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Optimal vaccination strategies against vector-borne diseases

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ABSTRACT

Using a process oriented semi-agent based model, we simulated the spread of Bluetongue virus by *Culicoides*, biting midges, between cattle in Denmark. We evaluated the minimum vaccination cover and minimum cost for eight different preventive vaccination strategies in Denmark.

The simulation model replicates both a passive and active flight of midges between cattle distributed on pastures and cattle farms in Denmark. A seasonal abundance of midges and temperature dependence of biological processes were included in the model. The eight vaccination strategies were investigated under four different grazing conditions. Furthermore, scenarios were tested with three different index locations stratified for cattle density.

The cheapest way to vaccinate cattle with a medium risk profile (less than 1000 total affected cattle) was to vaccinate cattle on pasture. Regional vaccination displayed better results when index cases were in the vaccinated areas. However, given that the long-range spread of midge borne disease is still poorly quantified, more robust national vaccination schemes seem preferable.

1. Introduction

Bluetongue has been recognised as a ruminant disease for more than one hundred years (Spreull, 1905), and is present at various levels on all continents except Antarctica (Tabachnick et al., 2004). Bluetongue displays its most severe economic impact when entering non-endemic areas where animal resistance to the disease is little, as was very evident with its invasion of temperate Europe in 2006 (Velthuis et al., 2006), and Australia in 1977 (Ward, 1994). Bluetongue is non-contagious and is transferred by *Culicoides* vectors (Tabachnick et al., 2004; Wilson et al., 2008). In the case of Denmark, the primary ruminant host of the disease is cattle; as these outnumber sheep ten to one. The dominant *Culicoides* species in Denmark, which are known to bite cattle, are the *Culicoides obsoletus* group and the *Culicoides pulicaris* group (Lassen et al., 2011).

Preventive vaccination strategies can have the objective to prevent or confine the disease to a minimum level; the latter is usually used in a veterinary perspective, where prevention is equivalent to a costly vaccination of all cattle. For the Bluetongue disease (BT) in 2008, Denmark chose initially to vaccinate regionally in order to prevent introduction from nearby countries. However, BT has previously displayed long distance introdof several hundred kilometres such as in Scandinavia, the UK, the Mediterranean and Australia (Sellers and Pedgley, 1977; Braverman et al., 1996; Mellor and Wittmann, 1998; Alba et al., 2000; Ducheyne et al., 2007; Burgin et al., 2012; Eagles et al., 2012); in these cases, regional vaccination close to borders would have had little effect. However, the basic concept of increasing the distance between infectious and susceptible cattle can also be implemented countrywide on a local scale, which is investigated in this paper in comparison

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with more traditional vaccination strategies. Increasing the distance between infectious and susceptible cattle on a local scale enables a vaccination campaign to cover large areas (i.e. country wide vaccination), while using a low number of total doses. In this paper, we aim to rank and quantify the effectiveness of eight vaccination strategies including specially designed strategies to maximise the distance between susceptible animals.

Vaccination has been used successfully to control outbreaks in Europe (Zientara et al., 2010). In Italy, a vaccination of 80% of all susceptible animals was able to efficiently halt and prevent transmission (Patta et al., 2004). However, the climate and the vectors differ between southern and northern Europe, and empirical results from Italy can therefore, not be transferred to Denmark. Szmaragd et al. (2010) concluded by simulation that for England, an 80% vaccination of cattle was necessary to halt an epidemic, and that a regional roll-out needed to be done at sufficient speed to prevent Bluetongue from spreading to non-vaccinated areas.

In this work, eight preventive vaccination scenarios are investigated with three areas of introduction into Denmark under four different grazing conditions, totalling 96 unique scenarios. For each scenario, the overall national vaccination cover is tested in steps of 10% with 1000 repetitions per step, in total 960,000 simulated introductions of BTV.

2. Methods

The model used for simulating the spread of disease is described in Græsbøll et al. (2012), and a description of Culicoides' flying parameters for midges are provided in Græsbøll (2013, App. B, SM1). Below a short resume of the model is described, with a detailed description of the vaccination scenarios.

The model is a semi-agent based stochastic process model: Individual midges are simulated to fly between cattle. The cattle can be located either on pasture or in stables on the farm's location. Between flying events, the viraemic stage and the probability of transmission of the virus are evaluated based on temperature, using the Markov Chain Monte Carlo (MCMC) method.

The vectors are simulated to fly in two distinct ways: Firstly, an active local flight mode where vectors fly at random on a length scale of hundreds of metres in order to locate cattle. Secondly, a passive mode where vectors can be carried several kilometres by the wind. Over small distances, vectors are assumed to be able to locate cattle with a 100% success rate. Therefore, all of Denmark is divided into a grid with cells of 300 by 300 metres. Within each grid cell, all of the vectors present can locate all of the cattle present. Vectors and hosts located within each grid cell are only discernable by disease status, and therefore, not individually tracked; hence, the term "semi-agent model". The grid also serves further technical purposes in the programming.

The overlaying of a grid on pastures in Denmark allows for each grid cell to be assigned a number of cattle, based on the known use of this cell. From the European Union's arable area subsidies programme, it was possible to obtain information about pasture areas and ownership of these in Denmark. From the Danish Central Husbandry Register (CHR), information about ownership of cattle could be obtained. Combining this information revealed which farmers could potentially put cattle out to pasture, and where these pasture areas were located. It was not known which farmers put their cattle out to pasture, so in each repetition of the simulation this was sampled randomly; also, the proportion of cattle put out to graze is likely to change in response to an outbreak.

Within each grid cell, the transmission of disease is determined by evaluating the probability; given the amount of infectious vectors/hosts and the temperature dependent bite and mortality rates of vectors. Furthermore, the virus development in the vectors and hosts is determined. The spread of the disease is especially dependent upon this, as the period it takes for vectors to become infectious is highly temperature dependent, and vectors most often die before they become infectious. The mortality rate of vectors is also temperature dependent. Furthermore, the vector to host ratio is seasonal with vector season starting at the end of May and ending in late November, displaying four generation peaks. The parameters and full model are presented in Græsbøll et al. (2012).

2.1. Vaccination scenarios

Eight preventive vaccination scenarios were selected to represent as different approaches to preventive vaccination as possible, and are defined as follows:

- P A percentage of cattle on all farms are vaccinated. All farms are vaccinated to the determined in-farm percentage.
- RH Random Holdings. Farms are selected at random to be vaccinated. All cattle belonging to the selected farms are vaccinated.
- NN Nearest neighbour vaccination. The two cattle farms closest to each other are identified and by random selection, one of these farms has all of their cattle vaccinated. Then, the two non-vaccinated cattle farms nearest to each other are located and again one is selected at random to be vaccinated. This pattern continues until a certain proportion of farms have been vaccinated.
- S Vaccination based on farm size. Beginning with the smallest farms in Denmark (in terms of number of cattle), a number of farms are selected to have all of their cattle vaccinated up to the specified vaccination cover.
- L Vaccination based on farm size. Beginning with the largest farm in Denmark, a number of farms are selected up to the specified vaccination cover.
- G Vaccination of all cattle put out to pasture for selected farms. Farms are selected at random with cattle on pasture until the specific vaccine coverage, and all cattle from these farms that are on pasture are vaccinated.
- SJ Regional vaccination of Southern Jutland bordering Germany. Farms in Southern Jutland are selected randomly until a specified coverage was reached.