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A large-scale epidemiological model of BoHV-1 spread in the Irish cattle population to support decision-making in conformity with the European Animal Health Law

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Abstract

We present a new modelling framework to address the evaluation of national control/surveillance programs planned in line with the European Animal Health Law (AHL) for livestock diseases. Our modelling framework is applied to the cattle sector in Ireland where there is need for policy support to design an optimal programme to achieve bovine herpesvirus type 1 (BoHV-1) free status under the AHL. In this contribution, we show how our framework establishes a regional model that is able to mechanistically reproduce the demography, management practices and transport patterns of an entire cattle population without being dependent on continuous livestock registry data. An innovative feature of our model is the inclusion of herd typing, thereby extending these beyond the categories of dairy, beef and mixed herds that are frequently considered in other regional modelling studies. This detailed representation of herd type-specific management facilitates comparative assessment of BoHV-1 eradication strategies targeting different production types with individual strategy protocols. Finally, we apply our model to support current discussions regarding the structure and implementation of a potential national BoHV-1 eradication programme in Ireland.

Keywords

regional, cattle, disease, model, BoHV-1, IBR, Ireland, eradication program

1. Introduction

The new Animal Health Law (AHL) and its implementation principles present new opportunities for the management of livestock diseases (European Commission, 2016). Among others, the AHL provides uniform guidance to livestock farmers across the EU on when a herd can be declared pathogen-free and which testing strategies can be used to determine the health status of a herd. Particularly for the bovine sector, this regulation allows the use of modern technologies for the monitoring of animal health activities. With the implementation principles laid down in the AHL, the herd management type has become an important criterion for shaping the sampling strategy of national surveillance and control programs. This requires not only a re-thinking by policy and decision makers, but also an update of epidemiological models which are tailored to support the decision-making process.

The use of epidemiological models representing the spread of infectious diseases in cattle populations assists with animal health decision-making and policy support. In recent years the development of these models has increased (Brock et al., 2020). In particular, regional models have been proposed because they allow possible consequences of decisions on the success or costings of a surveillance/control programme to be simulated across an entire region.

In the existing literature, different ways of representing the spread of pathogens in cattle populations at the regional level have been documented. We acknowledge the huge fundus of cattle disease management models on regional networks of farms, i.e. for foot-and-mouth disease (Boklund et al., 2013; Carpenter et al., 2011; Keeling et al., 2003; Tildesley et al., 2012; Ward et al., 2009). These models are implemented at the herd scale without considering herd management processes. Animal transports are either read from observed data or contact structures between certain types of herds are defined between which animal transports can occur arbitrarily.

Among the more detailed mechanistic models that take into account age structure and management practices within herds, many are spatially implicit in which the meta-population of connected animal sub-populations were considered without real geographical locations or real number of herds. Often, these are compartmental models where trading patterns have been assumed to be homogeneous in terms of topology and flows (e.g. Courcoul and Ezanno, 2010). Other approaches model between herd contacts data-driven according to national cattle movement databases (e.g. Beaunée et al., 2015; Qi et al., 2019; Thulke et al., 2018). More detailed approaches also model demographic processes, such as birth and death events, in a data-driven manner using cattle registry data (e.g. Iotti et al., 2019; Widgren et al., 2016). Data-driven modelling provides a realistic representation of interacting farms at a regional scale, and allows precise evaluation of the mechanisms involved in the spread of pathogens. However, the simulation horizon is constrained to the interval of available data, which complicates long-term predictions about the future of an eradication program.

Trade-related disease control interventions, e.g. restricting animal transports between certain farms, does interfere with the data-driven movements. A target herd for a move according to the data might not be accessible due to restrictions. The solution would be a generic transportation network incorporated into regional models of pathogen spread which still captures the basic trading principles in the available data. There have been efforts to create generic transport networks through the use of a virtual market that manages animal transports by supply and demand (Gethmann et al., 2019). However, the model did consider only first-tier farm management types and generated animal movement streams that still require corrective model manipulations.

Most regional cattle disease models are tailored to specific production systems, e.g. the dairy sector in Brittany, France, as developed by Beaunée et al. (2015) or Qi et al. (2019). Because other production systems are not included, it is not possible to evaluate the impact of national or regional programmes across production sectors. Furthermore, effective model-based decision-support may be complicated by the lack of detail about aspects of cattle herd management in the region. Hence,

it would be valuable to have a more detailed representation of management specific to herd type to assess animal disease control and surveillance activities under the AHL.

In this paper, we present a new modelling framework to overcome previous limitations in regional models. Our framework establishes a fully mechanistic regional model that is able to generically reproduce the demography, management practices and transport patterns of an entire cattle population without the need of permanent data-input. We apply our model to County Kerry, Ireland, which has been identified in previous analyses as a representative subset of the total Irish cattle population. The model results are prepared to support decision-making in the context of current discussions regarding the structure and implementation of a potential Irish BoHV-1 eradication programme.

2. Data & Methods

2.1. Datasets

Several datasets were analysed to gain an understanding of the dynamics of the Irish cattle population (Table 1). All data listed in Table 1 were obtained from the Animal Identification and Movement (AIM) database maintained by the Department of Agriculture, Food and the Marine (DAFM) of Ireland. In line with EU requirements, the AIM database includes records of all births, movements and disposals (i.e. origin, destination and date) and tracks every bovine animal in Ireland from birth or import to death or export (DAFM, 2018). In the database, each animal is recorded with its own unique identity (ID) or tag number, along with its sex, breed and birth date, as well as the IDs of its herd and dam.

From this database, three different datasets were generated that were considered important to describe the characteristics of the Irish cattle population. Taking into account the patterns of calving in Ireland outlined by Tratalos et al. (2017), we calculated herd-level demographic data for all cattle registered on three dates in 2017 (1st January, 1st May and 1st September). Birth data were drawn from 2016 to 2018 to gain an understanding of the calving characteristics. Movement data were extracted for each day in 2017 (1st January – 31st December 2017).

TABLE 1

2.2. The cattle population in Kerry

The data shown in Table 1 have been used to classify each individual herd in Ireland into one of 16 different herd types. A herd type was considered as a population of farms with broadly similar farming and management practices (Köbrich et al., 2003; Landais, 1998). These 16 herd types were identified from a previous analysis where expert knowledge was coupled with a machine-learning algorithm called self-organising-maps (SOMs). Detailed documentation of the classification procedure and a description of the identified herd types is described by Brock et al. (2021). In the following section, a brief description of these herd types is given.

Overall, the cattle population in Kerry was classified into 5 main herd types, some of which can be further divided into subgroups (Figure 1). The main herd types present in Kerry are dairy, beef, store, mixed and fattening herds, with beef herds accounting for the largest proportion (~ 45%) of all of the approx. 5000 registered herds.

Among dairy herds, four subgroups that differ in terms of their management are present. Typical dairy herds (D), which sell their male calves a few weeks after birth, are the most common dairy herd type in Kerry (Figure 1). In addition, there are dairy herds (DRm) that rear all their calves, including the male calves which are then sold as youngstock for fattening. Non-rearing dairy herds (DnR_C & DnR_nC) were also present in Kerry. These herds sell most of their calves, and either (DnR_C) move the female calves to external contract rearing farms (Rdf) where the calves are reared and later inseminated before being returned to their birth herd, or source replacement females through purchase of non-homebred animals (DnR_nC).

Five different types of beef breeding (suckler) herds are present in Kerry. Beef suckler to weanling (BSW) herds are the most common beef system in Kerry (Figure 1). These herds sell their male, and some female, calves after weaning (between six and eight months of age) to store or fattening herds. A proportion of females is kept for replacement. The beef suckling to youngstock (BSY) system is very similar to the BSW system, however these herds keep their offspring for a longer

period and sell them to fattening herds as yearlings. Non-rearing suckling to youngstock (BSY-nR) herds are a variation of the BSY herd type, with the difference being that most female calves are sold after weaning and replacement breeding females are purchased. With these latter herds, the main production objective is the rearing of bulls and steers for beef production. Although rarely represented in Kerry, beef pedigree herds (BP) are important for providing quality breeding stock to other commercial cattle producers in both the dairy and beef sectors. The suckling to beef (BSB) herds follow the full beef production cycle, from birth through to the age of slaughter.

The store/rearing group only comprise non-calving herds. Overall, five sub-types were identified within this group, which differ in terms of the animals these herd preferentially rear. Store dairy male (Sdm) herds typically purchase young male calves from dairy herds to rear before then selling them to fattening herds. Three different beef store herds are present, which differ in terms of their sex composition (rather than management practices): store beef males (Sbm), store beef females (Sbf) and store beef mixed (Sbmx) systems (Figure 1). These herds purchase beef animals as weanlings and rear them until they are sent to fattening herds. In rearing dairy female (Rdf) herds, young female dairy calves are introduced, reared and inseminated, before being returned to their birth herd (DnR_C) as pregnant heifers.

In Kerry 15% of the cattle herds registered are fattening (F) or dual purpose herds (M). F herds buy calves, weanlings, youngstock and cows from a wide range of herd types and fatten them until slaughter. M herds produce milk, but also have another cattle enterprise, solely focused on beef production.

FIGURE 1

2.3. Description of the model

A stochastic, regional, spatially explicit, individual-based model was developed to simulate the entire cattle population in Kerry. The model, called FarmECS-IBR, represents each of the ~5000 cattle herds and ~360,000 bovines, along with its herd type-specific management. The model is derived from the FarmNet model, which was applied to support national Bovine Viral Diarrhoea

Virus (BVDV) eradication programme decisions (Thulke et al. 2018). Following Brock et al. (2020b), the model is composed of three main components representing [1] biological processes, [2] management-related processes, and [3] pathogen-related processes. Biological processes such as ageing, pregnancy, fertility and mortality are represented at each time step for all individual animals. At the herd level, management-related processes such as grouping, breeding, buying and selling of animals are simulated for each herd. Pathogen-related processes such as infection, recovery and reactivation are simulated at the animal level. The simulation model runs in weekly time-steps and is implemented in Scala (<https://www.scala-lang.org/>). A complete technical documentation of the model according to the ODD protocol (overview, design concepts, and details) (Grimm et al., 2020, 2010, 2006) is available at <https://ecoepi.eu/CattleDisMM/#IBR-svepm21>.

2.3.1. Biological processes

Each individual animal in the model is subject to an ageing process with animal age increasing by one week per simulation step. Ageing can trigger other processes, for example transfer between management units. In order to better explain the biological processes that we have considered in our model, we provide Figure 2. The schema shows the life cycle of an individual animal in a self-breeding cattle herd from birth to death.

In the model, each newborn animal enters the calf cohort (Figure 2). The sex of each calf is determined stochastically at birth according to the sex ratio (50%). In the model, a calf is classified as a calf until it reaches a predetermined age threshold (26 weeks). It is then weaned and, depending on its sex, will either enter the grazing or heifer cohort. Female animals enter the heifer cohort and are reared until they are ready for breeding (sexually mature). In the model, this event is determined by an age threshold (57 weeks). After successful breeding, heifers become pregnant and enter the bred heifer cohort. In the model, the gestation length is fixed and set to 40 weeks. After calving, bred heifers become cows and the reproductive cycle continues until the animal dies through an age-dependent stochastic mortality process.

FIGURE 2**2.3.2. Herd management processes**

For each of the 16 herd types shown in Figure 1, a rule-based management scheme was implemented which is followed by all herds of the respective type. This management scheme determines, for example, how long herds of a certain type keep youngstock, at what age they sell them and whether herds maintain themselves through breeding of their own replacement females or by purchase. Table 2 provides an overview of the management rules for all 16 herd types represented in the model.

TABLE 2

All self-maintaining herds are subject to a breeding process (Table 2 for breeding herds). In the model, breeding occurs whilst a herd is in its breeding season, with timing influenced by the desired calving interval. For simplicity and in accordance with the findings by Tratalos et al. (2017), we represent each breeding herd in Kerry as spring calving because that was the general pattern for most herds in Kerry. Breeding is applied to all heifers if their age exceeds a minimum age threshold (57 weeks) and to all cows that have exceeded a predetermined waiting time (4 weeks) after their last calving whilst herds are in their breeding season.

After successful breeding, each farmer estimates whether the number of inseminated animals is sufficient to meet his/her annual production target. If the number of inseminated animals is higher than desired, the farmer has a surplus and sells excess bred animals. Due to unpredictable biological processes (e.g. mortality, infertility, abortion), the number of animals inseminated may not be sufficient. In this case, this is typically compensated for by purchasing animals from herds with a surplus.

What happens to newborn calves depends on the management rules that we have defined for each herd type. Some herds sell most of the calves that are not needed for replacement soon after birth to store herds where calves are reared. Other herds keep most of their newborn calves to sell at a later age as youngstock for fattening. Except for the BSB herds, all self-calving herds sell all their

male offspring to another herd. The timing of these animal sales varies between herd types, and can be read from Table 2. As an example, dairy herds (D) sell all their male calves at between two and 13 weeks of age. In contrast, dairy rearing male herds (DRm) keep their male offspring up to 104 weeks of age.

Animals not needed for replacement are predominantly moved to store or fattening herds. In the model, these herds are non-breeding and non-calving, and therefore completely dependent on the purchase of animals. Store herds rear their purchased animals until they reach a certain age at which point they are sold as youngstock to fattening herds. The current number of animals in each individual herd and the actual number of traded animals emerges from the herd-management rules.

2.3.3. Animal movements

In the model, animal movements emerge from the herd type-specific management rules and stochastic processes, e.g. mortality or infertility, and are driven by supply and demand. Categories of animal transport cohorts between farms were determined based on the identified herd types (Figure 3). The transport network in the model was derived from these cohorts. Figure 3 shows the predominant transport routes with the corresponding animal types. Time and volume of these transports is determined by the transport algorithm according to supply and demand in the respective time step of the simulation.

FIGURE 3

The sex of an animal, as well as the time (age) when the animal is to be sold, determines to a large extent the trading cohort to which animal is assigned. For example, male calves sold from dairy herds between 2 and 13 weeks of age are assigned to the calf dairy male (CDM) cohort. In the model, certain herd types, such as Sdm herds in this example, have a demand for exactly this trading cohort according to the availability of space within their premises (Figure 3).

Animals intended to leave a herd enter an open market, with ‘demand herds’ selecting ‘supply herds’ based on distance as well as demand and supply batch size. In the model, the open market is not represented as a physical market where animals from the entire region come together to be

distributed. It is represented as a virtual market, where each farmer registers his/her demand or supply in order to find the most suitable trading partner. The actual transport of animals is then direct, from farm to farm. If demand cannot be satisfied from the market at a certain time, it is satisfied by introduction of animals originating outside the modelled region. Using this logic, trade in the model is completely emergent from the management processes of each individual herd. Hence, animal movement data are not needed for representing animal movements. It was decided not to explicitly simulate animal movements via a physical market, as possible epidemiological consequences of animal transfer (e.g. virus reactivation) in the case of infections with BoHV-1 typically occur days after the movement.

2.3.4. Epidemiological processes

In the model, each animal is assigned to one of four BoHV-1 epidemiological states (Figure 4). Seronegative animals that have never been exposed to BoHV-1 are susceptible. If a susceptible animal becomes infected, it enters the primary infection state and will be a lifelong carrier of the virus. In the model, the infectious period of a primary infected animal is two weeks. During this period, the animal is highly contagious and poses a risk of infection to other susceptible animals. Following primary infection, hosts recover and become latently infected. These animals become seropositive but do not shed virus while in this latent state. The virus can be reactivated in latently infected animals, leading to secondary infection and viral shedding. In the model, secondary infection lasts for one week, with affected individuals again posing a risk of infection to susceptible animals, albeit a lower risk than from primary infected animals. After recovery from secondary infection, animals return to the latently infected state.

FIGURE 4

The event of getting infected with BoHV-1 is modelled stochastically by means of an individual infection probability. In the model, animals of specific management groups are split into separate management groups. For each animal in a specific management groups i , we calculate the individual probability of becoming infected as a combination of two frequency-dependent transmission rates as

$$P_{inf,i} = 1 - e^{-(r_{withinHerds} + r_{betweenHerds})} \quad (1)$$

The within management groups transmission rate ($r_{withinHerds}$) describes the rate at which an individual receives the infection from its own management groups i and all other management groups j is calculated as

$$r_{withinHerds} = \beta_{Pi}^{wP} \frac{Pi(i)}{n(i)} + \beta_{Si}^{wP} \frac{Si(i)}{n(i)} + \beta_{Pi}^{bP} \frac{Pi(j)}{n(j)} + \beta_{Si}^{bP} \frac{Si(j)}{n(j)} \quad (2)$$

while $Pi_{(\text{management group})}$, $Si_{(\text{management groups})}$ and $n_{(\text{management groups})}$ are the number of primary infected, secondary infected and total animals in the respective management groups, respectively. β_{Pi}^{wP} and β_{Si}^{wP} are the transmission coefficients for primary (Pi) and secondary (Si) infected within (wP) and between (bP) management groups.

In addition to within-herd infection, between-herd transmission is modelled as

$$r_{betweenHerds} = \beta_{Pi}^{bH} \frac{Pi_{(neighbours)}}{n_{(neighbours)}} \quad (3)$$

Here, $Pi_{(neighbours)}$ denotes all primary infected animals and $n_{(neighbours)}$ all total animals in the neighbouring herds. A neighbouring herd is defined as such if it lies within a defined radius of the coordinates of a herd recorded in the Irish herd register. According to expert knowledge the radius was set to 5km.

Latently infected animals have the potential to reactivate the virus which causes a secondary infection. Virus reactivation is simulated as a binomial random process, with a constant weekly reactivation probability

$$P_{Reactivate} = 1 - (1 - r^{reactivation})^{1/52} \quad (4)$$

$r^{reactivation}$ is the annual reactivation rate for all latently infected animals. If an animal is transported in the model the reactivation rate is increased at the time point when the moved animal enters the new herd. This is intended to reflect the increased stress associated with animal transport and thus an increased probability for virus reactivation as reported by Thiry et al. (1987).

TABLE 3

The model parameters related to the infection submodel are shown in Table 3. Wherever possible, they were taken from the literature. Otherwise, systematic simulations were carried out aiming to replicate patterns described in the literature (e.g. an endemic situation with ~80 % prevalence at herd level). Uncertain model parameters were discussed and refined with veterinarians from Technical Working Groups convened by Animal Health Ireland and researchers from UCD Centre for Veterinary Epidemiology and Risk Analysis (CVERA). A brief description of the performed simulations is shown in the supplement.

2.4. Model initialization, simulation and output

The model was initialized from a table listing the position, herd type, target size, breeding and outdoor period for each of the ~5,000 cattle herds in Kerry. Then, for each herd in the table, animals were created and added to the simulation. Important animal state variables, such as age, sex and breed were drawn randomly from predetermined distributions. A 20-year pre-simulation was then computed, to ensure a proper initial population structure and valid animal components and state variable values.

After the pre-simulation, and for the sake of model validation, the cattle population in Kerry was simulated for a period of 30 years. A simulation year has 52 weeks starting on 1st January and ending on 31st December, corresponding to weeks 1 and 52, respectively. In simulation year 30, we extracted the population composition of all herds in the model for the 3 points in time for which we have demographic data available (Table 1). Furthermore, we extracted the transport

network generated by the model for simulation year 30, which makes it possible to calculate the incoming and outgoing farm transport volumes for each of the represented herd types.

2.5. Model validation

The behaviour of the model has been qualitatively validated using a technique called pattern-oriented modelling (POM). POM, which was first described by Grimm et al. (1996), is a promising approach for gaining a mechanistic understanding of complex systems and validating models representing these systems. POM requires the model developer to define multiple patterns that can be observed in real world systems but which are not used to parameterise the model. The ultimate goal is then to reproduce these patterns accurately in the outputs of the model (Grimm et al., 2005, 1996; Grimm and Railsback, 2012).

In consultation with veterinarians and livestock experts from Ireland, we have identified two different data patterns. The first pattern we expect the model to replicate is the age structure of the cattle population in Kerry. Notice that age structure was not used as an input to the model. Rather, we have derived the “field-based” version of this pattern from the animal data listed in Table 1. The age distribution for each herd type in Kerry was recorded from the data based on 1st September in 2017 (Table 1) as follows: based on the date of birth of each tested animal, we calculated the age in days at the time of sampling. Animals were then grouped into age cohorts by year from 0 to 9. Animals older than 9 years were assigned to cohort >9. Animals were then aggregated according to the age cohort and herd type.

The second pattern the model is expected to replicate relates to the animal transport behaviour in Kerry. Again, trading volumes and relationships were not inputs to the model algorithm, rather herd-type specific management rules created demand and supply at the level of the individual herd. For the field-based pattern, we extracted the total annual transport volume between the five main herd types from the daily resolved animal transport data (dairy, beef, mixed, storage and fattening) for the year 2017.

After running the model for validation purposes, we analysed the model output in the same way as the herd register and movement data. At simulation week 34 (equivalent to September 1st) of year 30, we read the number of animals per herd type and age cohort grouped by years from 0 to >9. To achieve comparison between field and model regarding transport volume and network connectedness between herd types, we have read the total number of animals transported between the five main herd types.

As there was no data available for the calibration of the BoHV-1 infection model, we performed a systematic sensitivity analysis on selected model parameters of the BoHV-1 infection model (beta, reactivation rate). This was done to check the robustness of the model when modelling BoHV-1 intervention strategies under practical/real-world conditions (described in the following chapter). The original beta values (betaPrimaryInfectedWithinPool $\beta_{Pi}^{WP} = 1.1$ and betaSecondaryInfectedWithinPool $\beta_{Si}^{WP} = 0.55$), as well as the annual virus reactivation rate ($r^{\text{reactivation}} = 3\%$), identified as the main drivers of the infection model were systematically changed by +/-50% to check if the general dynamics (shape of the virus extinction curves & ranking of extinction time points) of the simulated BoHV-1 intervention strategies were maintained throughout the parameter combinations.

2.6. Modelling BoHV-1 intervention

Finally, the validated FarmECS-IBR model was applied to support the current discussions regarding the structure and implementation of a potential national BoHV-1 eradication programme in Ireland. Simulation experiments were conducted to compare alternative intervention strategies by their impact on herd-level prevalence. Each model run was started with a 30-year burn-in period following BoHV-1 introduction, to result in an endemic situation as described by Barrett et al. (2018); Cowley et al. (2011); O'Grady et al. (2011) and Sayers et al. (2015). From the 31st year onwards, seven different disease management scenarios were applied (Table 4).

TABLE 4

The scenarios modelled are either single interventions or a combination of up to three different intervention measures.

When the transport restriction intervention is applied, only seronegative animals are traded, excluding moves to slaughter. Each animal in the model intended for trade is serologically tested for BoHV-1 and moved only if the test result is negative (dependent on diagnostic specifications of the test, here assumed as perfect).

The culling intervention aims to eradicate BoHV-1 from low prevalence herds. Therefore, each herd gets fully tested once a year at a random date (census test) and when the within-herd prevalence is less than 15%, all sero-positive animals in the herd are culled.

The vaccination strategy aims to reduce prevalence within the herd by reducing active virus circulation. If used in combination with other intervention measures, vaccination is carried out in all herds with a within-herd prevalence above 15%, as determined by a full herd test carried out on a yearly basis and continues to the end of the program. If applied as a single intervention, vaccination is applied to all herds, irrespective of within-herd prevalence and throughout the entire simulation. At the animal level, the vaccine as simulated in the model is 90% effective, meaning that on average only 9 out of 10 vaccinated animals will have a certain level of protection after vaccination. The modelled vaccine suppresses virus activation and excretion from any infected animal, but does not protect against seroconversion if a vaccinated animal is in contact with an infectious animal.

It is important to note that these simulations are preliminary in terms of the scenarios modelled. The intervention measures described in Table 4 are idealised, assuming, for example, a full annual herd test per herd, or consistent annual vaccination regardless of the epidemiological status of the herds. We want to make clear that this does not fully replicate the requirements of the AHL in relation to establishing a herd as free from infection, but can help to gain a theoretical understanding of how specific intervention strategies can be used to reduce the overall prevalence

of BoHV-1 under Irish cattle management conditions. The scenarios show the utility of the model to explore this further, with the potential to refine the scenarios further to reduce potential program costs.

We were specifically interested in how the three best performing strategies would work under more practical/real-world conditions (e.g. in the absence of continuous vaccination or full-herd screenings). Therefore, we simulated the three best performing strategies again, but on this occasion assigning one of two BoHV-1 herd statuses to each herd in the model at the beginning of the programme. For this purpose, at the beginning of the programme, each herd was subjected to a BoHV-1 spot test (randomly testing 30 animals >9 months of age; as laid down in current discussions regarding Irish BoHV-1 control). Herds with a positive test result (at least one positive animal) were assigned to the first class and subjected to the intervention measures applied in the scenario. Herds with a negative spot test were classified as BoHV-1-free and all intervention measures were ceased. In the model, BoHV-1 free herds were subjected to annual BoHV-1 surveillance by performing an annual spot test. This approach allows for realistic estimates of the time to eradication, since the risk of non-detection of a new BoHV-1 introduction into a BoHV-1-free herd, for example, is included.

For each scenario, 20 iterations were performed to account for variability brought about by the stochastic processes in the model. For each scenario the proportion of sero-positive herds (containing one or more sero-positive animals) in the model were recorded on a weekly basis. Model outputs are compared between the scenarios.

3. Results

3.1. Model validation

3.1.1. Herd demography

Figure 5 shows the comparison between observed age structure data of the cattle population in Kerry (bold coloured lines) and our output data extracted from model population (faded coloured

lines). For each herd management type, the observed and simulated age structure is presented by sex, i.e. once for male (blue) and once for female (red) animals. We explicitly mention that the age-structure data from the Irish cattle register was not used as input data for the model. Rather, the age structure of each herd in the model emerges from the herd type specific management characteristics we implemented (Table 2).

In these age/sex distributions there is a high degree of similarity between observed and model data for those herd types that comprise the largest proportions of the total population (e.g. BSW and D). In all breeding herds, a right-skewed age profile can be seen. The high number of very young animals between 0-1 years of age is due to the number of calves retained in the herds. Logically, non-calving herds such as Fattener or Store herds have almost no animals in this age cohort because they only buy older animals. It is important to realise that age distributions differ substantially between the herd types, and these differences are reproduced by the herd-type specific rules used to manage the individual bovines of the herds listed in Table 2.

FIGURE 5

3.1.2. Transport patterns

We have created centred alluvial plots to show the transport flows between herd types, using different colours to represent the transport network (Figure 6). The thickness of the arrows is a measure of the transport volume. It can be seen that the ratio of the transport flows between observed data and our emergent simulation results is consistent. Major transport flows as observed in the data can be replicated by the simulation model. However, it can be seen that some transport streams in the simulation do not align as well with those in the data. For example, there are differences between the data and our simulation, especially in the transport behaviour of Stores herds.

When validating the model, we have paid attention to replicate further transport patterns which, according to our experts, have an influence on the epidemiological properties of the pathogen to be simulated. For example, we analysed the distribution of distances moved in trades between

herds as well as the number of trading partners a herd had per year. These additional comparisons are shown at <https://europei.eu/CattleDisMM/#IBR-svepm21>.

FIGURE 6

3.1.3. *BoHV-1 control strategies*

The herd-level seroprevalence of BoHV-1 for the simulated scenarios is shown in Figure 7. In the base-line scenario S1 (red line), no intervention strategies were applied and herd-level prevalence remained at a constant high level over the simulated years. This scenario indicates that without intervention there is no downward trend over the longer term in herd-level sero-prevalence, as predicted by the model. Hence, any difference between the graphs of S1 and the other modelled scenarios can be attributed to the intervention measures applied.

The transport restriction strategy (S2) alone (blue line) resulted in a decrease of herd-level prevalence (Figure 7a). If 100% of herds participated, a herd-level prevalence of 9% would be reached after 30 years. Based on this scenario, BoHV-1 will only be eradicated within the practical time horizon with additional interventions.

FIGURE 7

In contrast, as outlined in S4, annual and consequent BoHV-1 vaccination of all herds lead to the eradication of BoHV-1 from the cattle population in Kerry (green line). As a median value, continuous vaccination reduced herd-level prevalence from 80% to 0% within 25 years (after 28 years in 95% of the simulations).

All scenarios in which intervention measures were combined are more effective in reducing overall herd-level prevalence (Figure 7b). BoHV-1 eradication from the cattle population in Kerry was achieved most rapidly with the combination of transport restrictions and BoHV-1 vaccination and targeted culling in herds where prevalence is low ($< 15\%$) (S7 - cyan line). Leaving out the transport restrictions marginally increases the time to eradication by a median of two years (S6 - brown line). We would like to again emphasise that the results shown in Figure 7 are idealised

eradication measures, assuming, for example, a full annual herd test per herd, or consistent annual vaccination regardless of the epidemiological status of each herd.

In this study, the three best performing strategies (S4, S6 and S7) were simulated again, this time accounting for more practical/real-world conditions (e.g. absence of continuous vaccination or full-herd screenings). Figure 8 shows further comparison of the selected scenarios, indicating not only the course of BoHV-1 herd-level prevalence, but also the effort (number of vaccine doses used, number of culled animals, number of animals restricted from transport) that would have to be expended for each of the strategies.

Compared to the idealised representations, the time to achieve BoHV-1 freedom has increased in all strategies (Figure 8). Under more realistic conditions (vaccination of spot test positive herds only), a plain vaccination campaign (S4) would no longer lead to eradication. BoHV-1 eradication from the cattle population in Kerry was achieved after a median of 19 years when transport restrictions were combined with targeted BoHV-1 vaccination and culling in low prevalence herds (Figure 8c). Under non-idealised conditions, the omission of transport restrictions leads to a considerable extension of the eradication programme, by a median of ~5 years. The performed sensitivity analysis revealed that the ranking of the extinction times, as well as the shape of the extinction curves remain constant for the tested parameter combinations. Results of these systematic simulations can be found in the supplementary material.

FIGURE 8

4. Discussion

4.1. The FarmECS-IBR model in the context of other regional cattle disease models

Mechanistic simulation models are being increasingly used as tools to assist with animal health decision-making in the cattle sector. While the vast majority of models developed so far represent virus dynamics and intervention within single herds, only a few models have been developed to simulate the spread and control of diseases within entire regions (Brock et al., 2020b).

We propose a new and innovative spatially explicit, individual-based, regional cattle disease model. An innovative feature of our model is the inclusion of herd typing, thereby extending the basis of dairy, beef or mixed herds usually considered in other modelling studies (e.g. Beaunée et al., 2015; Qi et al., 2019; Thulke et al., 2018). We found that herd features relevant for epidemiological predictions may differ systematically between the herd types. In our model, sixteen different herd types were needed to represent existing management schemes of the cattle sector in Ireland. This detailed representation of herd type-specific management is an advantage to other approaches when it comes to the evaluation of detailed policies in the context of the AHL. With regard to BoHV-1, there are several possible pathways by which a herd or country may achieve the status of disease freedom. The explicit regulations and their implementation interact with specifics of the management regime in different herds. For example, bulk tank milk testing on its own can only be applied to dairy herds that have a minimum proportion of lactating cows. Contract rearing dairy herds (Rdf) would never fall into this category. However, bulk milk samples could be used in non-rearing dairy herds (DnR_C & DnR_nC). Such details become even more important when models are used to estimate program costs.

The herd specific management and animal transport rules alone generate animal numbers and age distributions in the individual herds that are consistent with the demography and transport data available from animal databases (Figure 5 & 6). Nevertheless, the model itself remains independent of direct data input. In this respect, it is possible to simulate trade structures that do not statically or randomly repeat observed data extracted from an animal movement tracing database (e.g. Beaunée et al., 2015; Thulke et al., 2018; Widgren et al., 2016). The generic management and transport scheduling facilitates active intervention within the modelled population, e.g. when specific animals must be removed according to a detailed treatment protocol. With our generic model implementation such off-management demands are easily satisfied without destroying the overall similarity of the model with real world data of a regional cattle population.

Flexible interventions on regional animal transports are required when it comes to evaluating the efficiency of restrictions of individual moves for virus eradication purposes (scenario S3). A different generic animal transport algorithm has been described with a model implantation by Gethmann et al., (2019). However, those authors had to balance demand and supply through randomly generated animal movements whereas we use rules based on herd and cohort type to do this. Trading partners are also grouped together on the basis of physical proximity and specific herd type when deriving trading batches. This reduced the number of trading partners leading to more realistic picture of pathogen spread within regional systems.

The limitations of our approach are mainly that it is challenging and time consuming to develop a management specific regional cattle disease model. An intensive participatory approach was followed during the conception and development of the simulation model. For this purpose, each model rule was discussed and agreed between the project partners from the start of the project. In addition, the developed model rules were verified with inventory and transportation data from only a single year (2017). This could lead to the model being overfitted to the current management situation and not reflecting changes to the overall Irish cattle system over time. Furthermore, the model is computationally intensive due to the detailed representation of the Irish cattle sector and the simulation of individual animals. That is why we constrained our model to County Kerry, representing ~5.000 cattle herds with approximately 360.000 animals. A single year of simulation, including all biological-, farming- and epidemiological processes took on average 45 seconds on a local machine (Processor: Intel Core i5-6200U CPU 2.4GHz, RAM: 16GB).

4.2. Model application in the context of BoHV-1 control

The development of herd-level prevalence under the transport restriction scenario (S2) shows the importance of having a more closed farming system or implementing quarantine measures for purchased animals. Without further measures, the prevalence at herd level decreased by about 90% (overall prevalence of 80% to 9% after 30 years of intervention; Figure 7a). Farmers therefore become aware of the risks associated with the introduction of BoHV-1 through the introduction of animals. In support of this, epidemiological studies report frequent animal purchases as a major

risk factor for a herd testing positive for BoHV-1 antibodies (Boelaert et al., 2005; van Schaik et al., 1998; Woodbine et al., 2009). Measures at a national level may include compulsory testing of purchased animals for BoHV-1, or more frequent surveillance of certified herds, to reduce the risk of moving the virus from herd to herd.

However, the model has shown that BoHV-1 eradication will not succeed if transport restrictions or targeted culling in low prevalence herds are when applied as single measures, rather than in combination.

The model output has shown that BoHV-1 eradication can be reached within the practical time horizon required of a national eradication programme if rigorous vaccination is included. Many studies have shown that vaccination can effectively reduce virus circulation and thereby decrease seroprevalence in a herd or population (Bosch et al., 1998; Mars et al., 2001). Hence, our scenario S4 (under idealised conditions) does effectively reduce both herd and animal-level prevalence through vaccination. The associated prevalence line shows the progressive fading out of seropositive animals over time in the absence of active virus circulation (Figure 7a). After a median of ~25 years, the virus is eradicated, without the requirement for other intervention strategies.

However, consistent vaccination of all herds on an annual basis is a costly and unrealistic scenario that is unlikely to be implemented in the real world. Consequently, we were interested to identify vaccination-only strategy that could feasibly work under field conditions (e.g. in the absence of continuous vaccination of all simulated herds). Simulations have shown that a vaccination strategy applied only to snap-shot test positive herds does not lead to eradication (Figure 8a). The simulation results of scenario S4 make clear that serological monitoring of animals intended for transport should be an important part of an eradication programme, especially towards the end of the programme, because large parts of the population are no longer immunised by either the field virus or the vaccine, which can lead to major disease outbreaks if seropositive animals are introduced.

Extending the vaccination strategy by, for example, targeted culling of seropositive animals in low prevalence herds (S6), or by also accounting for transport restrictions (S7), considerably shortens the time to eradication when assuming idealised and more realistic intervention strategies (Figure 7b and 8).

Under more realistic programme conditions, the time to eradication is substantially reduced if transport restrictions are also taken into account (a median of ~5 years). If transport restrictions are omitted, there is a slight increase in herd prevalence during the course of the eradication programme (S6), as field virus-infected animals can still be transported into herds where virus had previously been cleared. After the start of a program, when many herds have started vaccination it can be assumed that a vast majority of purchased field virus infected animals will have a certain level of protection (e.g. protection from disease and reduced likelihood of reactivation). Therefore, purchased animals will pose an increased outbreak risk to herds once vaccination protection in the overall population declines, i.e. towards the end (as compared to the beginning) of the programme. For this reason, the introduction of transport restrictions towards the end of an eradication programme appears to be an ideal supplement to counteract virus outbreaks in herds that are already free from BoHV-1.

Understanding the temporal dynamics of herd-level prevalence during an eradication program is an important component in our evaluation of the usefulness of individual interventions and their combinations. Our study, which accurately applies these intervention protocols to detailed herd management structures and trading behaviour in a cattle population, will contribute to effective planning for BoHV-1 eradication in cattle and continued disease-free status.

5. Conclusion

We present the first regional epidemiological model representing an Irish cattle population along with its specific herd type categories. The herd type specific management parameters (Table 2) allow a generic simulation of realistic age and sex distributions across all production types. In

contrast to existing cattle disease models, our tool facilitates comparative assessment of BoHV-1 eradication strategies targeting different production types with individual strategy protocols.

Our model allows a realistic simulation both of infection transmission and control/surveillance in the overall population. Hence, the BoHV-1 related simulation output provides scientific arguments, contributing to an informed debate of the structure and design of a BoHV-1 eradication strategy in Ireland. We have shown that the time to eradication can be substantially reduced if transport restrictions are taken into account in the planning of a BoHV-1 eradication programme.

Abbreviations

Herd types

D	Dairy
DnR_C	Dairy no rearing (contract)
DnR_nC	Dairy no rearing (no contract)
DRm	Dairy rearing males
M	Mixed
BP	Beef pedigree
BSY	Beef suckling to youngstock
BSY_nR	Beef suckling to youngstock no rearing
BSW	Beef suckling to weanling
BSB	Beef suckling to beef
Sdm	Store dairy males
Rdf	Rearing dairy females
Sbf	Store beef females
Sbm	Store beef males
Sbmx	Store beef mixed

F Fattening

Trading cohorts

CDM	Calf dairy males
CDF	Calf dairy females
PHD	Pregnant heifer dairy
PHB	Pregnant heifer beef
YFF	Youngstock for fattening
CBF	Calf beef female
CBM	Calf beef male

Conflict of interest

All authors declare that they have no conflict of interest

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Competing interest

The authors declare that they have no competing interests.

Data availability

Data for this study was obtained from the Animal Identification and Movement (AIM) database maintained by the Department of Agriculture, Food and the Marine (DAFM) in Ireland. The data was made available for research purposes and cannot be made publicly available.

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Tables & figures

Table 1 Data used to describe the Irish cattle system

Dataset	Description	Source
Herd population in 2017	List of all cattle registered in Ireland on three different dates (1 st Jan, 1 st May and 1 st Sep)	AIM database
All births from 2016 to 2018	List of all births during 2016 to 2018	AIM database
All animal transports in 2017	List of all animal movement in 2017	AIM database

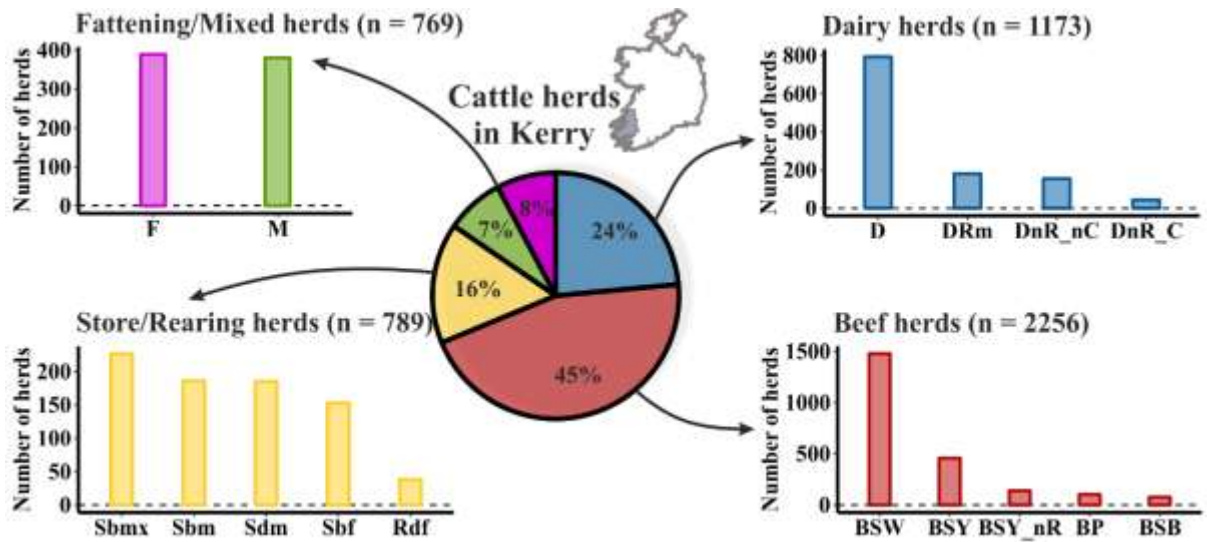


Figure 1 Herd types and their distribution in Kerry. The abbreviations of the herd types and their meanings are listed at the end of the paper.

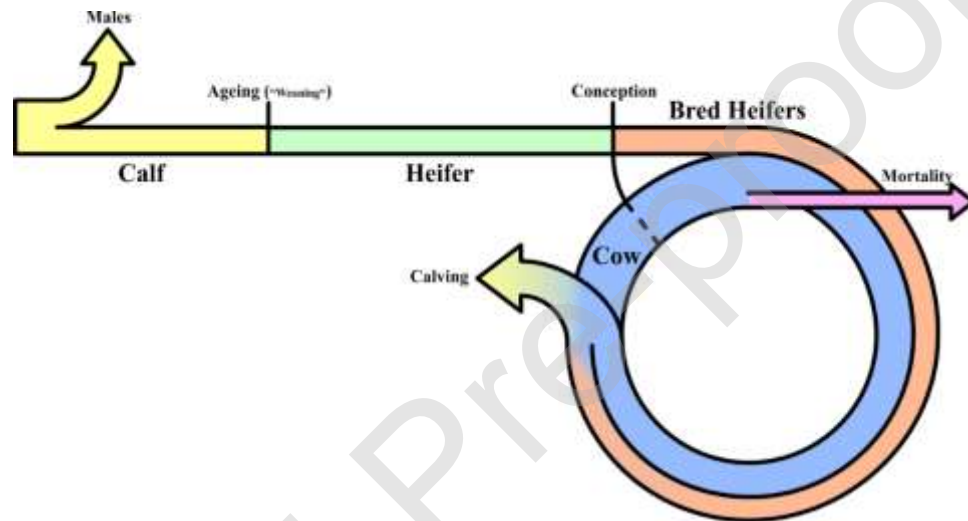


Figure 2 The typical life history of an individual female animal in a self-breeding cattle herd. A female calf becomes a heifer at the age of six months and remains in this cohort until conception. At 57 weeks of age heifers are started to be bred and after conception they enter the Bred Heifer cohort where they remain until calving.

Table 2 Management rules characterizing differences in herd management among the 16 herd types in Kerry. U(x,y) stands for a uniform distribution between the specified x and y values. Abbreviations for herd type and trade cohort (supply/demand for) as in Figure 3.

Herd type	Breeding/ calving	Prop. of female calves sold	Age to sell female calves (weeks)	Age to sell male calves (weeks)	Age to sell from store	Supply for	Demand for
Dairy	D	Yes/Yes	5%	U(4,8)	U(2,13)	-	CDM, CDF
	DRm	Yes/Yes	15%	U(4,8)	U(13,104)	-	YFF, CDF

Beef	DnR_C	No/Yes	85%	U(4,8)	U(2,6)	-	CDM, CDF	PHD
	DnR_nC	No/Yes	85%	U(4,8)	U(2,6)	-	CDM, CDF	PHD
	BSW	Yes/Yes	60%	U(26,39)	U(26,39)	-	CBM, CBF, YFF	-
	BSY	Yes/Yes	60%	U(60,104)	U(60,104)	-	CBF, YFF	-
	BSY_nC	No/Yes	90%	U(52,78)	U(52,78)	-	CBF, YFF	PHB
	BSB	Yes/Yes	-	-	-	-	-	-
Store/Rearing	BP	Yes/Yes	50%	U(78,104)	U(78,104)	-	CBF, PHB	-
	Sbm	No/No	-	-	-	U(78,104)	YFF	CBM
	Sbf	No/No	-	-	-	U(78,104)	YFF	CBF
	Sbmx	No/No	-	-	-	U(78,104)	YFF	CBM, CBF
	Sdm	No/No	-	-	-	U(78,104)	YFF	CDM
	Rdf	Yes/No	-	-	-	-	PHD	CDF
Other	M	Yes/Yes	-	-	-	-	YFF, PHD	-
	F	No/No	-	-	-	-	-	YFF

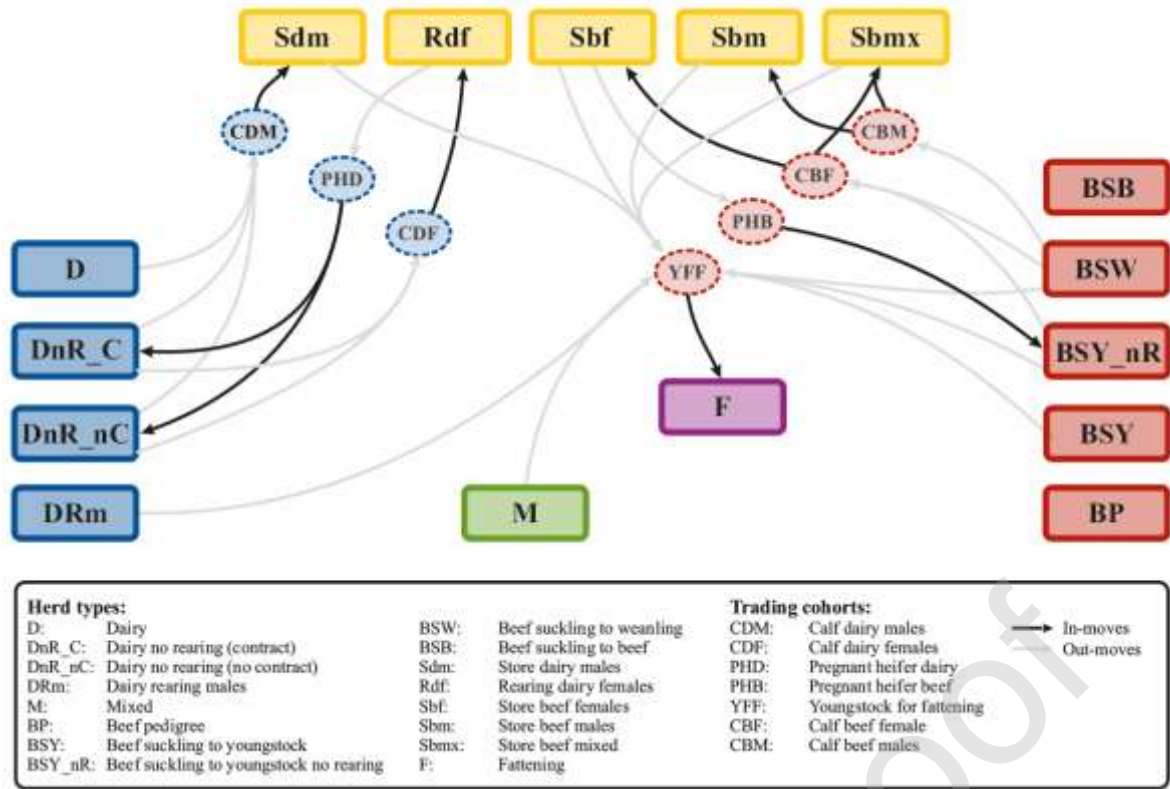


Figure 3 Typical animal transports under the cattle management system in Kerry. To assist with clarity in presentation, only primary movement cohorts are shown. Out-moves (supply) from herd types are indicated by grey lines while in-moves (demand) are indicated

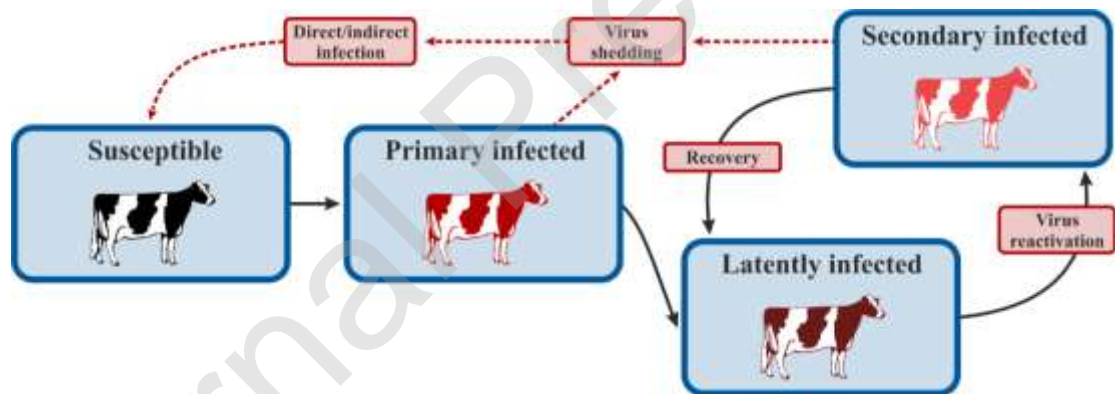


Figure 4 BoHV-1 infection states in the model.

Table 3 Overview BoHV-1 related model paramters

Paramter	Description	Value	Source/details
β_{Pi}^{wP}	Trans. rate primary infected animals within pools	1.1	Simulation experiments & expert input
β_{Pi}^{bP}	Trans. rate primary infected animals between pools	1.1*0.6	Simulation experiments & expert input
β_{Pi}^{bH}	Trans. rate primary infected animals between herds	0.02	Adapted from Thulke et al. (2018)
β_{Si}^{wP}	Trans. rate secondary infected animals within pools	0.55	Simulation experiments & expert input
β_{Si}^{bP}	Trans. rate secondary infected animals between pools	0.55*0.6	Simulation experiments & expert input
$\gamma^{reactivation}$	Yearly virus reactivation probability per latently infected animal	3%	Noordegraaf et al. (2002, 1998)
$\gamma^{reactivation}_{transport}$	Virus reactivation probability after transport	25%	Thiry et al. (1987) & expert input
t^{Pi}	Duration primary infection (weeks)	2	Bosch et al. (1997); Kaashoek et al. (1996); Kaashoek and Van Oirschot (1996)
t^{Si}	Duration secondary infection (weeks)	1	Bosch et al. (1997)

Table 4 Overview of simulated BoHV-1 control strategy scenarios (+; strategy applied)

Scenarios		Intervention measures		
		<i>Transport restrictions:</i>	<i>Culling strategy:</i>	<i>Vaccination strategy:</i>
		Only sero-negative animals are allowed to be traded	Sero-positive animals get culled in herds where prevalence is <15%	Animals get vaccinated in herds where prevalence is >15%
Single	<i>S1 – base</i>	-	-	-
	<i>S2 – transport</i>	+	-	-
	<i>S3 – culling</i>	-	+	-
	<i>S4 – vaccination</i>	-	-	+
Combined	<i>S5 – transport + culling</i>	+	+	-
	<i>S6 – culling +vaccination</i>	-	+	+
	<i>S7 – transport + culling + vaccination</i>	+	+	+

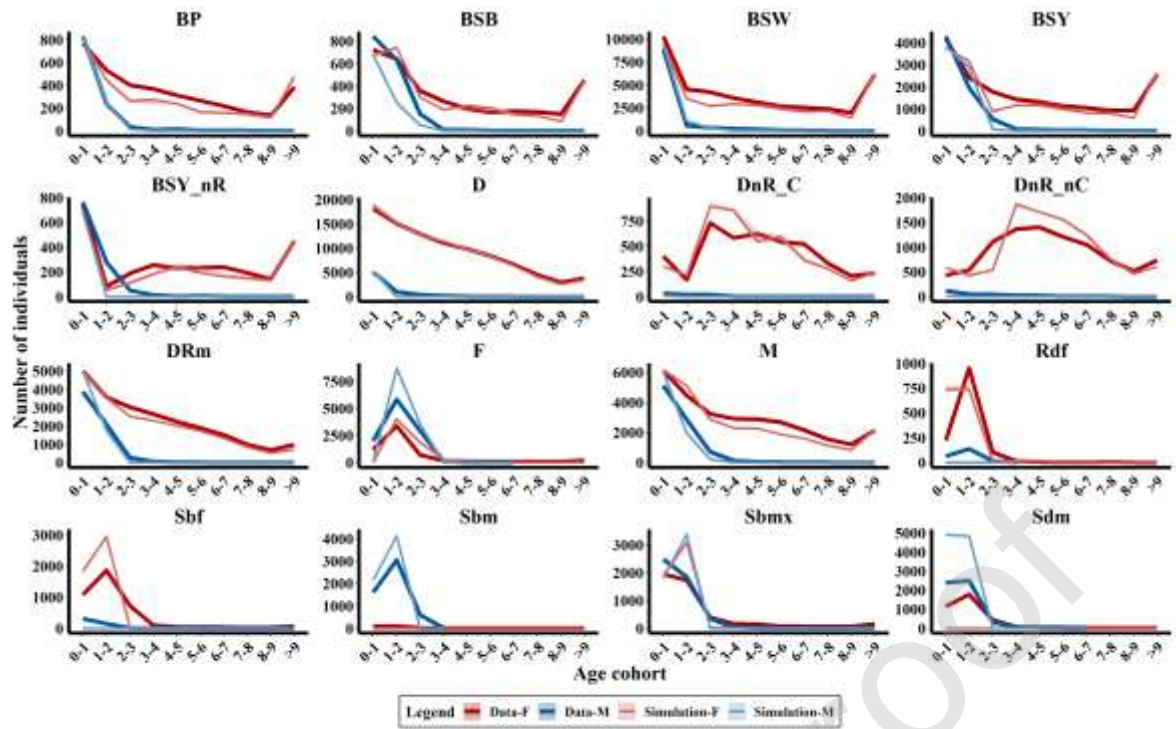


Figure 5 Comparison of observed (bold coloured lines) and simulated (faded coloured lines) age structure per herd type and sex. For the simulation, the median number of animals per age cohort is shown, calculated from a total of 10 model runs with identical parameter settings. An uncertainty band is also illustrated for the simulation runs (0.95 and 0.05 percentile), but this only becomes visible in herd types where the total number of animals is small, e.g. DnR_C or BP herds. The abbreviations of the herd types and their meanings are listed at the end of the paper.

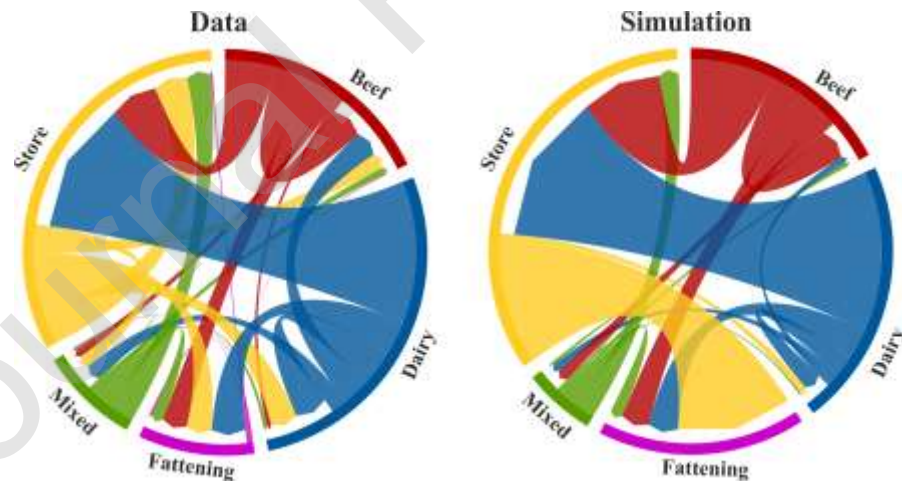


Figure 6 Comparison of observed (left) and simulated (right) transport flows per herd type. The thickness of the flows indicates the transport volume.

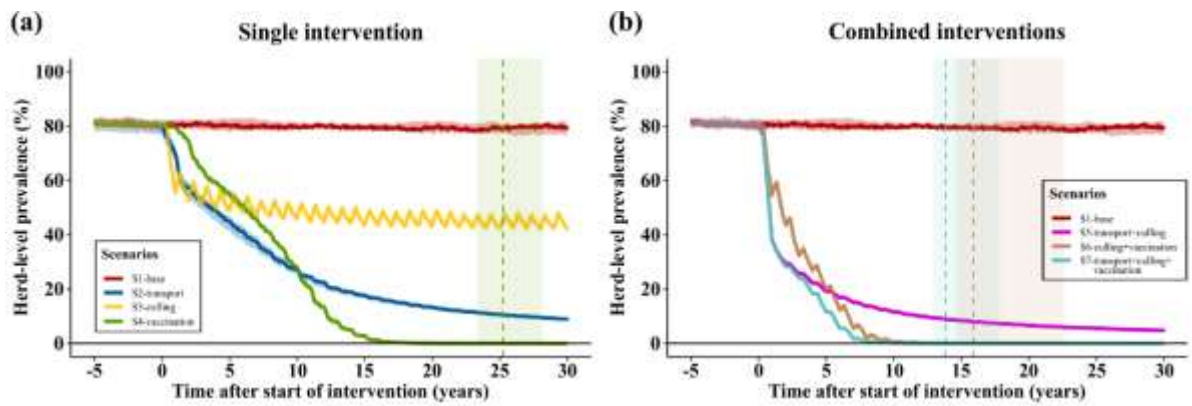


Figure 7 Comparison of the simulated idealised strategies to reduce herd-level prevalence in Kerry (all herds in Kerry). Each scenario was simulated for 30 years (subsequent to a 30-year burn-in). For each scenario, the solid coloured lines indicate the median herd-level prevalence in Kerry calculated for each model step over 20 iterations. In addition, the 95th and the 5th percentile for each scenario is plotted. The coloured vertical dashed lines indicate the time of virus eradication (median) along with the 95th and 5th percentile.

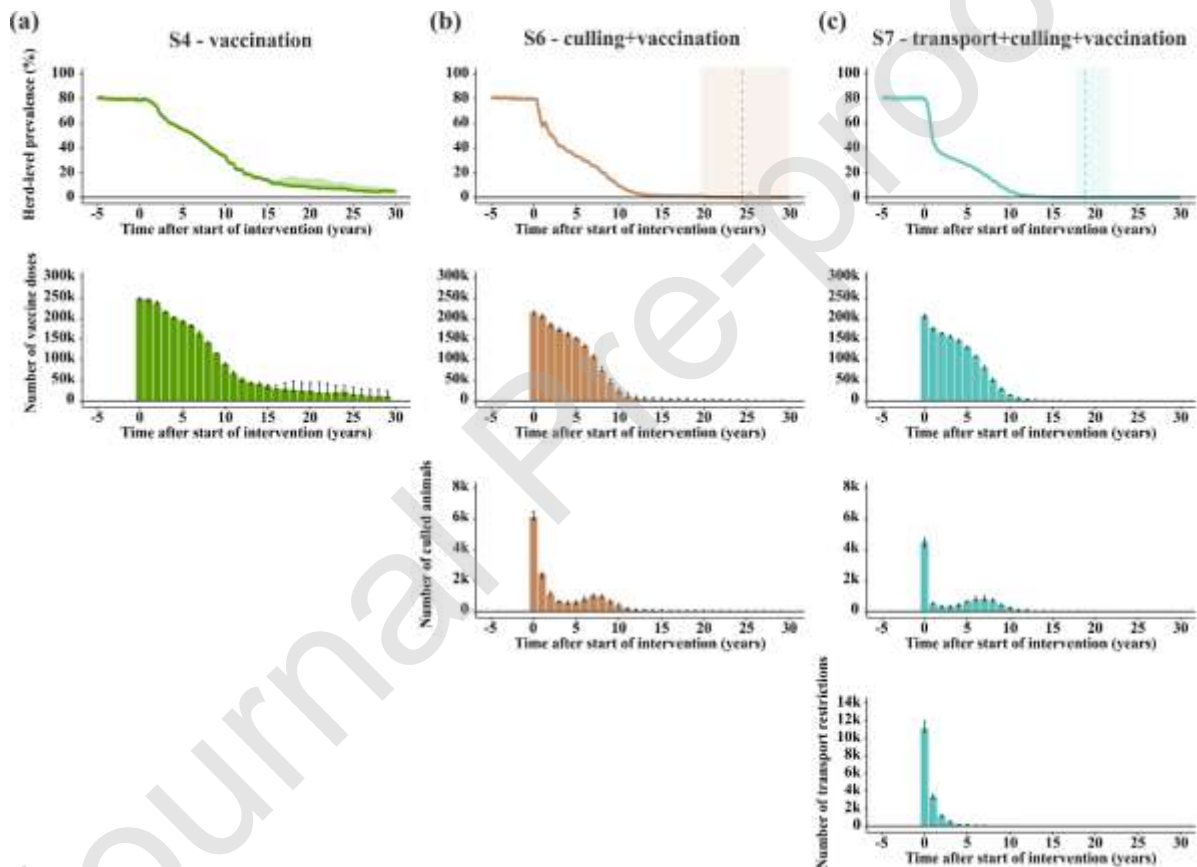


Figure 8 Comparison of the three best performing control strategies under practical/real-world conditions. For each scenario, the solid coloured lines indicate the median herd-level prevalence in Kerry calculated for each model step over 20 iterations (top row). In addition, for each scenario the 95th and the 5th percentile is plotted. The coloured vertical dashed lines indicate the time of virus eradication (median) along with the 95th and 5th percentile. In addition, the effort (number of vaccine doses used [second row], number of culled animals [third row], number of animals restricted from transport [fourth row]) that would have to be expended for each of the strategies is plotted, again showing the 95th and 5th percentile.