and vector epidemic models were discretised and evaluated using the Euler method with a time step of 0.1 days (extensive numerical simulations showed that lower time steps produced similar predictions).

Detection

Detection can occur by two means: (i) farmers report suspicion of clinical signs of bluetongue in their animals with a precision of p_{report}. Reporting is modelled as a binomial stochastic process of probability p_{report} and population is considered as the number of infected symptomatic individuals in the region each day; (ii) detection by a grid of farms with sentinel cattle since these are preferred by the Culicoides vector. These sentinel animals are assumed to be inspected by Government veterinary officers (note: this is a hypothetical assumption and use of sentinel animals is not currently practised in England or Wales). The weighted mean probability of detection in each time period by the grid of sentinel animals is:

$$p_{dt}^{j} = \frac{\chi^{j} n_{farm}^{k=0}\left(p_{dE}L_t^{j} + p_{dI}I_t^{j} + p_{dA}A_t^{j}\right)}{N^{j}} \qquad [7]$$

Conditional on the occurrence of the first infection, the event of discovery of the outbreak is modelled by comparing p^j_{dt} of each region daily with a random draw from a uniform distribution between zero and one. If the random draw is below p^j_{dt} the outbreak is considered detected and control measures start in the region where the case was detected, i.e. the region becomes a protection zone. We model these measures as the restriction of animal movements outside the region ($\Psi = 0$); introduction of a m_{detect} times more intensive sentinel monitoring program (including sheep) such that $m_{detect} \cdot \chi^j = \min(m_{detect} \cdot \chi^j, 1)$; infected detected animals are quarantined; animals with symptoms are reported at a rate of p_{report} and quarantined; and the farms in the region are sprayed with insecticides leading to an increase of vector mortality of m_{spray} times. Once the outbreak is eradicated control measures return to the initial levels.

Vaccination

The vaccine reduces the number of susceptible individuals. The new number of susceptible individuals at time t after the vaccination campaign at time t-1 in region j is:

$$S_t^j = S_{t-1}^j \delta \theta_{vac}^j$$

Where δ is the effectiveness of the vaccine; and θ^j_{vac} is the proportion of animals vaccinated in region j.

Economic impacts

The distribution of the net present value of the total economic costs (TC) is divided between costs before the incursion and detection of the disease and costs after the incursion and detection. The costs before are: expenditures on surveillance and vaccination programs. The costs after are: increased surveillance, the economic impacts caused by the disease on the hosts (infertility, abortions and reduced growth rate: $c_{BTV\text{-}host}$), impacts due to movement restrictions (with unit cost per animal of $c_{restric}$), costs due to animals deaths, insecticide treatment and lost value of their exports:

$$TC = \sum_{k=0}^{1}\sum_{j=0}^{1}\sum_{t=0}^{T} e^{-\rho t}\left[\begin{array}{l}\left(1-\varphi^j\right)\left[\chi_t^j N_t^{jk=0} c_d + \theta_{vac} S_t^{jk} c_{vac}\right] + \\ \varphi^j\left(m_{\text{detect}}\chi^j N_t^{jk} c_d + I_t^{jk} c_{BTV-host}^j + N_t^{jk} c_{restric} + D_t^{jk} c_{rum}^j + N_t^{jk} c_{\text{insect}} + C_{lm}^j\right)\end{array}\right] \quad [8]$$

Where: T: time horizon considered; ρ: discount rate; c_d: unit cost of inspection of one host; c_{vac}: unit cost of a vaccine dose; c_{rum}: market price of a host; and C_{lm}: daily gross values of the livestock export trade market loss. The regions where BTV is detected lose the value of their export markets until the outbreak is eradicated.

Analysis of robustness of surveillance programs using info-gap theory

Decision-makers in Government or industry may face severe uncertainty when making decisions regarding the design and implementation of exotic and emerging animal disease surveillance programs. We adopt an information-gap (info-gap) approach (Ben-Haim, 2006) to assess the robustness of the model to different surveillance levels. Info-gap theory was developed by Ben-Haim (2006) to assist decision-making in situations where the information about some areas of the system modelled is highly deficient. As an advantage to other probabilistic methods of uncertainty modelling, info-gap does not require underlying assumptions about the distributions of uncertainty of the parameters. Info-gap has been successfully applied to several fields such as conservation ecology (Nicholson and Possingham, 2007), invasive species introductions and control (Carrasco, et al., 2010, Moffitt, et al., 2008, Yemshanov, et al., 2010) or terrorism prevention (Moffitt, et al., 2005). Primary limitations of the info-gap framework are the need to determine a performance requirement and the absence of any obvious economic efficiency criteria to help in that determination.

Three main components are required for info-gap analysis: (a) a mathematical process model (described in the previous section), (b) a performance requirement and (c) a model of uncertainty. We assume that the government agency wants to adopt a surveillance protocol that guarantees that the maximum total costs (TC) due to the epidemic are less than an unacceptable threshold (TC_{max}). We further distinguish three thresholds or aspiration levels according to their degree of exigency: *low exigency* where the government aims to guarantee that TC are below 60% of the value of the cattle population (TC_{max_low}); *medium exigency* where TC are below 50% of such value (TC_{max_medium}); and *high exigency* where TC are below 40% (TC_{max_high}). These values are chosen as illustrative examples – other conditions, such as the prioritisation of finite resources amongst competing demands, would also be important in practice. The performance requirement is:

$F_{0.999}(TC) \leq TC_{max}$. [9]

Because the epidemic models are stochastic, a distribution of outcomes instead of a single value is obtained for each horizon of uncertainty. We selected the 99.9th percentile of the distribution to be compared with the performance criteria.

The model for uncertainty expresses what is unknown about the parameters in the process model. It is an unbounded family of nested sets of possible values. Each set corresponds to a degree of knowledge-deficiency according to the level of nesting (Ben-Haim, 2004). We consider that the parameters $p_{incursion}$, ρ_{mix} (that affects the disease transmission), p_{report}, the actual lack of knowledge of the extent of the high risk area θ_{mis} (modelled as mismatched allocation of vaccines and detection efforts that are allocated to the unintended region), γ (dispersal of the vector between regions), and p_{dA} (assuming $\theta_{asym} = 1$) present severe uncertainty. The corresponding info-gaps models are expressed as the sets: $U_{pincursion}(\alpha, p_{incursion}^{be})$, $U_{\rho mix}^{j}(\alpha, \rho_{mix}^{be})$, $U_{\theta mis}^{j}(\alpha, \theta_{mis}^{be})$, $U_{preport}^{j}(\alpha, p_{report}^{be})$ and $U_{pdA}^{j}(\alpha, p_{dA}^{be})$. α is the information-gap between what is known and what needs to be known for an ideal solution and the superscript "be" indicates are our best estimates of the model parameters.

The greater is α the greater the range of possible variation. The value of α is unknown and unbounded and expresses the idea that possibilities expand as the info-gap grows, imbuing α with its meaning of "horizon of uncertainty" (Ben-Haim, 2004).

We evaluate the horizon of uncertainty α using an exponential function instead of a linear function to emphasize the sampling of the parameter space for small values. The evaluation is done in such a way that the worst possible scenarios are studied, e.g. increasing $p_{incursion}$, ρ_{mix} θ_{mis} from their original value to a value close to one (right hand side of equation [10]) and decreasing p_{report} and p_{dA} from their original value to a value close to zero (left hand side of equation [10]) following:

$$e^{-c\alpha}\vec{\theta}^{be} \leq \vec{\theta}^{be} \leq \min\left[\left(d - e^{-c\alpha}\right)\vec{\theta}^{be}, 1\right]; \quad \alpha \in [0,1] \qquad [10]$$

where c and d are scale constants. For an adequate sampling of the parameter space we set $c = 2$ and $d = 10$. Info-gap theory identifies as the best policy the one that is most robustly satisficing (Ben-Haim, 2006), i.e. the goal is not to minimize the NPV of total costs but to maximise the

reliability of an acceptable outcome. The most robust policy will be the one that presents most immunity to unacceptable outcomes. We employ a robustness function $\widehat{\alpha}$:

$$\widehat{\alpha}(policy_i) = \max\left[\alpha:\ \max_{\vec{\theta}^{be}\in U_{\vec{\theta}^{be}}(\alpha,\vec{\theta}^{be})}\left\{F_{0.999}\left(\mathrm{TC}\left[\chi^j\right]\right)\right\} \leq TC_{\max}\right] \qquad [11]$$

$\widehat{\alpha}$ is equal to the maximum value of α, in such a way that the 99.9th percentile of the NPV of total costs fulfils the performance criterion given different surveillance levels and uncertainty in the parameters $p_{incursion}$, ρ_{mix} , p_{report}, θ_{mis}, γ, and p_{dA} (represented as $\vec{\theta}^{be}$).

Results

Robust surveillance under severe uncertainty on the spatial transmission of the disease

The most robust policies when the effect of farms connectedness by movement of animals and vectors is severely uncertain were those involving vaccination of the high risk region (Figure 1 A). A vaccination policy covering 40% of the population would be able to avoid increases in the 99.9^{th} percentile of the discounted total costs even if the mixing among animals was perfect, i.e. all the cattle and sheep confined in the same location. In reality, for many emerging diseases no vaccines will be available and surveillance will be the only option. In this case, the least robust surveillance strategy would be to deploy detection efforts on the low risk region. Even a "do nothing" policy results more robust (Figure 1 A), indicating that in the case of bluetongue in England and Wales it is more cost-effective not to search at all than mounting a detection campaign of the same high intensity in both the high and low risk regions. In contrast a strategy focusing on the surveillance of the high risk region was almost as robust as strategies involving vaccination, and total costs did not increase even under perfect mixing.

Robust surveillance under severe uncertainty on the probability of incursion

As the horizon of uncertainty regarding the probability of incursion increases, making the probability of incursion greater in the high risk region, the most robust policies are those that involve vaccinating the high risk region (Figure 1 B). Surprisingly, in the case of no vaccine availability, surveillance activities not only do not increase the robustness of the management policies but they make them less robust. The reason is that, under very high probability of incursion, the epidemics cannot be mitigated by surveillance, i.e. even if surveillance activities allow for control of a few incursions, many others will not be detected in time and the epidemic will occur. The delay obtained by surveillance activities does not compensate their cost (see Figure 1B where strategies involving surveillance and no vaccination are less robust with regard to the medium and low aspiration level than implementing no action in the "do nothing" strategy). Thus, any knowledge that constrains the upper limit of the risk of incursion may be of great importance in deciding upon an optimum surveillance or vaccination strategy.

Robust surveillance under severe uncertainty on the capacity of farmers to report the disease

In the case of some diseases, a proportion of infected animals can present clear clinical signs after a period of incubation of the disease. If the farmers are well informed and vigilant about the potential occurrence of these symptoms, their active reporting can be a low cost and extremely effective way to detect the early emergence of disease (Figure 1C). In contrast with Figure 1 A, B and D and Figure 2 where we assumed that farmers could not detect or report the disease, active reporting is shown to be able to reduce the 99.9^{th} percentile of total cost to a third (compare Figure 1 A and B with Figure C for $\alpha = 0$, with a reduction from £B 1.5 to £B 0.5). All the policies appeared very robust due to farmers active reporting. The strategies involving surveillance of the low risk region (which is much larger in magnitude to the high risk region), were considerably less robust because outlays were applied to an activity that did not increase the effectiveness of detection or the initiation of control.. Interestingly, these results hold even for very low probabilities of accurate reporting by farmers, showing the high potential of involving the farmers on the detection of emerging diseases.

Robust surveillance under severe uncertainty on the detection effectiveness

To be able to evaluate the effect of lower detection effectiveness clearly, we set the proportion of asymptomatic animals to one, which led to a drastic downward shift of the expected costs (Figure 2 B and C). The results demonstrated how, even if the effectiveness of detection is very low, a policy of surveillance in the high risk region is of comparable robustness to policies using vaccination (Figure 2 B).

Robust surveillance under severe simultaneous uncertainty on incursion, transmission, vector dispersal and detection

We evaluated an info-gap framework where all the uncertain parameters were varied simultaneously. The results showed patterns consistent with the analysis of the individual horizons of uncertainty for the policies of surveillance of both regions and the low risk region (that were less robust) and surveillance of the high risk region and vaccination (which were more robust). The main difference resided in the "do nothing" scenario that as expected was a robust alternative. The reason is that diseases that present a high probability of incursion and transmission within and between regions, render non cost-effective the attempt to control them.

Robust surveillance under severe uncertainty regarding the extension of the high risk region

Uncertainty on the actual extension of the high risk region leads to unintended allocation of vaccines and surveillance in regions where the probability of entry is low. Strikingly, the results showed that a policy of only surveying the high risk region was robust to uncertainty in the knowledge of the extension of the high risk region for values of α between 0.2 and 0.5 (Figure 1 D). The reason is that even if a large proportion of surveillance efforts are misallocated to the low risk region, the proportion correctly allocated to the high risk region still has an important protective impact and a small amount of surveillance in the low risk region is also beneficial. This is not the case of vaccine allocation because allocation of vaccine to the low risk region instead of the high risk area reduces the capacity of the vaccine to control the epidemic in the high risk region. As a result, a policy of surveillance of the high risk region unexpectedly appears more robust than a policy of vaccination (Figure 1 D).

Robust surveillance under severe uncertainty on the probability of vector dispersal

Vector dispersal might lead to spread of the disease between regions. Under severe uncertainty, a policy of surveillance in both regions (which is very costly) appeared very robust with respect to the medium aspiration threshold (Figure 2 A). Intuitively, for high levels of vector dispersal between regions the probability of interregional infection is high, making it advisable to conduct surveillance in both regions. This can be noted in Figure 2 A, where for values of α greater than 0.8, the values of the 99.9^{th} percentile of discounted costs increases for all strategies except for surveillance of both regions which decreased the discounted costs. This result is somewhat surprising since, for the rest of horizons of uncertainty considered, a policy of surveillance in both regions with high intensity appeared very costly and less robust..

Discussion

Here we developed an epidemic-economic model in a landscape with two interconnected regions with a heterogeneous risk of incursion and spread of an emerging disease. We employed info-gap theory to assess the robustness of surveillance strategies for animal disease control. Using the case study of bluetongue incursion in England and Wales, new insights for robust surveillance strategies were obtained. Knowledge of the pathways of entry of a disease, the spatial distribution of climatic variables that increases the probability of disease incursion and the structure of the production system that promotes disease spread allows in many cases to differentiate between low and high risk regions. Accounting for the spatial heterogeneity of the risk of disease incursion and spread represents an opportunity to identify robustly protective and cost-effective surveillance strategies.

The results predicted that, in a landscape divided by a small high risk region and a large low risk region, the most robustly protective policies involved vaccination of 40-50% of the animals in the high risk region. The model suggests that vaccination could contribute to limiting the size of an outbreak and reduce the risk of spread to the larger low risk region. In addition, consistent with epidemic theory, vaccination policies were able to avert large outbreaks even for high probability of incidence of new incursions and perfect mixing among individuals. However, it must be borne in mind that these results are predicated on our underlying assumptions, which include a considerable horizon of uncertainty in respect of the risk of incursion. If that risk were constrained then the vaccination strategy might be predicted to be less robust. Likewise, if our costs for surveillance were importantly over or under-estimated then different conclusions might result. This can be investigated further through sensitivity analysis. We chose relatively high threshold for exigency in the info-gap model – in reality, investment in surveillance for BTV would compete with limited resources for other surveillance priorities and a lower value might be imposed. However, where a surveillance strategy such as promoting the reporting of suspect clinical signs by farmers might also serve to detect multiple diseases, then the value of the approach would increase.

In the case of new diseases, vaccines are not likely to be available and surveillance for early detection is one of the main mitigation options. The results showed that intensive surveillance of the high risk region was robustly protective but intensive surveillance on both

regions was not a robust policy and that, under severe uncertainty regarding probability of incursion and transmission, it was even less robust than doing nothing (unless in the case of high interregional vector dispersal which is discussed below). Our results regarding the robustness of surveying high risk regions are in agreement with results in the related field of invasive alien species surveillance. Hauser and McCarthy (2009) showed that regions with a high probability of invasive species occurrence and great benefits associated with detection should have intensive surveillance. In our case, surveillance of the high risk region implies high avoided costs because of prompt detection of incursion and the opportunity for rapid control, preventing further transmission to the second much larger region. Interestingly, surveillance of the high risk region was a very robust strategy even under perfect mixing of individuals within regions. This result can be interpreted from a reverse angle: a surveillance strategy accurately targeted to the high risk areas can achieve the same results as a presumably much more costly preventive policy consisting of the restriction of the spatial movement of animals between farms to reduce disease transmission.

The results regarding the robustness of the surveillance of the high risk region did not imply that the low risk region should not have any surveillance efforts. In the case of severe lack of knowledge of the extension of the high risk region, an unintended proportion of the surveillance efforts were allocated to the low risk region. This resulted in a robust policy that also prevented infrequent outbreaks in the low risk region that could potentially spread and if totally undetected, could affect a large proportion of the population in the low risk region. However, this is an unlikely scenario for BTV in England or Wales. This logic did not apply to vaccine allocation between regions. Vaccine misallocations into the low risk region due to the lack of knowledge of the extent of the high risk region led to a less robust policy than a strategy of surveillance in the high risk region. This result is consistent with the control of a disease in two interconnected regions for which the administration of treatment to equalize the infection level in both patches has been shown to be the worst possible strategy to minimise the overall level of infection. It is instead more beneficial to focus on the control of the area with the lowest infection level (Rowthorn, et al., 2009). Similarly, not focusing campaigns in the high risk area converted vaccination into a non robust strategy because it led to two reduced campaigns incapable of preventing the epidemic from taking off in either of the regions (instead of just one campaign preventing the take off of the epidemic in the high risk region). This serves to illustrate

the value of knowledge that enables accurate identification of high risk areas. Where a seasonal effect is also present, as in the case of BTV, then high risk can be attributed to space and time.

The characteristics of the connectivity between regions was shown to be very relevant for the adequate selection of surveillance policies, as in the case of the election of the optimal harvesting strategy in patchy and infected wildlife populations (Horan, et al., 2005). In the case of bluetongue, vector dispersal between regions cannot be directly controlled whereas animal movements between regions can be stopped. The info-gap analysis regarding the dispersal characteristics of the vector showed that, when interregional dispersal is very high, intensive surveillance of both regions was a robust strategy because infection of one region will most likely lead to the infection of the rest of the regions. However, experience in Northern Europe indicates that very high inter-regional transmission of BTV is unlikely in reality. If this was the case, the distinction between both risk regions becomes vague and the robustness of policies focusing on surveillance of the high risk region is dampened.

Surveillance campaigns focusing on the high risk region were shown to be robust to increasingly worse scenarios; however, they could not obtain a substantial decrease in the expected costs due to the disease. In contrast, farmers' inspection and reporting was shown to be by far the most effective way for early detection and control of emerging diseases leading to a substantial reduction of expected costs. This was the case even if the capacity of the farmers to correctly identify and report the disease was very limited. Indeed, in practice new outbreaks of epidemic disease such as BTV, Foot & Mouth Disease, Classical swine fever and Avian Influenza have frequently been discovered through the observation and reporting of suspect clinical signs by vigilant livestock farmers. These results are consistent with examples of past successful eradication campaigns where public involvement in outbreak detection thorough information campaigns has been shown to be a very effective way to prevent harmful non-indigenous species from invading new environments. For instance reports by members of the public of small outbreaks of Colorado potato beetle in the UK has helped to maintain the UK Colorado beetle free status for over 100 years (Bartlett, 1980). In this sense, modelling efforts integrating farmers' adoption of biosecurity measures (Gramig and Wolf, 2007, Hennessy, 2007, Hennessy, 2008) with epidemic theory and surveillance systems present a big potential to obtain further insights on the designing of robust surveillance strategies through public involvement.

Our modelling approach has some limitations. Epidemic compartmental models assume perfect mixing of individuals in the population. In the case of animal diseases, the hosts are confined in farms and the mixing is relatively limited to movement of animals between farms. Bluetongue, however, is a vector-borne disease and the vector can move freely between farms, although distances play a role in the mixing of the vectors. To account for spatial structure we applied a metapopulation approach with two subpopulations and incorporated a parameter in the force of infection reflecting difficulties in transmission due to imperfect mixing. However, greater spatial resolution of the model could be obtained by considering each individual farm as a single subpopulation (e.g. Szmaragd, et al., 2009). At the risk of not capturing interesting spatial interactions (such as the relationship between the incubation period and the biting rate with temperature), we preferred to keep the spatial structure of the model simple to answer more general questions on robust surveillance and to provide for a modelling framework that could be easily modified and applied to other diseases without extensive data demands.

Info-gap theory is a simple and intuitive way to formalise the analysis of robustness of mathematical models that shifts the objective of the agency from minimisation of costs to a satisfactory and protective behaviour. Info-gap is however not free of limitations, such as the difficulty to select the performance criteria and the election of the origin of the horizon of uncertainty. Nonetheless, the use of parameters from literature provides for a good starting point for the analysis of robustness of the model.

Conclusions and future research

This paper contributes to the literature on the economics of disease surveillance. Specifically we focus on the case of surveillance system for exotic and emerging diseases, where there are important gaps on the information required to make appropriate decisions. If the aim of an agency is safeguard the possibility of disaster under severe uncertainty over detection and spread of an animal disease, then an important feature of the system is its robustness. In other words the system should be designed to prevent total losses to society beyond a given level of performance. Specifically, we considered the economic and epidemiological conditions that make surveillance strategies between heterogeneous regions or patches robust. Our approach, combining epidemic-economic models with info-gap theory, is novel and generated decision-making insights for robust surveillance of emerging animal diseases. We applied this model to data concerning Bluetongue disease in England and Wales, making assumptions about possible

strategies and costs for illustrative purposes. The paper is not intended to reflect official policy in UK. The main conclusion of this study is robustness is not greatly affect by lack of surveillance in low risk areas, but it critically depends on farmer involvement in surveillance.

We believe our approach is an alternative to the recently proposed risk based surveillance systems (Stärk, et al., 2006). Moreover our modelling framework can be particularly useful and relevant for decision makers charged with the duty of developing a surveillance system that detects new diseases and or known diseases in new environments.

In this paper we only considered two types of regions, a low and a high risk area, and we did not fully considered the interactions between vector and animal movements. In the future we aim to look in more detail at the spatial and time dimension of this problem. We think that it may be useful to adapt a network approach where each farm is a node linked with each other and there are flows of animals and vectors. This should gives an even more detailed and practical sense on how a robust surveillance should be designed.

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Table 1. Epidemic and entomological parameters of the model for the surveillance of BTV outbreaks in the UK. Values expressed as ranges were modelled as uniform distributions.

Parameter	Parameter description	Cattle	sheep	Source
N	Total number of susceptible individuals in England and Wales	5,978,229	23,222,000	[b]
μ	Incubation period (days)	0-7	0-21	[a]
ε, ε_A	Infectious period for infected symptomatic and asymptomatic (days)	20.6	16.4	[d]
η	Mortality of the host due to the disease	0.003;	0.3	[j]
Θ_{asym}	Proportion infected becoming asymptomatic	0.96	0.4	[j]
b	Probability of transmission from vector to host	0.8-1.0		[e]
β	Probability of transmission from host to vector	0.001-0.15		[g]
σ	Biting preference for cattle with respect to sheep	9		[h]
ω	Mortality of the vector	0.1-0.5		[i]
	Ratio of vectors to host	0-5000		[e]
r	Vector recruitment rate	0.1-0.5		[f]
a	Biting rate	0-0.5		[e]
γ	Proportion of vectors dispersing beyond the protected zone	10^{-6}		[l]
Ψ	Proportion of animals moved daily between regions to live destinations	$1.68 \cdot 10^{-5}$	$3.64 \cdot 10^{-5}$	[k]
μ_{vec}	Incubation period of the vector (days)	4-26		[c]

[a] Estimated from (Bonneau, et al., 2002); [b] (DEFRA, 2009, Welsh Assembly Government, 2009); [c] (Gerry and Mullens, 2000); [d] (Goldsmit, et al., 1975); [e] (Gubbins, et al., 2008); [g] (Nunamaker, et al., 1997); [h] assumed from studies showing that there is a preference of the vector to bite cattle (Nevill, 1978); [i] (Birley and Boorman, 1982); [j] (DEFRA, 2007); [f] assumed similar to the mortality rate (Savini, et al., 2005); [k] we use as a surrogate the number of animals moved out of the current surveillance zone to live destinations if restrictions stop in England (DEFRA, 2007). The animal movements have been estimated as 63000 cattle and 113000 sheep per year. Movements to slaughter are assumed not to affect epidemic dynamics. The probability is the proportion of moved animals with respect the total population outside the surveillance zone; [l] Wind contributed to explain the BTV epidemic in northern Europe in 2007 with establishment of local virus circulation at distances of 35–85 km (Hendrickx, et al., 2008). These hops indicate a leptokurtic spread where a few individuals can disperse long distances. We assume that a proportion of 10^{-6} vectors will be able to disperse between regions daily.

Table 2. General parameters of the model for the surveillance of BTV outbreaks in the UK.

Parameter	Parameter description	value	Source
$p_{incursion}$	Daily probability of first infection into the system per region (^{0}low risk region; ^{1}high risk region)	^{0}0.001096; ^{1}0.000137	a
T	Time horizon (years)	20	
ρ	Discount factor	0.035	b
B_{exC}	Average value of cattle meat exports from the UK (2006 and 2007) ($ millions)	90.631	c
B_{exS}	Average value of sheep meat exports from the UK (2006 and 2007) ($ millions)	393.212	c
p_{exHR}	Proportion of exports associated to high risk region	0.2078	d
C_{lm}	Daily gross values of the livestock trade market loss (£)	180000	f
$c_{BTV\text{-}host}$	Loss of value of infected symptomatic animals due to loss of fertility, abortions and or reduced growth rate (£) (^{0}cattle; ^{1}sheep)	^{0}75; ^{1}20	e
c_d	Unit cost of inspection of one animal (£)	3.33	j
c_{rum}	Value of an animal at slaughter (£) (^{0}cattle; ^{1}sheep)	^{0}600; ^{1}60	e
$c_{restric}$	Daily cost due to restrictions on movement per animal (£) (^{0}cattle; ^{1}sheep)	^{0}0.082; ^{1}0.0082	e
c_{vac}	Unit cost of vaccine per dose and year (^{0}cattle; ^{1}sheep)	^{0}1.32; ^{1}0.66	g
δ	Effectiveness of the vaccine	0.95	
n_{farm}	Mean number of animals per farm	30	
p_{dI}	Probability of correctly detecting infected symptomatic	1	
p_{dA}	Probability of correctly detecting infected asymptomatic	0.8	
p_{dE}	Probability of correctly detecting exposed	0.6	
c_{insect}	Daily cost of insecticide application per animal (£)	0.081	h
m_{spray}	Increase in vector mortality due to spraying	3	i
m_{detect}	Factor of increase of the proportion of surveillance after detection	10	
p_{report}	Probability of accurately reporting BTV symptoms by the farmer	0.9	
TC_{max_low}	Low exigency aspiration level (£ millions)	179.347	

TC_{max_medium}	Medium exigency aspiration level (£ millions)	89.673
TC_{max_high}	High exigency aspiration level (£ millions)	17.934

[a] In the case of the high risk region, we assume that the outbreaks of BTV in Ipswich, Cambridge, Kent and Sussex in 2007 responded to independent entries and represented the risk under current climate for the last ten years; in the low risk region we assume that one independent entry is expected to occur in next 20 years; [b] (Treasury, 1997); [c] (FAO, 2010); [d] The area of a protected zone of 100 km radius is expressed as a proportion of the area of Wales and England, assuming that given that a sample of the size of the high risk region is very large, the distribution of holdings can be approximated as homogeneous; [e] 5% of the animal value (DEFRA, 2007); [f] Calculated as $(B_{exC} + B_{exS})\, p_{exHR}\, (365)^{-1}$; [g] two 1ml doses are needed per cattle and 1ml dose per sheep at a cost of £ 0.66 per ml (DEFRA, 2010); [h] We assume a cost of insecticide of £3 and a cost of application of £14 per 30 animals holding. Applications are done once a week; [i] insecticides will have high effectiveness in the holdings applied but not on the rest of vectors in the environment that will easily replace the controlled population making this parameter highly uncertain; [j] The mean travelling costs (3 visits per farm), the wage costs of DEFRA personnel is assumed to be £30 per a 30 animals farm. The laboratory costs for the serological analysis is assumed £70 per sample analysed that allow to detect the disease in a farm of 30 animals.

Figure 1. Evaluation of the robustness of vaccination and surveillance policies under severe uncertainty in: A) transmission of the diseases within each region (ρ_{mix}); B) probability of incursion of the disease in the high risk region ($p_{incursion}$); C) rate of reporting of the farmers (p_{report}); and D) lack of knowledge of the extension of the high risk region (θ_{mis}). HRR: high risk region; LRR: low risk region; TC net present value of the total costs expressed in billions of £. The probability of reporting by the farmers was set to zero except in plot C. The proportion of farms survey was set as 0.003 and the proportion of animals vaccinated was set at 0.4 in the regions indicated by the policies in the legend.

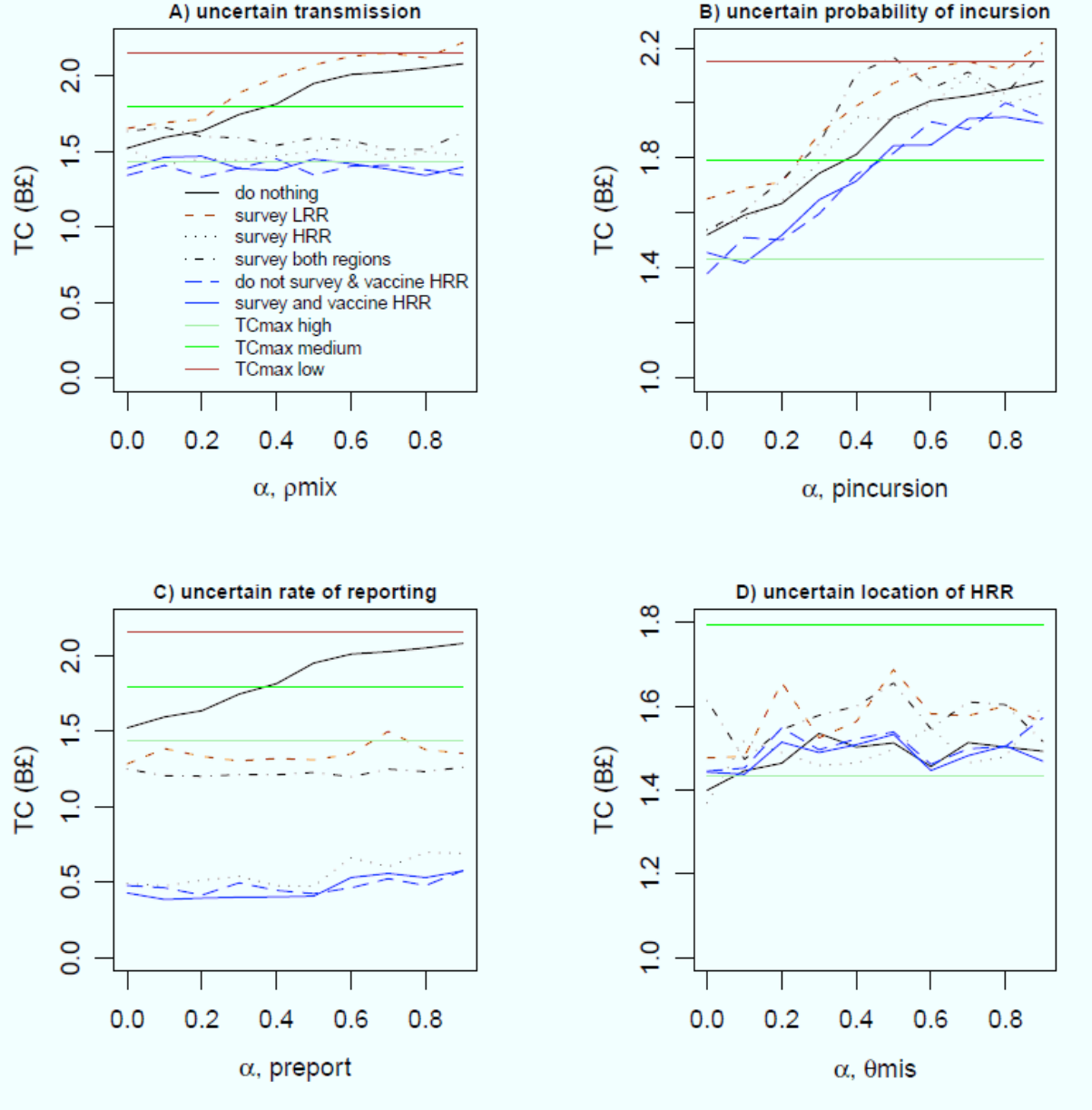

Figure 2. Evaluation of the robustness of vaccination and surveillance policies under severe uncertainty in: A) vector dispersal within regions (γ); B) effectiveness of detection measures (p_{dA}); C) simultaneous severe uncertainty in the parameters $p_{incursion}$, ρ_{mix} , p_{report}, θ_{mis}, γ, and p_{dA}. D) The levels of vaccination and surveillance were varied to assess changes in robustness. The proportion of asymptomatic individuals was set to zero in plots B) and D) to assess the effect of increasingly less effective detection measures (represented by p_{dA}). HRR: high risk region; LRR: low risk region; TC net present value of the total costs expressed in billions of £. The probability of farmers reporting was set to zero.