



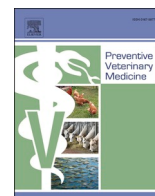
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The effect of risk-based trading and within-herd measures on *Mycobacterium avium* subspecies *paratuberculosis* spread within and between Irish dairy herds

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ABSTRACT

Johne's disease (bovine paratuberculosis) is an endemic disease caused by *Mycobacterium avium* subspecies *paratuberculosis* (*Map*). *Map* is transmitted between herds primarily through movement of infected but undetected animals. Within infected herds, possible control strategies include improving herd hygiene by reducing calf exposure to faeces from cows, reducing stress in cows resulting in a longer latently infected period where shedding is minimal, or culling highly test-positive cows soon after detection. Risk-based trading can be a strategy to reduce the risk that *Map* spreads between herds. Our objective was to assess whether within-herd measures combined with risk-based trading could effectively control *Map* spread within and between dairy cattle herds in Ireland. We used a stochastic individual-based and between-herd mechanistic epidemiological model to simulate *Map* transmission. Movement and herd demographic data were available from 1st January 2009–31st December 2018. In total, 13,353 herds, with 4,494,768 dairy female animals, and 72,991 bulls were included in our dataset. The movement dataset consisted of 2,304,149 animal movements. For each herd, a weekly indicator was calculated that reflected the probability that the herd was free from infection. The indicator value increased when a herd tested negative, decreased when animals were introduced into a herd, and became 0 when a herd tested positive. Based on this indicator value, four Johne's assurance statuses were distinguished: A) $\geq 0.7 - 1.0$, B) $\geq 0.3 - < 0.7$, C) $> 0.0 - < 0.3$, and D) 0.0. A is the highest and D the lowest Johne's assurance status. With risk-based trading some of the observed movements between herds were redirected based on Johne's assurance status with the aim of reducing the risk that a non-infected herd acquired an infected animal. Risk-based trading effectively reduced the increase in herd prevalence over a 10-year-period in Ireland: from 50% without risk-based trading to 42% with risk-based trading in the metapopulation only, and 26% when external purchases were risk-based as well. However, for risk-based trading to be effective, a high percentage of dairy herds had to participate. The most important within-herd measures were improved herd hygiene and early culling of highly infectious cows. These measures reduced both herd and within-herd prevalence compared to the reference scenario. Combining risk-based trading with within-herd measures reduced within-herd prevalence even more effectively.

Abbreviations: c, Rapid culling of test-positive cows of the highly infectious state; D, Typical dairy herds; DnR-C, Non-rearing dairy herds with contract rearing; DnR-nC, Non-rearing dairy herds without contract rearing; DRm, Dairy herds that also rear male calves; e30, Improved herd hygiene with calf exposure to general farm environment reduced to 30%; e70, Improved herd hygiene with calf exposure to general farm environment reduced to 70%; h, 50% of herds with the highest out-strength; I_H, Highly infectious state; I_L, Latently infected state; I_M, Moderately infectious state; I_T, Transiently infectious state; l, 50% of herds with the lowest out-strength; M, Mixed herds; *Map*, *Mycobacterium avium* subspecies *paratuberculosis*; p25, 25% of the herds have a herd indicator; p50, 50% of the herds have a herd indicator; p75, 75% of the herds have a herd indicator; R, Resistant; rI, No risk-based trading; rII, Risk-based trading within the metapopulation only; rIII, Risk-based trading within the metapopulation and of external purchases; S, Susceptible state; s, Slower progression from the latently infected to the moderately infectious state; SdR, (Store) herds that rear dairy females/contract rearing herds; t, Test herds twice a year.

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1. Introduction

Johne's disease (bovine paratuberculosis) is an endemic disease caused by *Mycobacterium avium* subspecies *paratuberculosis* (*Map*). This disease has a large economic impact on the dairy sector worldwide due to milk losses, early culling and increased mortality (Garcia and Shalloo, 2015). Heavy shedding and clinical signs, e.g., weight loss, decreased milk production, and diarrhoea, can be triggered by a stressful event such as first calving, but are sometimes never observed (Whitlock and Buergelt, 1996).

Diagnosing infected animals is difficult because the sensitivity of available tests is low. Depending on the stage of infection, it ranges from 15% to 71% (More et al., 2015a; Barkema et al., 2018). Infectious animals can therefore remain undetected in a herd. *Map* is transmitted between herds primarily through movement of these infected but undetected animals (Rangel et al., 2015; Marquetoux et al., 2016). Once an infected animal is introduced into a herd, the herd can remain infected for a long time (Marcé et al., 2011a). There is an estimated probability of persistence of 42.7% 15 years after the introduction of a single infected animal into a typical spring calving Irish dairy herd (Biemans et al., 2021).

Within infected herds, possible control strategies (bio-containment) include improving herd hygiene by reducing calf exposure to faeces from cows (Sweeney, 1995; Donat et al., 2016), reducing stress in cows resulting in a longer latently infected period where shedding is minimal (Kurade et al., 2004; Crossley et al., 2005), or culling highly test-positive cows as soon as possible after detection (Lu et al., 2010; Konboon et al., 2018; Jordan et al., 2020).

With respect to spread between herds, risk-based trading can be a strategy to reduce the risk that carriers enter a *Map* free herd (bio-exclusion) (Gates and Woolhouse, 2015; Ezanno et al., 2022). With such a strategy, each herd is assigned a 'Johne's assurance status' based on the probability that it is free from infection. With risk-based trading in place, destination herds with a high Johne's assurance status (that is, herds with a high probability of being free from infection) should avoid acquiring animals from a source herd with a lower Johne's assurance status (Jordan et al., 2020; Ezanno et al., 2022).

Epidemiological modelling can be used to investigate these strategies, as it enables us to better understand *Map* spread both within a herd (Marcé et al., 2011a, 2011b; Biemans et al., 2021) and between herds (Beaunée et al., 2015; Ezanno et al., 2020; Biemans et al., 2022), and to assess a range of different control strategies (Beaunée et al., 2017; Ezanno et al., 2022). The use of an epidemiological model is a conceptual approach that allows us to investigate and combine control measures focusing on bio-containment and bio-exclusion. This would never be possible in a field study where, for example, the level of participation among farmers, the low sensitivity of diagnostic tests, and the long period between infection and the onset of clinical symptoms can be limiting factors.

Here, we used a stochastic individual-based and between-herd mechanistic epidemiological model developed for western France (Camanes et al., 2018; Ezanno et al., 2022). In this model, within-herd management and infection dynamics for each herd are represented, and herds are linked through trade movements. Recently, a rewiring algorithm was added to this model, making it possible to change trade movements from those observed in the data through to movements based on the relative risk of source and destination herds to be *Map*-free (Ezanno et al., 2022). This model was adapted to represent the Irish dairy farming system (Biemans et al., 2022) which is predominantly highly seasonal (Tratalos et al., 2017). Furthermore, animals are traded much more frequently compared to France, i.e., > 2 million trade movements over ten years in Ireland (Biemans et al., 2022) compared to about 1 million trade movements over nine years in France (Ezanno et al., 2022) for a similar number of herds.

For France, based on an assumed starting herd prevalence of 90%, the herd prevalence was 82% after nine years when trade movements

were redirected between herds based on their within-herd prevalence status (Ezanno et al., 2022). For Ireland, herd prevalence is assumed to be lower with estimates ranging from 20.6% in 2005 (Good et al., 2009) to 28% in 2013–2014 (McAloon et al., 2016). Therefore, in this study, we focused on redirecting trade movements between herds based on the probability that many herds are free from infection.

Our objective was to assess whether the within-herd measures of improved herd hygiene, reduced stress, and faster culling of test-positive animals, and the between-herd measure of redirecting trade movements based on Johne's assurance status could effectively control *Map* spread between dairy cattle herds in Ireland.

2. Material and methods

2.1. Data

We extracted movement and herd demographic data from the Animal Identification and Movement database of the Irish Government's Department of Agriculture, Food and the Marine for the period 1st January 2009 – 31st December 2018 (the study period). These data were used to select the herds included in our dataset, which we subsequently refer to as 'the metapopulation'. Herd selection is described in detail in Biemans et al. (2022) and is summarised briefly here. We only selected herds in which more than half of all animals were of a dairy breed. Also, more than 30% of the animals in the herd had to be female, and movement data needed to be available for each year of the study period. Only female animals were modelled, with the exception of the introduction of some male animals for breeding. Herds that did not trade female animals with other herds were excluded. Finally, herds with fifteen animals or less, or five adults or less, were considered to be non-commercial dairy herds and were excluded. The inclusion of bulls was only considered for those herds that purchased bulls (83% of the herds). Bulls had to be purebred dairy or beef, they had to enter the herd via trade, and beef bulls had to come from a breeding herd. Bulls had to be at least one year of age upon entering a herd, and they had to remain in a herd for at least five months (one breeding season). Only bulls that stayed in a herd with a maximum length of four years for beef bulls and two years for dairy bulls were considered to be selected. It was assumed that about half of the cows would be serviced by a bull, with twenty cows per bull. In total, 13,353 herds, with 4,494,768 dairy female animals, and 72,991 bulls were included in the metapopulation. Herds were classified as one of six possible herd types (Table 1), as described in Brock et al. (2021).

The movement dataset consisted of 2,304,149 animal movements of which 17% were animals moved between herds in the metapopulation, 20% were animals moved from a herd outside of the metapopulation to a herd in the metapopulation, and 63% were animals moved from a herd in the metapopulation to a herd outside of the metapopulation.

For each herd in the metapopulation, herd parameters for size and exit rates were calculated from the data. Herd size was calculated on the 1st of January 2009. For each age group (see section "Within-herd model"), exit rates were calculated for each three-month period, in each year; January – March, April – June, July – September, October – December. Whenever a birth was registered in the data, a newborn calf (which could be susceptible or infected depending on the status of the dam) was added to the herd.

2.2. Within-herd model

The within-herd model is a stochastic individual-based model with a discrete time step of one week that is adapted from Camanes et al. (2018) and Biemans et al. (2021). The code is available under the Apache 2.0 license (Supplementary file 1). The within-herd model is fully described in Biemans et al. (2022). In brief, the model accounts for herd structure and infection dynamics. Animals belong to one of six age groups: newborn calves, unweaned calves, weaned calves, young

Table 1
List of herd types. For a full description of these herd types please refer to Brock et al. (2021).

Herd type	Abbreviation	Description
Typical dairy	D	Female dairy calves are reared to become replacement heifers and male calves are sold at an early age.
Dairy no rearing – contract	DnR-C	Sell most of their calves, with female dairy calves being moved to external rearing herds. Female calves return to their birth herd as pregnant heifers.
Dairy no rearing – no contract	DnR-nC	Cows are bred to beef bulls and most of their calves are sold. Replacement animals are bought from herds with a surplus of cows or pregnant heifers.
Dairy rearing males	DRm	Female dairy calves are reared to become replacement heifers. Male calves are not sold, however, they are assumed to be kept in a location different from the female animals and are therefore not included in the data.
Mixed	M	Both milk and beef production activities. Both pure-bred dairy females and cross-bred dairy and beef animals are present. We assumed that the milk and beef production activities were managed in separate locations and that contact between dairy and beef animals was negligible. Beef animals are therefore not included in the data.
Store dairy rearing	SdR	Female dairy calves are reared and inseminated before returning to their birth herd.

heifers, bred heifers, and cows. Animals progress to the next age group at a certain age or at a defined time in the year. Animals also belong to one of six health states: susceptible (S), resistant (R), transiently infectious (I_T), latently infected (I_L), moderately infectious (I_M), and highly infectious and possibly clinically affected (I_H). Susceptibility decreases exponentially with age (Windsor and Whittington, 2010) and animals are assumed to be resistant after reaching one year of age. Animals with health state I_T , I_M , and I_H are infectious and shed *Map* in their faeces and after calving in their colostrum/milk. The quantity of *Map* shed is heterogeneous between animals of the same state (Giese and Ahrens, 2000; Mitchell et al., 2015). *Map* can be transmitted *in utero*, via ingestion of contaminated colostrum or milk, and via contact with a faeces-contaminated environment. This is either the local environment or the general indoor farm environment. Transmission via the local environment is defined as the infection risk of the environment in which an animal resides contaminated by animals that are/were present in the same place but not necessarily at the same time. The local environment can either be indoor or on pasture. Transmission via the general indoor environment is defined as the infection risk of all indoor farm environments contaminated by animals that are/were not necessarily present at the same place or time. Details of all model parameters are in Supplementary file 2.

2.3. Between-herd model

The between-herd model is fully described in Biemans et al. (2022) and the code is available under the Apache 2.0 license (Supplementary file 1). In brief, movements of animals from and to a herd in the metapopulation were modelled as observed in the data. Thus, the data defines the date that a movement occurs, the age of the animal that is moved, and the source and destination herds. The animal to be moved is selected randomly from the relevant age group in the source herd, and thus can be of any health state. When there is, due to chance, no animal present in the correct age group, an animal of the closest age group is selected. If an animal is coming from a herd outside of the metapopulation, its health state is drawn from a distribution that corresponds to the proportion of animals in each health state in the same age group within the entire

metapopulation. It is therefore assumed that the average risk of introducing an infected animal is the same within and from outside of the metapopulation. When an animal was moved via a market, the movement is represented as if it occurs directly from the source herd to the destination herd.

2.4. Johne's assurance status based on the probability of freedom from infection

For each herd, a weekly indicator is calculated that reflects the probability that the herd is free from infection (P_{free}) (Martin, 2008; More et al., 2013). This indicator takes values between 0 and 1, where 0 indicates confirmed infection and 1 indicates assurance of freedom from infection within the constraints of test sensitivity. The indicator value increases when a herd tests negative, decreases when animals are introduced into a herd, and becomes 0 when a herd tests positive (Martin, 2008; More et al., 2013; Jordan et al., 2020). Based on the indicator value, four Johne's assurance statuses are distinguished:

- A: $\geq 0.7 - 1.0$.
- B: $\geq 0.3 - < 0.7$.
- C: $> 0.0 - < 0.3$.
- D: 0.0.

Where A is the highest and D the lowest Johne's assurance status.

At the start of the simulations, all herds have an indicator value of $1 - \text{herd prevalence} = 1 - 0.3$, with the herd prevalence value based on the estimated 28% in 2013–2014 (McAloon et al., 2016; Meyer et al., 2019; Sergeant et al., 2019):

$$P_{free}(t = 0) = 0.7$$

2.4. Yearly testing

Herds are tested once a year. All animals of 2 years of age and older that were present in the herd at the moment of testing are first subjected to a serum ELISA test with a sensitivity of 0.15 for I_T and I_L animals, 0.47 for I_M animals, and 0.71 for I_H animals, and a specificity of 0.985 for all animals (More et al., 2015b). In our simulations, health state specific sensitivities are used because we know the actual health state of the animal and we assume that animals in a more severe health state (i.e., animals that shed more) have a higher probability of testing positive. The number of animals in a herd with health state I_x (where $x = T, L, M$, or H) that are ELISA test positive is calculated using a binomial distribution with parameters $n = \text{number of animals in health state } I_x$ and $p = \text{ELISA test sensitivity for health state } I_x$. The number of animals that test faecal culture positive is then calculated using a binomial distribution with parameters $n = \text{number of animals in health state } I_x$ that tested ELISA positive and $p = \text{faecal culture test sensitivity for health state } I_x$. For faecal culture, we used a sensitivity of 0.23 for I_T and I_L animals, and 0.74 for I_M and I_H animals, and a specificity of 1.00 for all animals (More et al., 2015b).

If the number of faecal culture positive animals in the herd is > 0 (More et al., 2013),

$$P_{free}(t) = 0.0$$

If there is no ELISA positive animal in the herd, or if there are ELISA positive animals in the herd but there is no faecal culture positive animal (Martin, 2008; More et al., 2013),

$$P_{free}(t) = \frac{P_{free}(t-1)}{(1 - (1 - P_{free}(t-1)) \times SE_{herd}(t))}$$

where $P_{free}(t-1)$ is the indicator value of the previous week and SE_{herd} is the herd sensitivity. SE_{herd} is calculated as (More et al., 2013; Meyer et al., 2019; Sergeant et al., 2019):

$$SE_{herd}(t) = 1 - \left((1 - SE_{overall}) \times \frac{n(t)}{N(t)} \right)^d$$

where $SE_{overall}$ is the individual animal sensitivity, n is the number of animals of 2 years of age and older tested, N is the number of animals of 2 years of age and older present in the herd at the moment of testing, and d is the expected number of infected animals in an infected herd. In our model, d does not have to be an integer. $SE_{overall}$ and d are calculated as (More et al., 2013; Meyer et al., 2019; Sergeant et al., 2019):

$$SE_{overall} = SE_{ELISA} \times SE_{faecal\ culture} = 0.15 \times 0.65 \approx 0.1$$

Here we used an average value for the test sensitivities instead of specific test sensitivities per health state because we assume that in reality we do not know the actual health state of animals that tested negative.

$$d = N \times Prevalence_{design} = N \times 0.05$$

where $Prevalence_{design}$ is the design prevalence, i.e., the minimum prevalence in a population which could be detected with a certain probability (Martin, 2008; More et al., 2009; Cameron, 2012).

Herds that tested positive have an indicator value of $P_{free} = 0.0$. With these herds, only when all eligible animals test negative in the following three consecutive years is the value increased to $P_{free} = 0.1$, e.g., if a herd has faecal culture positive animals in year 1 $P_{free}(t = \text{year } 1) = 0.0$, if in the three years thereafter all animals in this herd test negative, the indicator values become $P_{free}(t = \text{year } 2) = 0.0$, $P_{free}(t = \text{year } 3) = 0.0$, and $P_{free}(t = \text{year } 4) = 0.1$.

2.4.1. Weekly animal introductions

In test positive herds, the introduction of animals does not affect the indicator value, i.e., in test positive herds, the P_{free} is always 0.0.

In test negative herds, the reduction of the indicator value with the number of animals introduced is calculated on a weekly basis. Two introduction types are distinguished: standard-risk introductions and low-risk introductions; $\#StandardRiskIntro$ is the number of animals introduced within the previous week in the destination herd coming from a source herd with a lower Johne's assurance status, and $\#LowRiskIntro$ is the number of animals introduced within the previous week in the destination herd coming from a source herd with an equal or higher Johne's assurance status. The risk of introducing an infected animal into the destination herd is calculated as (More et al., 2013; Meyer et al., 2019):

$$P_{intro}(\Delta t) = 1 - (discountStandardRisk(\Delta t) \times discountLowRisk(\Delta t))$$

with

$$discountStandardRisk(\Delta t) = (1 - Prevalence_{animal})^{StandardRiskIntro(\Delta t)}$$

$$discountLowRisk(\Delta t) = (1 - Prevalence_{animal} \times LowRiskMultiplier)^{LowRiskIntro(\Delta t)}$$

where $Prevalence_{animal}$ is the animal level prevalence of 0.032 (McAloon et al., 2016). The $LowRiskMultiplier$ of 0.5 reflects the assumed reduced risk of introducing an infected animal from a source herd with an equal or higher Johne's assurance status. The probability of freedom from infection is calculated weekly as (Martin, 2008; More et al., 2009, 2013; Meyer et al., 2019),

$$P_{free}(t) = 1 - \left((1 - P_{free}(t-1)) + P_{intro}(\Delta t) - (1 - P_{free}(t-1)) \times P_{intro}(\Delta t) \right)$$

If due to this calculation $P_{free}(t) < 0.1$, it is set to $P_{free}(t) = 0.1$. Thus, in a test negative herd the indicator value never falls below 0.1.

2.5. Risk-based trading

Risk-based trading means that some of the observed movements between herds were redirected based on Johne's assurance status with the aim of reducing the risk that a non-infected herd will acquire an infected animal (bio-exclusion). The trade movement redirection algorithm is fully described in Ezanno et al. (2022). The algorithm aims to change some of the animal movements as observed in the data so that a destination herd receives its animals from a source herd with a similar or better Johne's assurance status. To do so, every week, all animal movements per age group were summarized with regard to the Johne's assurance statuses of the source and destination herds. Next, animal movements from herds with a lower status to herds with a better status are identified and switched where possible with a relevant alternative so that the source herd has an equal or better status than the destination herd. For movements for which there was no alternative there were two possibilities: 1) the movement was kept as observed in the data, or 2) the source herd sent the animal to a herd outside of the metapopulation and the destination herd received an animal from a herd outside of the metapopulation (referred to as an external purchase) with an equal or better status. Therefore, the probability of receiving an infected animal from a herd outside of the metapopulation was equal to the average proportion of infected animals in the age group of the traded animal in herds within the metapopulation with an equal or higher status than the destination herd.

The fact that multiple animals could be moved between two herds at the same time was neglected because the majority of the herds in the metapopulation sold or bought only one or two animals at a time (Supplementary file 3).

Three trading options were considered (details in Supplementary file 4):

- No risk-based trading;
- Risk-based trading within the metapopulation only;
- Risk-based trading within the metapopulation and of external purchases.

In the no risk-based trading (rI) scenario, animals are moved between herds in the metapopulation as observed in the data. In the scenario with risk-based trading within the metapopulation only (rII), movements were changed where possible for the source herd to have an equal or better status than the destination herd. Movements for which there was no alternative were kept as observed in the data. rII represents a scenario where all herds in the metapopulation were provided with an indicator for the probability of freedom, but risk-based trading was optional. Under this scenario we assumed that a herd preferred to buy from a herd with an equal or higher Johne's assurance status, but that if this was not possible would buy from a herd with a lower Johne's assurance status. In the scenario with risk-based trading within the metapopulation and of external purchases (rIII), movements were changed where possible for the source herd to have an equal or better status than the destination herd. For movements without an alternative, the source herd sends the animal to a herd outside of the metapopulation and the destination herd receives an animal from a herd outside of the metapopulation with an equal or better status. Under this scenario we therefore assumed that external purchases could be controlled in the same way as purchases within the metapopulation. rIII represents a scenario where all herds in Ireland were provided with an indicator for the probability of freedom, meaning that herds outside of the metapopulation had a Johne's assurance status as well. Under this scenario we assumed that there were always enough options for a herd to buy from a low-risk herd.

2.6. Within-herd measures

We also investigated three on-farm control measures aimed at

controlling *Map* spread within herds. First, via improved herd hygiene through reduced (70% or 30%) calf exposure to the general farm environment. Second, by assuming improved on-farm conditions that reduce stress in cows resulting in a slower progression (104 weeks instead of 52 weeks) from the latently infected (I_L) stage to the moderately infectious (I_M) stage. Thus, a longer latently infected period where shedding is minimal. Third, by culling highly (I_H) infectious faecal culture test-positive cows within one month after detection.

2.7. Scenarios

First, we investigated the three risk-based trade options separately (reference scenarios):

- 1) No risk-based trading (rI).
- 2) Risk-based trading within the metapopulation only (rII).
- 3) Risk-based trading within the metapopulation and of external purchases (rIII).

Second, we combined the three risk-based trading options with the three within-herd measures applied to all herds:

- 1) Improved herd hygiene where calf exposure to the general farm environment was reduced to 70% (e70-I/e70-II/e70-III) or 30% (e30-I/e30-II/e30-III).
- 2) Slower progression from the I_L to the I_M stage (sI/sII/sIII).
- 3) Rapid culling of I_H test-positive cows (cI/cII/cIII).

Third, we investigated three different scenarios within risk-based trading option II:

- 1) Only a percentage of the herds have a herd indicator but all herds are subjected to risk-based trading. A percentage of herds, 75% (p75-II), 50% (p50-II), or 25% (p25-II), is chosen at random, and for these herds the indicator value and corresponding Johne's assurance status is calculated weekly and herds can trade according to the rules belonging to the status they have. The remaining herds that do not have an indicator all have Johne's assurance status D and can only trade according to the rules belonging to Johne's assurance status D.
- 2) Only a specific subset of herds is subjected to risk-based trading; the other herds can trade freely. The 50% of herds with either the highest (hII) or lowest (l-II) out-strength were subjected to risk-based trading. The out-strength measures the number of animals sold by a herd (outgoing movements). For each herd, the out-strength was calculated for every year and then averaged over the ten-year period. Herds that did not belong to the subset could trade freely, meaning that trade was simulated as observed in the data, even if they traded an animal with a herd in the subset. For herds outside of the subset no animal movements were redirected.
- 3) Test herds twice a year (tII) to have improved understanding of the actual Johne's assurance status. Herds were tested once in the first three months of the year and once in the three months following the month of June.

In total, 21 different scenarios were assessed (Table 2); an overview of all parameters relevant to these scenarios is given in Supplementary file 5.

2.8. Simulation settings and model outputs

Amongst 4006 candidate herds that were most likely to be infected (Biemans et al., 2022), 24% of the total number of herds were randomly chosen to be initially infected. An initial herd prevalence of 24% in 2009 was in agreement with field observations, with an estimated herd prevalence of 20.6% in 2005 (Good et al., 2009) and 28% in 2013–2014 (McAloon et al., 2016). The within-herd prevalence among those

Table 2
Overview of the 21 scenarios simulated.

	Risk-based trading option	Within-herd measure/ additional option	Symbol
1	No risk-based trading	–	rI
2	No risk-based trading	Exposure to environment reduced to 70%	e70-I
3	No risk-based trading	Exposure to environment reduced to 30%	e30-I
4	No risk-based trading	Slower progression from I_L to I_M	sI
5	No risk-based trading	Rapid culling of I_H test-positive cows	cI
6	Risk-based trading within metapop. only	–	rII
7	Risk-based trading within metapop. only	Exposure to environment reduced to 70%	e70-II
8	Risk-based trading within metapop. only	Exposure to environment reduced to 30%	e30-II
9	Risk-based trading within metapop. only	Slower progression from I_L to I_M	sII
10	Risk-based trading within metapop. only	Rapid culling of I_H test-positive cows	cII
11	Risk-based trading within metapop. only	75% of herds have a herd indicator	p75-II
12	Risk-based trading within metapop. only	50% of herds have a herd indicator	p50-II
13	Risk-based trading within metapop. only	25% of herds have a herd indicator	p25-II
14	Risk-based trading within metapop. only	RBT for 50% highest out-strength herds	hII
15	Risk-based trading within metapop. only	RBT for 50% lowest out-strength herds	l-II
16	Risk-based trading within metapop. only	Test herds twice a year	tII
17	Risk-based trading within metapop. + ext. purch.	–	rIII
18	Risk-based trading within metapop. + ext. purch.	Exposure to environment reduced to 70%	e70-III
19	Risk-based trading within metapop. + ext. purch.	Exposure to environment reduced to 30%	e30-III
20	Risk-based trading within metapop. + ext. purch.	Slower progression from I_L to I_M	sIII
21	Risk-based trading within metapop. + ext. purch.	Rapid culling of I_H test-positive cows	cIII

initially infected herds was drawn from a Gaussian distribution $N(-0.42, 0.12)$, keeping only values below 0.7. *Map* transmission within and between herds was simulated for ten years, matching the temporal extent of the movement data. For each scenario, we simulated 10 stochastic repetitions.

For the three reference scenarios we investigated the following: the distribution of herds over the Johne's assurance statuses over time, the evolution of the average indicator value per Johne's assurance status over time, the percentage of herds in which at least one infected animal is present (herd prevalence) and the percentage of herds with a > 5% within-herd prevalence among > 2 year-old animals over time, and the number of infectious trade movements between pairs of Johne's assurance statuses. The average in-degree (number of herds that the herd of interest receives animals from) and out-degree (number of herds that the herd of interest sends animals to) of the reference scenario with no risk-based trading were compared to the two reference scenarios with risk-based trading. For all scenarios we investigated the herd prevalence after 10 years and percentage of herds with a > 5% within-herd prevalence among > 2 year-old animals after 10 years versus the movements in the metapopulation that were redirected as percentage of the total number of movements. Herd prevalence and percentage of false negative herds over time was compared for testing once versus twice a year. Finally, we investigated the relation between herd type and the number of movements redirected.

The model was developed in C++ Standard 14 (Stroustrup, 2000). Model outputs were analysed and visualised in R version 4.1.2 (R Core

Team, 2021), using packages dplyr (Wickham et al., 2021) and viridis (Garnier, 2018).

3. Results

3.1. Johne's assurance status over time

After 10 years of simulations, the majority of herds had either status A (45–59%) or status D (24–41%), depending on the risk-based trading scenario (Fig. 1A). The percentage of herds with status B increased rapidly to 29% in the first year. From this point onwards, the percentage of herds with status B decreases steadily until it reaches to 8–12% after 10 years. Herds that introduce a lot of animals either test positive and are assigned status D, or keep testing negative and become status C.

For all three risk-based trading scenarios, the progression of the average indicator value per Johne's assurance status is very similar (Fig. 1B). The biggest change over time was observed for herds with status A, for which this value increased over time from 0.7 at the start of the simulations to 0.9 at the end.

3.2. Herd prevalence over time

With no risk-based trading, the herd prevalence was 49.9% on average after ten years of simulations (Fig. 2A). With risk-based trading in the metapopulation only, the herd prevalence was 41.7% on average. With risk-based trading of external purchases as well, the herd prevalence was stable at 26.3% on average, this value was reached within the first year of simulations. For the percentage of herds with > 5% prevalence among > 2 year-olds in the metapopulation, a decrease from 18.7% to 15.7% was observed for all three risk-based trading scenarios during the first three years of simulations (Fig. 2B). This initial decrease occurred because only few infected animals were present in newly-infected herds, also more than 50% of the infected animals traded were less than two years of age. Thereafter, this value increased to 24.4% for no risk-based trading (rI), 21.7% for risk-based trading in the metapopulation only (rII), and to 18.1% for risk-based trading of external purchases as well (rIII).

After 10 years, average within-herd prevalence among > 2-year-old animals within infected herds was 12.7% with no risk-based trading (rI), 14.1% with risk-based trading in the metapopulation only (rII), and 17.5% with risk-based trading in the metapopulation and of external

purchases (rIII) (Fig. 3).

For all reference risk-based trading scenario (rI/rII/rIII) and combinations of these scenarios with within-herd measures (e70-I/e70-II/e70-III/e30-I/e30-II/e30-III/sI/sII/sIII/cI/cII/cIII), average herd prevalence decreased and average within-herd prevalence increased with more intense risk-based trading. Within-herd prevalence was lowest (6–7%) for the scenarios where calf exposure to the general farm environment was reduced to 30% (e30-I/e30-II/e30-III). The herd prevalence and within-herd prevalence for the scenarios where only part of the herds had a herd indicator (p75-II/p50-II/p25-II) or where only a specific subset of herds was subjected to risk-based trading (hII/l-II) were very similar to the reference scenario without risk-based trading (rI), with herd prevalence of 45–50% and within-herd prevalence of 12.6–13.6%.

3.3. Movements redirected

The percentage of movements where an infected animal was moved between herds was 7.3% without risk-based trading (rI), 7.1% with risk-based trading in the metapopulation only (rII), and 6.6% with risk-based trading in the metapopulation and of external purchases (rIII). For all three scenarios, source herds with status D were responsible for the vast majority of infectious trade movements (Table 3). However, the majority of these animals were sold to a herd outside of the metapopulation. Except for destination herds with status D and herds outside of the metapopulation, the number of infectious animals received decreased with a more stringent risk-based trading scenario. Compared to source herds with status A or B, herds with status C traded twice as many (Table 3A and B) or a similar number (Table 3C) of infectious animals, even though the percentage of herds with this status was relatively low (Fig. 1A). For rI, the percentage of infectious trade movements from a source herd was 0.5% for status A, 2.1% for status B, 6.1% for status C and 21.8% for status D. Similarly for rII, the percentage of infectious trade movements from a source herd was 0.4% for status A, 2.4% for status B, 6.0% for status C and 22.1% for status D. For rIII, the percentage of infectious trade movements from a source herd was 0.3% for status A, 1.8% for status B, 2.8% for status C and 23.6% for status D.

Fig. 4 shows the in-degree and out-degree per herd for the three risk-based trading scenarios. For 54.2% of the herds in the metapopulation the in-degree was the same with (rII/rIII) and without (rI) risk-based trading. For 41.6% (rII) or 43.5% (rIII) of the herds, the in-degree increased with on average 0.60 or 0.63 herds per year, respectively.

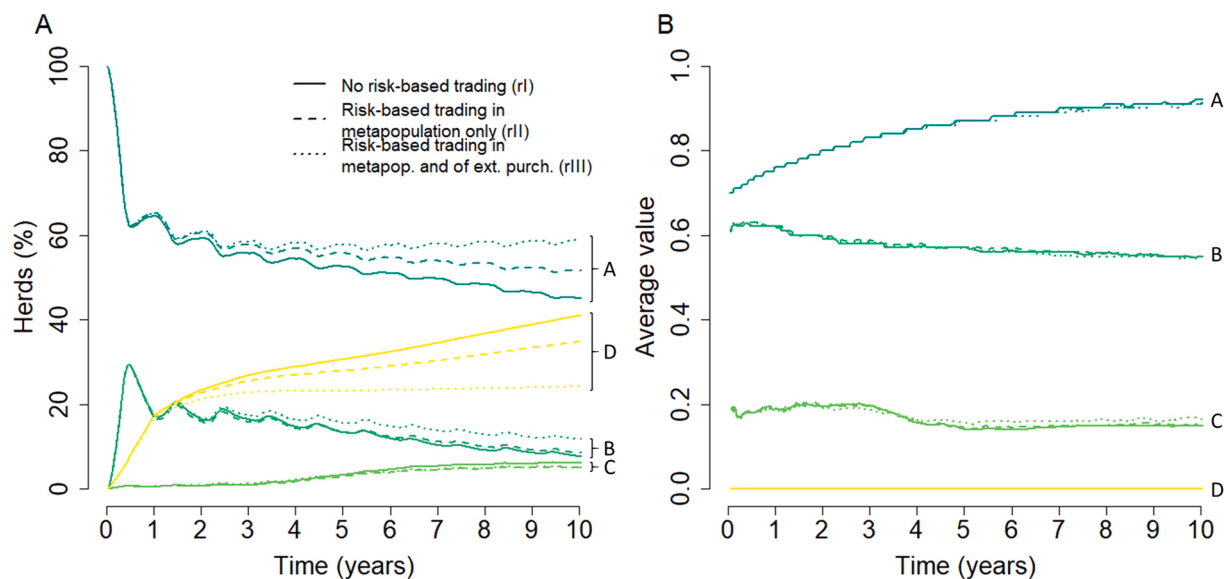


Fig. 1. Johne's assurance status over time for the three reference scenarios. (A) Distribution of herds over Johne's assurance statuses (A, B, C, D) over time. (B) Average indicator value per Johne's assurance status (A, B, C, D) over time.

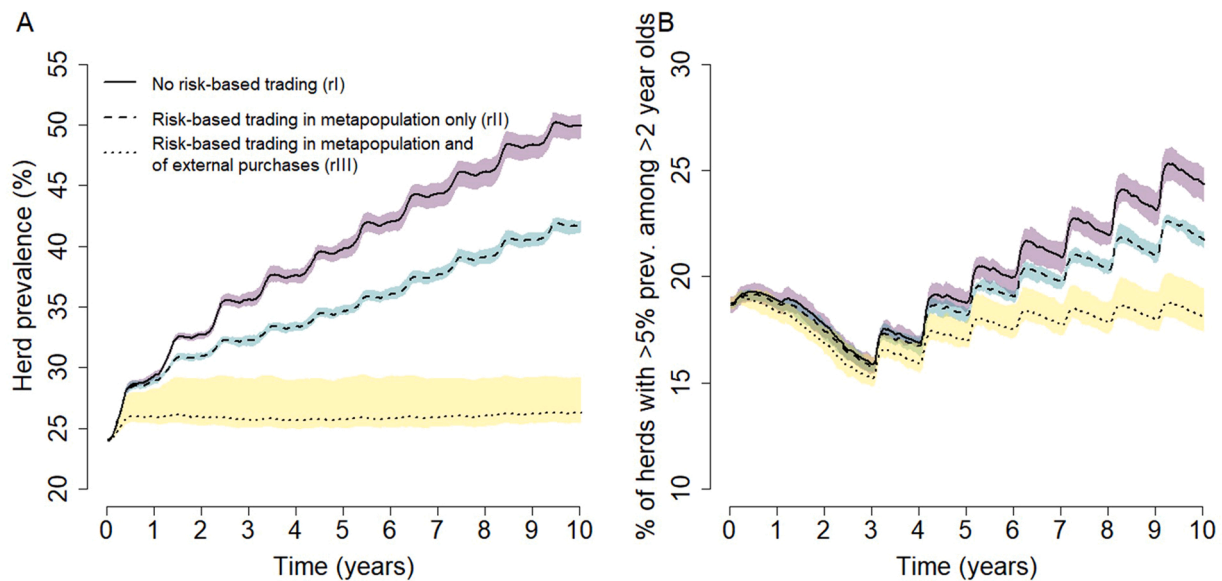


Fig. 2. Herd prevalence over time for the three risk-based trading scenarios. (A) Percentage of herds in which at least one infected animal (of any age) is present. (B) Percentage of herds with an > 5% within-herd prevalence among > 2-year-old animals. Lines indicate the mean value calculated over ten replicates, shading shows the range from the minimum to the maximum value in the ten replicates.

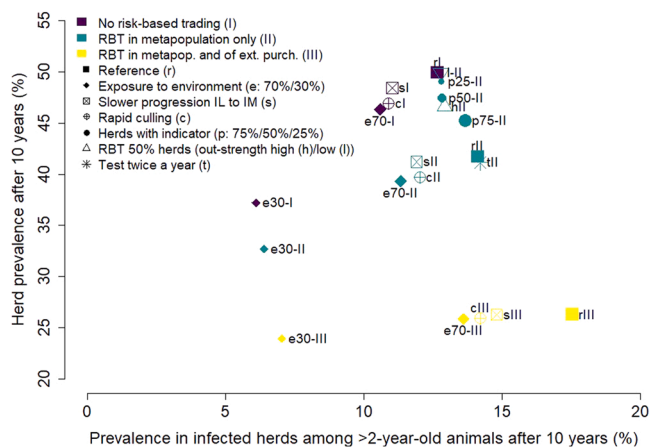


Fig. 3. Herd prevalence versus the within-herd prevalence in infected herds after 10 years for all 21 scenarios (Table 2). Herd prevalence was calculated as the percentage of herds in which at least one infected animal (of any age) is present.

For 44.7% (rII) or 43.2% (rIII) of the herds in the metapopulation, the out-degree was the same as without risk-based trading. For 47.5% (rII) or 47.6% (rIII) of the herds, the out-degree increased with on average 0.55 or 0.53 herds per year, respectively.

Fig. 5 presents the relation between herd prevalence after 10 years of simulations and the percentage of movements within the metapopulation that was redirected. Without risk-based trading, all within-herd measures (e70/e30/s/c) effectively reduced herd prevalence compared to the reference scenario (rI). With risk-based trading in the metapopulation only (rII), this effect was less pronounced. With risk-based trading in the metapopulation and of external purchases (rIII), within-herd measures to reduce herd prevalence were no longer effective, with e30 as an exception. In the rII scenario, and in combinations of this scenarios with within-herd measures, between 4.6% and 4.8% percent of the movements were redirected. In the rIII scenario, and in combinations of this scenarios with within-herd measures, between 5.2% and 5.4% percent of the movements were redirected. However, it should be noted that an additional 20% of all movements coming from a

herd outside of the metapopulation, were also risk-based.

For the scenarios where only a random part of the herds had a herd indicator but all herds were subjected to risk-based trading (p75-II/p50-II/p25-II) or the scenario where 50% of herds with a high out-strength were subjected to risk-based trading (hII), the herd prevalence after 10 years lay in-between rI and rII (45.3%–49.1%). This indicates that the more herds participate, the more effective risk-based trading becomes. However, which herds participate is important as well. Herd prevalence for the scenario where 50% of herds with a low out-strength were subjected to risk-based trading (l-II) was equal to the scenario with no risk-based trading at all.

3.4. Accuracy of classification

The percentage of herds with an infected animal present but not identified by a test (false negative herds) after 10 years of simulation was on average 8.3% for the reference scenario with risk-based trading in the metapopulation only (rII), 9.7% for this scenario together with a slower progression from I_L to I_M (sII), and 7.1% for this scenario when testing twice a year (tII) (Fig. 6). Average within-herd prevalence among > 2-year-old animals within infected herds after 10 years, however, was 14.2% for scenario rII and tII, but 11.9% for scenario sII (Fig. 3), while herd prevalence after 10 years was between 41.1% and 41.7% for all three scenarios (Fig. 5). Thus, compared to scenario rII and tII, for scenario sII a similar herd prevalence was observed even though Johne's assurance status was less accurately classified; in contrast, the within-herd prevalence was lower.

3.5. Herd type

Table 4 shows the number of herds per herd type for which movements were redirected. With risk-based trading in the metapopulation only (rII), for 26.7% of the herds no movements were redirected over the ten-year simulated period. For 19.1% of the herds, less than one outgoing movement was redirected, and for 13.6% of the herds, less than one incoming movement was redirected, on average. Furthermore, for 18.7% of the herds more than 10 outgoing movements were redirected, and for 18.5% of the herds more than 10 incoming movements were redirected. The median average value for the number of redirected movements per herd was 1.4 for outgoing movements and 2.0 for

Table 3
Infectious trade movements between pairs of Johne's assurance statuses. Numbers shown are for one representative replicate of the scenario.

A. No risk-based trading (rI)		Destination Johne's assurance status					
Source		A	B	C	D	Outside	Total
Johne's assurance status	A	505	243	71	200	1764	2783
	B	133	171	42	216	1982	2544
	C	100	81	73	588	3380	4222
	D	3144	2439	1762	21,190	127,968	156,503
	Outside	3169	2609	2083	20,876	0	28,737
Total		7051	5543	4031	43,070	135,094	194,789
B. Risk-based trading in the metapopulation only (rII)		Destination Johne's assurance status					
Source		A	B	C	D	Outside	Total
Johne's assurance status	A	515	228	38	62	1674	2517
	B	13	259	91	409	2118	2890
	C	5	23	105	978	3163	4274
	D	304	322	469	23,788	126,677	151,560
	Outside	3421	2677	2068	19,710	0	27,876
Total		4258	3509	2771	44,947	133,632	189,117
C. Risk-based trading in the metapopulation and of external purchases (rIII)		Destination Johne's assurance status					
Source		A	B	C	D	Outside	Total
Johne's assurance status	A	460	172	58	35	1521	2246
	B	0	341	82	191	1702	2316
	C	0	0	106	361	1803	2270
	D	0	0	0	26,494	122,897	149,391
	Outside	1150	1192	575	16,074	0	18,991
Total		1610	1705	821	43,155	127,923	175,214

incoming movements. The percentage of DnR-C herds with more than 10 outgoing movements redirected was relatively high (40.3%) compared to other herd types. Similarly, the percentage of DnR-nC herds with more than 10 incoming movements redirected was relatively high (45.3%) compared to other herd types.

4. Discussion

Risk-based trading effectively reduced the increase in herd prevalence over a 10-year period in Ireland. Only about 5% of the movements were redirected. However, for risk-based trading to be effective, many (all) herds must participate and Johne's assurance statuses must be accurately determined. When risk-based trading was combined with within-herd measures, the reduction in herd prevalence was even more pronounced.

For our simulations we used an adapted version of the stochastic individual-based and between-herd mechanistic epidemiological model developed to simulate *Map* transmission between herds in western France (Camanes et al., 2018; Ezanno et al., 2022). Some important differences exist between the Irish and French dairy sector. First, the Irish dairy farming system is predominantly seasonal (Tratalos et al., 2017), whereas in France calves are born all-year-round. Second, in Ireland, animals are traded twice as frequently compared to France (Biemans et al., 2022; Ezanno et al., 2022). And third, in Ireland, most dairy herds are assumed to be free from infection (Good et al., 2009; McAloon et al., 2016), while in France most dairy herds are assumed to be infected, albeit with a very low within-herd prevalence (Beaunée et al., 2017; Ezanno et al., 2022). Ezanno et al. (2022) investigated risk-based trading as well, and observed a decrease in herd prevalence for all scenarios compared to the control scenario. With regard to within-herd measures, improving herd hygiene was as effective as early culling in France. However, it should be noted that calf exposure was reduced from 35% to 10% in Ezanno et al. (2022), and in our study from 100% to 70% or 30%. For the early culling scenario, they assumed that 10%, 25%, or 50% of the test positive I_M and I_H cows were randomly

chosen to be culled within one month after detection, while in our study 100% of the test positive I_H cows were culled within one month after detection. Despite these differences, the effect of these within-herd measures combined with risk-based trading in an Irish context was found to be very similar to those in France.

In this study, we chose to limit the simulated period to the ten years for which we had data. Theoretically, we could have extended the simulated period to see whether an equilibrium would be reached for herd prevalence, the distribution of herds over the four statuses, etc. However, even though this is a simulation study, real data from 2009 to 2018 was used to simulate animal movements between herds, to simulate the number of births per week, and to calculate the exit rates. Extending the simulated period beyond these ten years could be achieved by duplicating the data from 2009 to 2018. But a choice must be made on which years to duplicate. Data from 2009 might not be representative for 2019 given that cattle numbers have increased since 2009, i.e., from 6.6 million in 2010 to just over 7.3 million in 2020 (Anon, 2020). Duplicating data from 2018 only, could be another option because it is the most recent. Irrespective of which years are duplicated, one should be very careful when interpreting the results of an extended simulation since they might not be accurate. For each herd, herd size is calibrated once at the start of the simulations in 2009. Over time, however, simulated herd size starts to deviate from actual herd size due to missing data, under reporting, etc. (Biemans et al., 2022, additional file 3). When running the model for a period longer than ten years, especially when using data from another year, the discrepancy between simulated and actual herd size will only grow. Because we cannot be certain that the results obtained in that case are still accurate, we choose to restrict simulated period to the ten years for which we had data.

In our study, Johne's assurance status was defined based on an indicator value for the confidence of freedom from infection. Based on this indicator, four Johne's assurance statuses are distinguished, A: $\geq 0.7 - 1.0$, B: $\geq 0.3 - < 0.7$, C: $> 0.0 - < 0.3$, and D: 0.0. At the start of the simulations all herds started with status A, based on test results and the number of animals introduced over time, herds were distributed over all

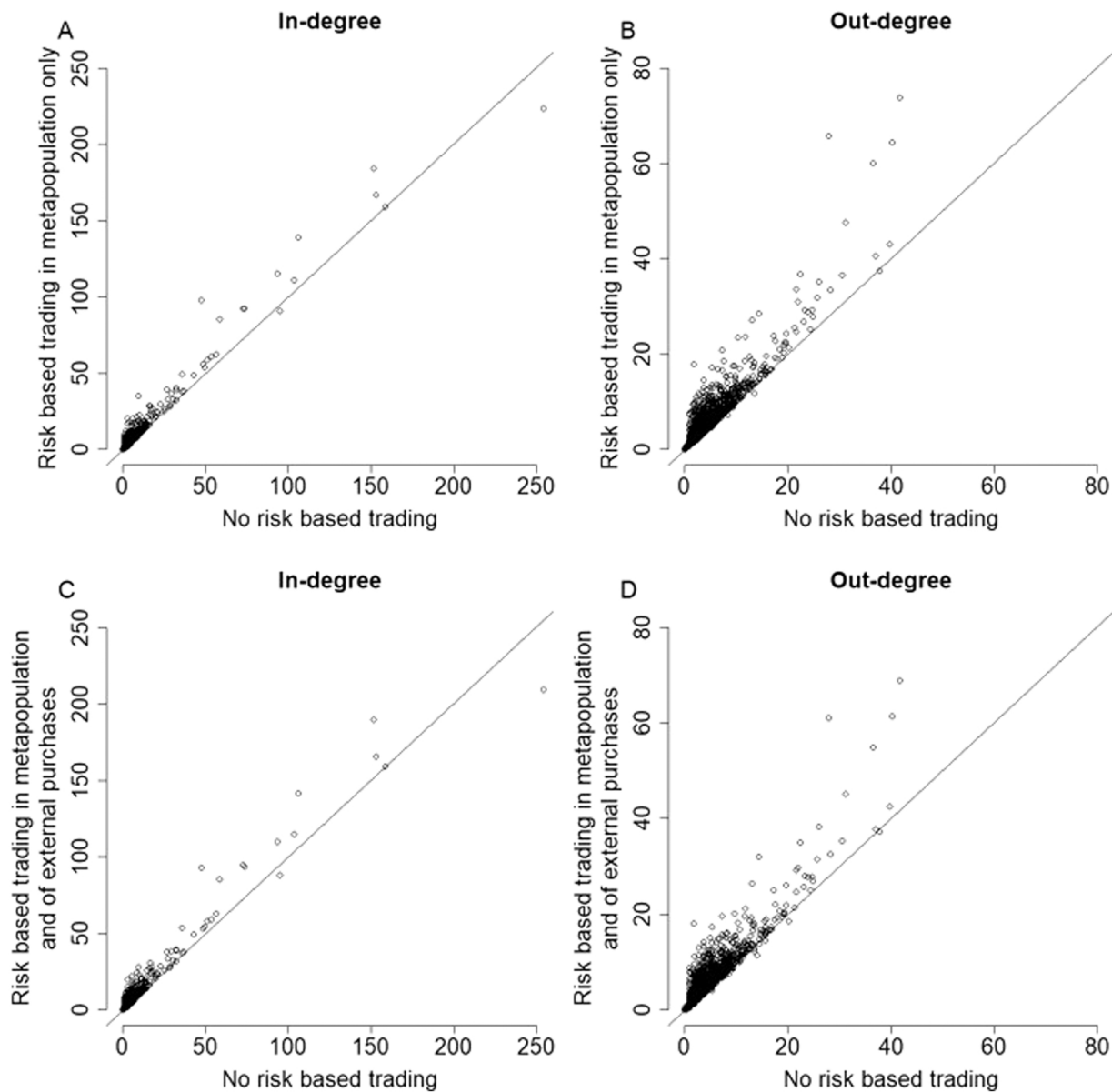


Fig. 4. In-degree and out-degree per herd for three risk-based trading scenarios. Under each scenario, for each herd the in-degree (A and C) and out-degree (B and D) were calculated yearly as an average over 10 replicates and this yearly average was subsequently averaged over the ten years. Each point represents one herd. Points on the line have the same in-degree/out-degree with and without risk-based trading. Points above the line have a higher in-degree/out-degree with risk-based trading compared to no risk-based trading. Points below the line have a lower in-degree/out-degree with risk-based trading compared to no risk-based trading.

statuses. However, at the end of the simulations the number of herds per status was far from equal, with the majority of herds having status A, followed by status D (Fig. 1). It would be worthwhile to investigate the need for four different statuses for risk-based trading, or whether three statuses (A, B+C, D) would suffice. An advantage of merging statuses B and C is the increase in trading options for herds with status C, possibly resulting in a reduced number of movements that need to be redirected. However, the risk of merging these statuses is an increase in herd prevalence. The number and percentage of infectious animals sold by herds with status C is relatively high (Table 3) especially given that the percentage of herds with this status is relatively low (Fig. 1). Another option could be splitting status D into several classes based on within-herd prevalence. In France, risk-based trading based on within-herd prevalence was found to reduce the proportion of infected herds and the number of newly infected herds over a nine-year period, especially when targeting herds that persistently have a low prevalence (Ezanno et al., 2022). Defining Johnne's assurance status based on confidence of

freedom combined with within-herd prevalence might reduce herd prevalence even further.

Under the scenario risk-based trading in the metapopulation only (rII), risk-based trading was optional. We assumed that a herd preferred to buy from a low-risk herd, but if this was not possible would buy from a high-risk herd. If risk-based trading would be optional, money would also play a role. Farmers might be willing to accept the risk of introducing *Map* if the animals from herds with a lower status were less expensive than animals from herds with an equal or better status (Bennett and Balcombe, 2012). Some farmers may decide to choose wealth over health, paying a lower price and accepting the risk of introduction of infection, while others might choose health over wealth, paying a higher price but minimizing this risk (Colman et al., 2020). The trading strategy a farmer chooses to follow will affect their trading behaviour, which will in turn affect the herd prevalence over time. Whether this divergence in trading strategies occurs depends on the burden of adverse health effects that a farmer is willing to accept before

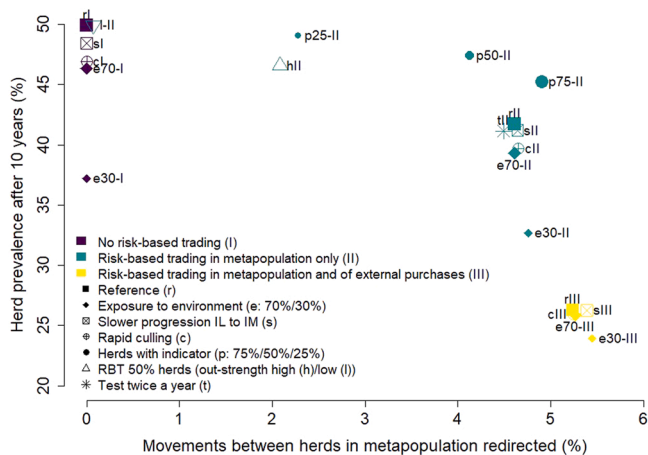


Fig. 5. Herd prevalence after 10 years versus the percentage of movements redirected for all 21 scenarios (Table 2). Herd prevalence was calculated as the percentage of herds in which at least one infected animal (of any age) is present.

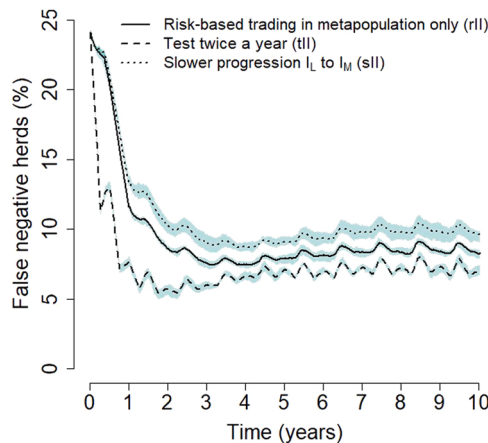


Fig. 6. Percentage of false negative herds over time. In a false negative herd, infected animals are present but they are not identified by a test.

seeking better trading options (Colman et al., 2020).

Under the risk-based trading scenarios, spatial distance between trading herds was not taken into account. This might have led to animals being moved over larger distances than observed in the data. In Ireland, 66% of animal movements were between herds located less than 50 km from each other (Tratalos et al., 2020). Whether farmers are willing to trade over larger distances to reduce infection risk could depend on the costs (Bennett and Balcombe, 2012; Colman et al., 2020). Future work on risk-based trading between dairy herds in Ireland could consider taking spatial distribution, costs of risk-based trading, and establishing systems to share status information between trading partners into

account as well.

For all reference risk-based trading scenarios, and the combinations of these scenarios with within-herd measures, the average herd prevalence after ten years was lower while the average within-herd prevalence was higher with more intense risk-based trading (Fig. 3). For example, under the no risk-based trading (rI) scenario, herd prevalence was 49.9% and average within-herd prevalence was 12.7% after ten years. In contrast, the scenario with risk-based trading in the metapopulation and of external purchases (rIII), herd prevalence after ten years was 26.3% and average within-herd prevalence was 17.5%. Risk-based trading is thus very effective in preventing spread between herds but does not prevent spread within herds. In scenario rI (no risk-based trading), 49.9% of the animals that entered a herd with status D came from a herd with status D, whereas the equivalent figure in scenario rIII (with risk-based trading) was 61.4% (Table 3). Thus, risk-based trading leads to increased trade between infected herds (status D). These herds are selling and buying infected animals, and are unable to reduce infection through trade, leading to an increased average within-herd prevalence after ten years compared to no risk-based trading. This increase in average within-herd prevalence can be prevented by combining risk-based trading with within-herd measures. For example, when risk-based trading in the metapopulation and of external purchases was combined with improved herd hygiene (e70-III), herd prevalence after ten years was 25.9% which is similar to the 26.3% with risk-based trading only (rIII), and average within-herd prevalence was 13.6% which is close to 12.7% without risk-based trading (rI).

Improving herd hygiene and early culling of highly infectious cows were found to be very effective within-herd measures, having positive effects on both herd and within-herd prevalence. Several studies have already shown the positive effects of improved herd hygiene and early culling (Doré et al., 2012; Donat et al., 2016; Wolf et al., 2016; Beaunée et al., 2017; McAloon et al., 2017; Biemans et al., 2021). Combining these two measures has been shown to be even more effective (Konboon et al., 2018; Ezanno et al., 2022). Whether this is also the case in an Irish context, especially when combined with risk-based trading, could be a topic for further exploration.

We found that an increase to the duration of the latent period had a positive effect on within-herd prevalence but no effect on herd prevalence (Fig. 3). Relevant to this, we assumed that reduced stress in cows could result in a slower progression of disease from the latently infected stage to the moderately infectious stage. In mouflon, stress due to movement might have contributed to the start of *Map* shedding in animals that were previously diagnosed as MAP-negative (Priblyova-Dziedzinska et al., 2014). In cattle, onset of clinical symptoms may occur due to stress induced by calving, feed changes, or movement (Animal Health Diagnostic Animal Health Diagnostic Center, 1999). However, a relation between calving associated stress and *Map* shedding levels was not observed (Kauffman et al., 2014).

The model used in this study was developed to simulate transmission between dairy herds. Therefore, only herds belonging to one of six dairy herd types (Brock et al., 2021) were included in the model (Biemans et al., 2022): typical dairy herds (D), mixed herds (M), dairy herds that

Table 4

Number of herds per herd type with movements redirected; for the scenario with risk-based trading in the metapopulation only (rII).

Herd type	# total	# herds with > 0 outgoing movements redirected (% of herd type)	# herds with > 10 outgoing movements redirected (% of herd type)	# herds with > 0 incoming movements redirected (% of herd type)	# herds with > 10 incoming movements redirected (% of herd type)
D	6299	5220 (82.9)	1577 (25.0)	4199 (66.7)	1004 (15.9)
M	3509	1988 (56.7)	179 (5.1)	2740 (78.1)	742 (21.1)
DRm	2364	1584 (67.0)	368 (15.6)	1674 (70.8)	448 (19.0)
DnR-C	799	699 (87.5)	322 (40.3)	593 (74.2)	106 (13.3)
DnR-nC	380	297 (78.2)	55 (14.5)	346 (91.1)	173 (45.5)
SdR	2	2 (100.0)	1 (50.0)	2 (100.0)	2 (100.0)
Total	13,353	9,790 (73.3)	2502 (18.7)	9554 (71.5)	2475 (18.5)

also rear their male calves (DRm), non-rearing dairy herds (DnR-C and DnR-nC), and herds that rear dairy females (SdR). We observed that for 87.5% of the source DnR-C herds and for 74.2% of the destination DnR-C herds at least one animal movement was redirected (Table 4). Furthermore, for 40.3% of the source DnR-C herds, more than ten movements were redirected. DnR-C herds sell most of their calves, with female dairy calves being moved to external contract rearing herds, e.g., SdR herds. The female calves return to their birth herd as pregnant heifers, a process known as contract rearing. Since DnR-C herds have a contract with SdR herds to rear their young stock, it is very unlikely that they will send their calves to a different farm when a movement is not allowed because of risk-based trading. One solution could be to exclude from risk-based trading only those movements that are related to such contracts. Another option is to exclude DnR-C and SdR herds from risk-based trading altogether. However, this might have an effect on herd prevalence because DnR-C and SdR herds have a higher out-degree and out-strength compared to all other herd types (Biemans et al., 2022). Excluding these high out-strength herds would lead to a scenario similar to subjecting only the 50% of herds with a low out-strength to risk-based trading (I-II), which was found to be completely ineffective (Fig. 5). Thus, if risk-based trading were to be implemented, a solution would need to be found for herds that engage in contract rearing.

5. Conclusion

We used a stochastic individual-based and between-herd mechanistic epidemiological model to simulate *Map* transmission between dairy herds in Ireland. We used this model to assess whether within-herd measures and redirecting trade movements based on John's assurance status could effectively control *Map* spread. Risk-based trading effectively reduced the increase in herd prevalence over a 10-year period in Ireland. However, for risk-based trading to be effective, a high percentage of dairy herds must participate. Combining risk-based trading with within-herd measures was even more effective. Improving herd hygiene and early culling of highly infectious cows were found to be the most important within-herd measures affecting both herd and within-herd prevalence.

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Declarations of interest

None.

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Appendix A. Supporting information

Supplementary data associated with this article can be found in the online version at doi:10.1016/j.prevetmed.2022.105779.

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