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Eradicating BVD, reviewing Irish programme data and model predictions to support prospective decision making

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ABSTRACT

Bovine Viral Diarrhoea is an infectious production disease of major importance in many cattle sectors of the world. The infection is predominantly transmitted by animal contact. Postnatal infections are transient, leading to immunologically protected cattle. However, for a certain window of pregnancy, *in utero* infection of the foetus results in persistently infected (PI) calves being the major risk of BVD spread, but also an efficient target for controlling the infection.

There are two acknowledged strategies to identify PI animals for removal: tissue tag testing (direct; also known as the Swiss model) and serological screening (indirect by interpreting the serological status of the herd; the Scandinavian model). Both strategies are effective in reducing PI prevalence and herd incidence. During the first four years of the Irish national BVD eradication programme (2013–16), it has been mandatory for all newborn calves to be tested using tissue tag testing. During this period, PI incidence has substantially declined. In recent times, there has been interest among stakeholders in a change to an indirect testing strategy, with potential benefit to the overall programme, particularly with respect to cost to farmers. Advice was sought on the usefulness of implementing the necessary changes. Here we review available data from the national eradication programme and strategy performance predictions from an expert system model to quantify expected benefits of the strategy change from strategic, budgetary and implementation points of view. Key findings from our work include (i) drawbacks associated with changes to programme implementation, in particular the loss of epidemiological information to allow real-time monitoring of eradication progress or to reliably predict time to eradication, (ii) the fact that only 25% of the herds in the Irish cattle sector (14% beef, 78% dairy herds) would benefit financially from a change to serosurveillance, with half of these participants benefiting by less than EUR 75 per annum at herd level or an average of EUR 1.22 per cow, and (iii) opportunities to enhance the effectiveness of the current programme, particularly in terms of time to eradication, through enforced compliance with PI removal as currently outlined in programme recommendations. The assembled information provides scientific arguments, contributing to an informed debate of the pros and cons of a change in eradication strategy in Ireland.

1. Introduction

Bovine Viral Diarrhoea virus (BVDV) causes high production losses due to reproductive, enteric and respiratory disease in many cattle sectors of the world (Moennig et al., 2005). The infection is predominantly transmitted by animal contact. In most animals, exposure leads to transient infection, followed by immunological protection. However, during a defined window of gestation, *in utero* infection results in the production of persistently infected (PI) calves (Coria and McClurkin, 1978; McClurkin et al., 1984; Moennig and Liess, 1995). PI animals shed large amounts of BVDV throughout their lives (Coria and McClurkin, 1978; Houe,1995), and are considered about 10 times more infectious than animals with transient (non-persistent) infection (Moerman et al., 1993; Cherry et al., 1998). The high infectivity of PI individuals drives perpetuation and incidence of endemic BVD (Tråvén et al., 1991; Ersbøll et al.,2010).

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A number of national BVD control or eradication programmes have been initiated, leading to reduced PI animal occurrence and a substantial decrease in herd-level incidence (Lindberg and Houe, 2005; Ståhl and Alenius, 2012). Two primary diagnostic methods are applied in BVD control programmes, as reviewed previously (Graham et al., 2014), with the principal difference relating to whether PI animals are detected directly or indirectly. Direct strategies use virological testing to clarify the infection status of individual animals (the "Swiss model", Presi and Heim (2010)). This approach is commonly referred to as tissue tagging or tag testing, with testing conducted on all new-born calves to directly identify PI animals. Indirect strategies use preliminary serological screening tests to determine herd BVD status (the "Scandinavian model", Lindberg and Alenius (1999)). This approach relies on testing of either serum of animals of a certain age or pooled milk, from individual animals or from the tank (bulk milk). Independent of the method applied to identify and remove PI animals, any national BVDV programme has to be systematic, with a focus on eradication, this being the regional extinction of the BVD virus (Lindberg et al., 2006; Laureyns, 2014).

The Irish eradication programme is broadly based on the "Swiss model" using direct antigen-based tests to identify BVDV-positive animals. After a voluntary phase in 2012 (Graham et al., 2014; Graham et al., 2015b), the programme has been compulsory since the start of 2013. By 2016, an increasing number of farms achieved negative herd status (NHS) which is defined as demonstrated absence of PI animals in the herd during the preceding 12 months using complete cohort tag testing and the known negative status for each single animal in the herd using programme data (http://animalhealthireland.ie/?page_id=4916, last visited August 2017). NHS status allows targeted application of specialised programme measures to enhance eradication, and is only marginally related to proof of freedom in the sense of post-eradication surveillance.

For some time, there has been interest among stakeholders in a change to an indirect testing strategy, with potential benefit to the overall programme, particularly with respect to direct costs to farmers. In this context, serosurveillance has been suggested by stakeholders, namely serological testing of a subsample of animals in each herd. Consistent with approaches taken in other BVD control programmes (Rossmanith et al., 2010; Truyers et al., 2010; Norström et al., 2014), it was assumed that serosurveillance would be conducted once annually. The required number of samples per group has varied between different national programmes, typically being in the range of 5–10 (Lindberg and Houe, 2005). In Ireland, it is proposed that 10 young stock from each management group will be sampled with a cut-point of two positive tests results to achieve a herd-level sensitivity (HSe) and specificity (HSp) of 99.5% and 100% respectively. The HSe and HSp were estimated using HerdAcc (Jordan and McEwen, 1998) based on a cohort size of 50 animals, a design prevalence of 50% and test sensitivity and specificity of 96.9% and 97.8% respectively.

The interest from stakeholders raises the potential for a substantial shift in strategy in the national programme. On initial assessment, however, limited data were available to support such a change. The current systems were working well, in part due to the substantial resource that had been committed to facilitate direct testing of all calves within 20 days after birth, and of subsequent herd and PI management. Further, there was no apparent difference between the current and proposed approaches with respect to the potential for programme fatigue. It was clear that this question could only be answered by considering – and quantifying – the benefit(s) that might accrue from the proposed strategy change.

Experiences from national BVD eradication programmes applying different control methods (Hult and Lindberg, 2005; Houe et al., 2006; Presi et al., 2011; Duncan et al., 2016) demonstrate that the two alternative testing approaches are equally effective in reducing national BVDV incidence. Further, using a modelling-based approach recently described by Thulke et al. (2017), model simulations indicated little difference in terms of time to eradication with a change to serosurveillance during the course of a compulsory tagging programme, on the proviso that key constraints to eradication (including the prompt removal of PI animals shortly after birth) are appropriately managed. Moreover, limited differences were found in costs associated with diagnostic testing when comparing the current and proposed strategies. In the Irish programme, this is because costs attributable to the price of testing were in a ratio of ~1:3 in favour of tissue tag test, whereas the number of tests applied during model simulations were in a ratio of ~2.5:1 in favour of serological testing (Thulke et al., 2017). In summary, experiences from the existing programme and insights from modelling both suggest that these benefits may accrue with a programme change to serosurveillance after the fourth year of universal tag testing. However, in order to support decisions with respect to this question, there is a need for a detailed understanding of the implications of a change in strategy. These issues are of practical importance, noting the likely difficulties that will be faced during the final stages of a disease eradication programme, the so-called 'tribulations of the last mile' (Del Rio Vilas et al., 2017).

A final decision concerning which of these two options to implement will be influenced by expectations, previous experiences and an interpretation of the risk profile with regards to costs, benefits and practical constraints. Assessments in advance in support of such decisions are only possible by projecting recent efforts and strategic successes into plausible future outcomes. Previously, Houe (2003) indicated that individual national assessments are needed when considering economic issues regarding BVD eradication. We note, however, that the literature is not consistent in this regard (Pinior et al., 2017).

Here we address this decision problem in greater detail by asking: (i) what issues are relevant when changing the testing strategy in the context of an active national programme?; and (ii) where might we expect savings to accrue when changing from direct to indirect testing methods for BVDV detection? In addition, we also consider whether other pathways – apart from a change to the national testing strategy – might be feasible to reduce the impact on industry during the eradication programme. In particular, we focus on the issue of PI removal following detection, and its impact on time to eradication.

The objective of this study was to combine accessible literature, programme data and outcomes from an epidemiological expert system modelling to elucidate important criteria for decision making (risks, economic costs and benefits) that support the debate regarding the potential introduction of an alternative BVD eradication method after four years of compulsory tag testing of all newborn calves for some herds, i.e. either continued tissue tagging in all herds until final eradication of the virus from Irish cattle herds, or selective application of sample-based serosurveillance in NHS herds and continued tissue tagging otherwise.

2. Materials and methods

The understanding sought through this study was derived from a mixed methods approach using observational data about the field programme in Ireland, the predicted future programme performance derived from expert system modelling, cost calculations elicited from programme data, as well as qualitative and quantitative information accessible from the existing body of BVD literature. Arguments from literature are referenced to the original source, noting that an exhaustive systematic review of BVD references was beyond the scope of our study. For the latter, the interested reader may consult Pinior et al. (2017) and related work.

2.1. Data

Several different data sources were used during a review of details relevant to a potential change in national testing strategy, relating to

the cost and performance of the ongoing national control programme in the Irish cattle sector, testing efforts needed as part of the two strategy alternatives according to herd size and calving parameters, as well as movement patterns and contiguity structures driving the expert system model.

We accessed several databases including (a) the Irish Cattle Breeding Federation (ICBF) database, including all herd-level information to model the Irish cattle population (i.e. herd seasonal calving pattern, number of animals of breeding age, the dominant production purpose); (b) the Land Parcel Information System (LPIS) database, identifying potential neighbourhood contact structure (i.e. which pastures potentially enable over-the-fence contact between animals of different farms); and (c) the Animal Identification and Movement (AIM) database, which records all calf registrations and cattle movements in Ireland (i.e. movement dates, source-destination pathways including moves via markets, age and sex of the animal). LPIS and AIM are maintained by the Irish Government's Department of Agriculture, Food and the Marine (DAFM). Indicators of programme performance since the initiation of the mandatory measures in 2013 were obtained from Animal Health Ireland (AHI) (e.g. Devitt et al. (2014), Graham et al. (2015b), Clegg et al. (2016), Graham et al. (2016)), including the number of tests, PI animal detections, PI calf survival records, and individual-level data on the epidemiological history of every animal in positive herds. The following costs were used, based on data provided by AHI: individual animal tissue tag test at EUR 2.50 for herds with NHS and otherwise EUR 3.00-3.40 excluding postage (i.e. ear notch collection is performed by the herd owner as part of initial calf registration), and individual animal blood test of EUR 7.66, including sample collection by veterinarian on farm and lab fee but excluding farm visit fee and postage. With this latter estimate, it was assumed that the visit would be combined with other veterinary activities in the same season, to minimise costs. Otherwise, a veterinary farm visit fee would need to be added at each sampling date. In other national programmes, the costs will vary, including the cost difference between individual tissue and serological testing. Estimated average annual losses from BVD in Irish dairy and suckler herds was found in the literature i.e. Stott et al. (2012), or on the AHI website.

2.2. Expert system model outline

The expert system model FarmNet-BVD is fully documented and appended as online Supplementary material (www.ecoepi.eu/FarmNet-BVD), and followed the ODD-protocol (Objective, Design, Details; (Grimm et al. 2006; Grimm et al. 2010)) which prescribes documentation standards for complex system models. The following provides a brief description, noting that detailed information is available in the online supplement.

The expert system model builds on previously published BVD models (Courcoul and Ezanno, 2010; Tinsley et al., 2012; Damman et al., 2015). The model paradigm combines the multi-compartment matrix representation of herds (Damman et al., 2015), reflecting animal numbers by management and BVD status (Supplement Fig. S2) and the dynamic network representation of animal movements (Tinsley et al., 2012) with herds as nodes and individual movement records as temporary edges. The spatial component of the model operates on the true locations and neighbourhood structures. Cattle management and BVD transitions are simulated on a weekly time scale while animal movement follows daily reported data. The model is designed to simulate the BVD dynamics of the complete national cattle industry, i.e. 6 million Irish bovines, whilst also representing critical individual-based events e.g. cows gestating or transient infections. The temporal simulation performance was maintained using new model solutions for scheduling individual-based events (i.e. first-in-first-out queues, Supplement Fig. S2) and the processing of non-infected herds (i.e. island of proxy herds, Supplement Fig. S3). The model implementation facilitates real time graphical output of spatial BVD prevalence, time-series of herd-level prevalence, individual numbers of PI animals, annual cumulative PI detections, and numbers of diagnostic tests applied in the simulated programme. The output data were used to verify model behaviour with existing observations of the Irish eradication programme, and were fed into final analysis of predictions.

The model is driven by data input, i.e. herd characteristics (calving season, animals at breeding age, production purpose, spatial location and contiguous pastures) and animal-level movement records. Where accessible, model parameters follow those suggested by the literature, including reported ranges. Otherwise, if data or literature reference were lacking, the authors provided expert opinion of Irish farming systems, including dairy and beef rearing practices.

Model herds comprise multiple compartments representing management stage: Cows (CO), Calves (CA), Grazing animals for slaughter (GR), Heifer first year (H1), Heifer second year (H2), Heifer breed (HB), and Cattle for fattening prior to culling (FF). Every management cohort is sub-grouped according to the infection status: Susceptible, Immune, Transient, PI, and for calves, the status of maternal antibodies (MAB+). If all combinations are in use, model herds will have animals in 29 subcohorts i.e. 7 management x 4 infection + 1 MAB. The individual animal perspective was taken for gestation schedules, for the movements of animals pregnant with a PI, and in order to manipulate the fate of each PI. Seasonal management as occurs in the Irish cattle sector is represented as an annual cycle of events (Fig. 1), basically organising the regular and stochastic transitions between compartments (after Damman et al. (2015)).

Transportation of animals in the model simulations is driven by annual datasets comprising all Irish cattle movements between 2011 and 2014. These annual datasets are randomly applied for each year of simulation − both in retrospective and prospective years. In simulation years prior to the simulated programme interventions (i.e. before 2013), the objective was an endemic level of BVD infected farms, including herd-level patterns of immunity. Most data were not available prior to the programme, including herd status, immunity status, and annual movement records. Therefore, the movement of animals was generated by combination of the accessible annual movement records and the first herd database completed in the programme. Into the future of the programme, i.e. from August 2016 onwards, past herd distribution and annual movement datasets were again used tacitly knowing that both will probably undergo certain changes over the intervening 3–5 years.

The direct control option is implemented mimicking the protocol for tissue tag testing that is applied in the Irish national programme: every calf in the model has to be tested within 3 weeks after birth and removed 4 weeks later, following a positive confirmatory test (i.e. referring to the programme rule of financial support only for removal between weeks 5–7). Indirect testing was not needed to be simulated in this study (the interested reader may consult the model documentation for model details). In the model, Trojan introduction i.e. movements of *in utero* PIs (Reardon et al., submitted) can be excluded using a pre-movement test option in non-free herds. This option suppresses the off-herd movement of cows pregnant with a future PI calf, which in reality might be achieved by generalised movement restrictions applied to farms with non-negative BVD status. In all simulations we assumed diagnostic tests with perfect sensitivity and specificity.

The model represented farmer non-compliance to prompt removal of PI animals (i.e. keeping of PI animals beyond 7 weeks post-detection). To do so, for every PI calf scheduled as born, the date of final removal is assigned by randomly drawing from PI survival data of the Irish BVD eradication programme (Supplement Fig. S6). The survival curves represent all detected PI animals independent of whether they were retained or not i.e. including early and late removals (Clegg et al., 2016). The very late removal dates, i.e. > 6 months in the survival data, were replaced in the model by so-called retention herds. Retention herds in the model keep PI animals until they die, e.g. due to slaughter. Manipulations of the PI removal time away from observed values (in

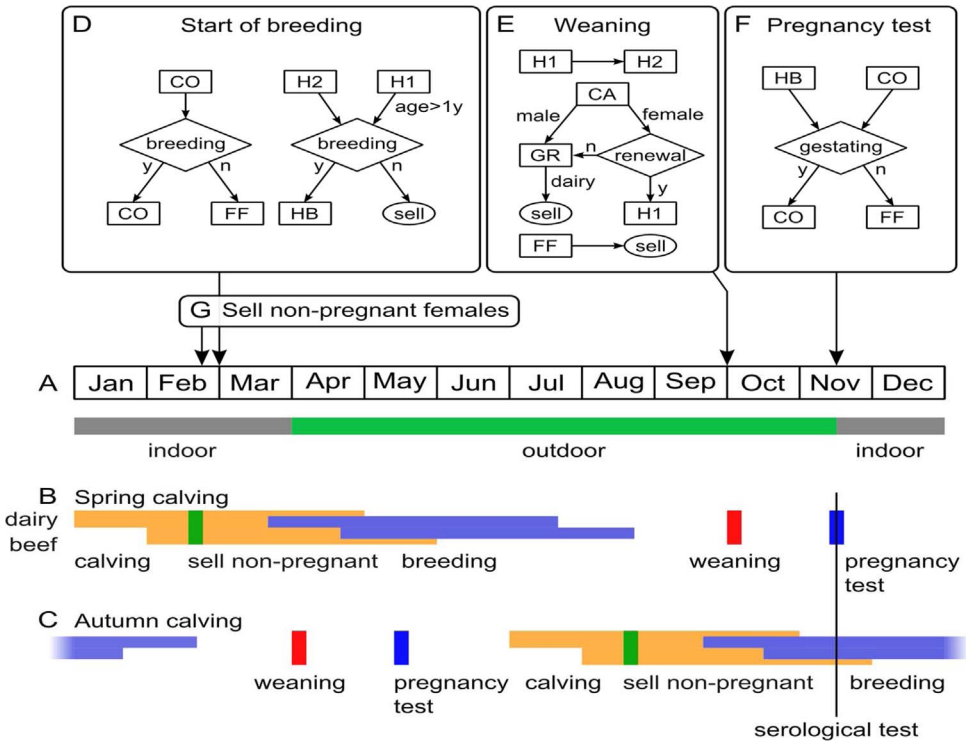

Fig. 1. Schematic depiction of the herd management model applied in 2016 to provide quantitative predictions of the number of newborn PI animals if BVD is circulating in Irish breeding farms under different control measures. The Figure describes event and process scheduling. A: Running months and associated pasturing schedule for herds with outdoor rearing; B and C: Typical management schedule for Irish dairy (upper line) and beef herds (lower line) applying spring (B) and autumn calving cycles (C). Event timing and logic of the model function, D: Breeding; E: Weaning; F: Pregnancy test; and G: Sell non-pregnant cows. For detailed explanation of the annual herd management scheme see the complete model documentation appended as online supplement (www.ecoepi.eu/FarmNet-BVD).

scenarios) were achieved by assigning fixed time of removal relative to birth, i.e. 1 st week, 7th week, and a reduction in the proportion of retention herds.

2.3. Simulation scenarios

Simulation experiments were conducted comparing the development of the PI cohort on a global scale for alternative reinforcement strategies. For each run, a 30 year burn-in period was simulated, ending in an endemic situation as well as an emerging proportion of herds with immune animals. Subsequently, the tissue tag testing strategy was applied for 10 years of simulation. During the first three years, measures and retention are adjusted to the history of the Irish national programme i.e. 2013–2015. During this period, PI removal times mimic recorded survival, and the herd-level proportion of retention farms was halved in 2014 and further reduced by two thirds in 2015 (Clegg et al., 2016). From the fourth year onwards, future tag testing is simulated until the end of 2022 but applying different scenarios as follows:

S0–'Worst case scenario': PI animals were managed in future years as in 2015 i.e. PI removal was continued unchanged in all years, using PI survival data from 2015 as described and an unchanged cohort of retention herds. S1–'Scenario retention reduction': The proportion of retention herds was reduced from year to year by two thirds i.e. as observed for 2015. S2–'Scenario early removal': From 2017 onwards, it is assumed that all PI calves are removed within the week of birth and the proportion of retention herds has dropped to zero, i.e. PI detection was followed by immediate removal without any retest or logistic delay. S3–'Scenario forced removal': From 2017 onward, it is assumed that all PI calves are removed within seven weeks after birth and the proportion of retention herds dropped to zero, i.e. PI calves are detected and removed according to regulation, possibly including confirmatory retesting. S4–'Scenario forced removal & movement restrictions': As 'Scenario forced removal' (S3) but additionally untested calves and *in utero* PIs in any herd with non-negative BVD status are prevented from moving, i.e. calves with missing tag test and pregnant animals would be excluded from being traded off herds without a negative BVD status (NHS herds).

For every scenario, 96 repetitions were run each using alternative parameter configuration reflecting uncertain specifications of sensitive transmission parameters (see the supplemented ODD model documentation, Tables S1–S4 and Local sensitivity): PI mortality (annual disease related fatality rate); within-group transmission due to a PI (seasonally dependent mixing of compartments); between-pasture transmission due to a PI (direct and indirect transmission to other animals in the same or other management group of the same herd); between-herd transmission due to a PI (direct and indirect transmission to other animals in other, contiguous, herds). Parameter variations were set symmetrically around those values calibrated with sector-wide herd-level prevalence similar to that before the start of the control programme in Ireland (Cowley et al. (2012); see local sensitivity in the Supplementary material). From the model output, the simulated number of new PI animals born in each year is recorded and compared with those detected during the Irish programme (http://animalhealthireland.ie/?page_id=229). In order to integrate parameter uncertainty with the final outcome, the absolute value in the middle of the fourth year of the simulated eradication programme is rescaled to the observed number of PI calves at this point in time. The proportionality factor was taken forward to the subsequent simulation data points. The variability of the annual prediction of newborn PI calves due to parameter uncertainty was finally expressed as box-whisker-plots around the simulated median per year.

2.4. Calculation of herd-level costs for alternative test strategies

Analyses were carried out for all Irish herds in which calves were born in 2015. Data on the characteristics of calves (birth herd, sex, breed and date of birth) and their movements between June 2013 and December 2015 were drawn from the AIM database. Herds were classified as being of beef or dairy enterprise type if ≥66% of their stock were from beef or dairy breeds respectively, calculated using their end-of-year herd profiles for 2014 and 2015 (Good et al., 2009; Tratalos et al., 2017a). Other herds were classified as 'mixed', except in those few herds with no stock at the end of the year in both 2014 and 2015, which were classified as 'unknown'.

For every individual Irish herd, the required number of tissue tag tests was determined based on the number of calves born each year. Based on birth dates and applicable movements in 2015, we calculated the number of young stock, i.e. 6–12 months and 9–18 months old, that were present in their birth herd in October 2015. These calculations were used to qualify whether 10 young stock were still present in the herd at the time of blood sampling. Based on separate calculations (Tratalos et al., submitted), October was the optimal month for serological testing, this being the month when the maximum number of herds had sufficient young stock for serological testing.

Sample size per herd required for serological screening is dependent on the relationship between the number of calving cows in the herd and the number of separately managed groups to sample each by 10 bloods. As no detailed data on the management group structure was accessible for each herd, sample numbers were calculated under 2 alternative assumptions: M∞ – only one management group in the herd, and M50 – one group for every 50 cows, which covers the range likely to be found in Irish herds. This analysis will be disclosed in full and with greater detail elsewhere (Tratalos et al., submitted).

3. Results

Descriptive analysis of the performance indicators using recordings of the Irish national eradication programme are summarised in Fig. 2. The programme effectiveness was roughly 75%, i.e. a decline in absolute numbers from about 14k (9.5k) detected PI animals (herds) in 2013 down to 3.3k (2.5k) after four years of mandatory tissue tag testing.

The absolute annual efficacy of the programme was calculated and is shown in Fig. 2A. Awareness measures in 2015/2016 resulted in a doubling of efficacy (bar charts: approximately 4k PIs identified and removed in 2016 instead of approximately 2k in 2015) and maximum efficiency of eradication efforts (line graph: about 50% reduction from previous year in 2016 while less than 30% in the years before). This programme performance was achieved in the face of substantial non-compliance with the requirement for timely removal (i.e. retention, (Graham et al. 2015a; Clegg et al. 2016)). According to the animal notification system, some PI animals were present in the population for more than 100 weeks (700 d in Fig. 2B).

Table 1 presents the BVD status of the 6.1 million cattle that were present in Irish breeding herds during the years of the Irish BVD eradication programme (that is, at any point since the start of 2013), based on knowledge available at the mid-2016. Not only are more than 99% of breeding herd animals considered to be BVD negative (Direct and Indirect negative), but as few as 0.01% are confirmed PI.

The model predictions regarding the number of newborn PI calves in the Irish cattle population from August 2016 onwards are summarised in Fig. 3. All simulations assume continued tissue tag testing until the end of the simulation. The scenarios increase by intensity of enforcement towards timely removal of detected PI animals. The profiles presented show the expected yearly number of newly detected PI calves. The first panel refers to the reference model assuming no enforcement (S0), and represents a continuation of the levels of retention seen at the end of the third year, 2015, of the Irish programme. The continued level of long-term delay in PI removal post-detection prevents the simulated eradication programme from approaching a zero PI incidence despite ten years of continued tissue tag testing.

From year five (i.e. 2017) onwards, in the simulated Scenario S1 (annual reduction of long-term PI retention by 50%, continued as achieved between 2015 and 2016 during the Irish programme), PI incidence was reduced to near zero after ten years of tissue tag testing (2nd panel Fig. 3). The next panel shows the same output data but for Scenario S2, assuming from the fifth year (i.e. 2017) onwards all detected PI animals will be removed within 4 weeks after birth. The simulated annual PI incidences dropped to near zero after 8 years of tissue tag testing (i.e. year 2020 in the Irish programme). Scenario S3 assumed that from the fifth year (i.e. 2017) onwards, there was forced but more practical removal of PI calves, namely in the first two months of their life. This slowed down the approach to zero. Scenario S4 was the same as S3 but also included, from the fifth year (i.e. 2017) onwards, the prevention of the movement of risk animals (i.e. untested calf or *in utero* PI) from herds not having BVD free status. This brought the decline of annual incidence in newly detected PI calves back to the favourable levels seen with Scenario S2, which assumed removal in the month of birth.

Table 1
The BVD status of the 6.1 million cattle that were present in Irish breeding herds during the years of the Irish BVD eradication programme, based on knowledge available as of 22 August 2016. The original data record more details facilitating epidemiological interpretation of e.g. break-down findings (Source: D. Graham, AHI programme investigations; http://animalhealthireland.ie/?page_id=227). 'Unknown' are animals (1) born before 1 st January 2013 without being tested and not calved or (2) calves that are born less than 35 days ago still without any (valid) test result. 'Suspect' animals are dams of animals with a current non-negative result.

Animal status	Number animals	Percentage of bovine population
Direct negative	4,511,282	73.76%
Indirect negative	1,544,556	25.26%
Unknown	57,662	0.94%
Suspect	1770	0.03%
Positive	552	0.01%
Total population	6,115,792	100.00

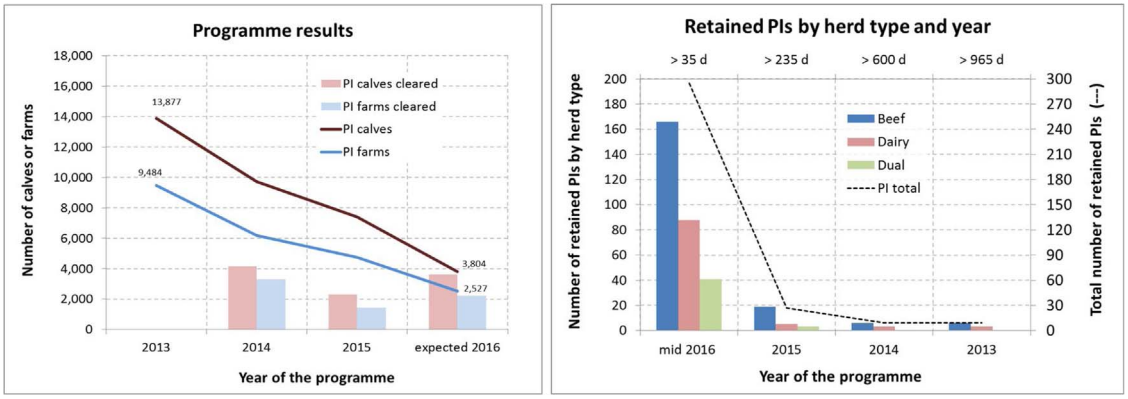

Fig. 2. Efficacy of the first years of the national eradication programme in Ireland (2013–2016). Left panel: Annual numbers of PI calves detected (red line) and herds with at least one PI calf detected (PI farm, blue line) illustrating a decrease of PI burden by about 75%. The bar chart details the absolute annual impact of the programme measures on PI calf numbers (pink) and PI herd numbers (light blue). Right panel: Frequency distribution at mid-2016 of PI animals detected during each year of the programme still alive in the herd for more than 7 weeks following first detection (top axis translates into number of days in retention). (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article.)

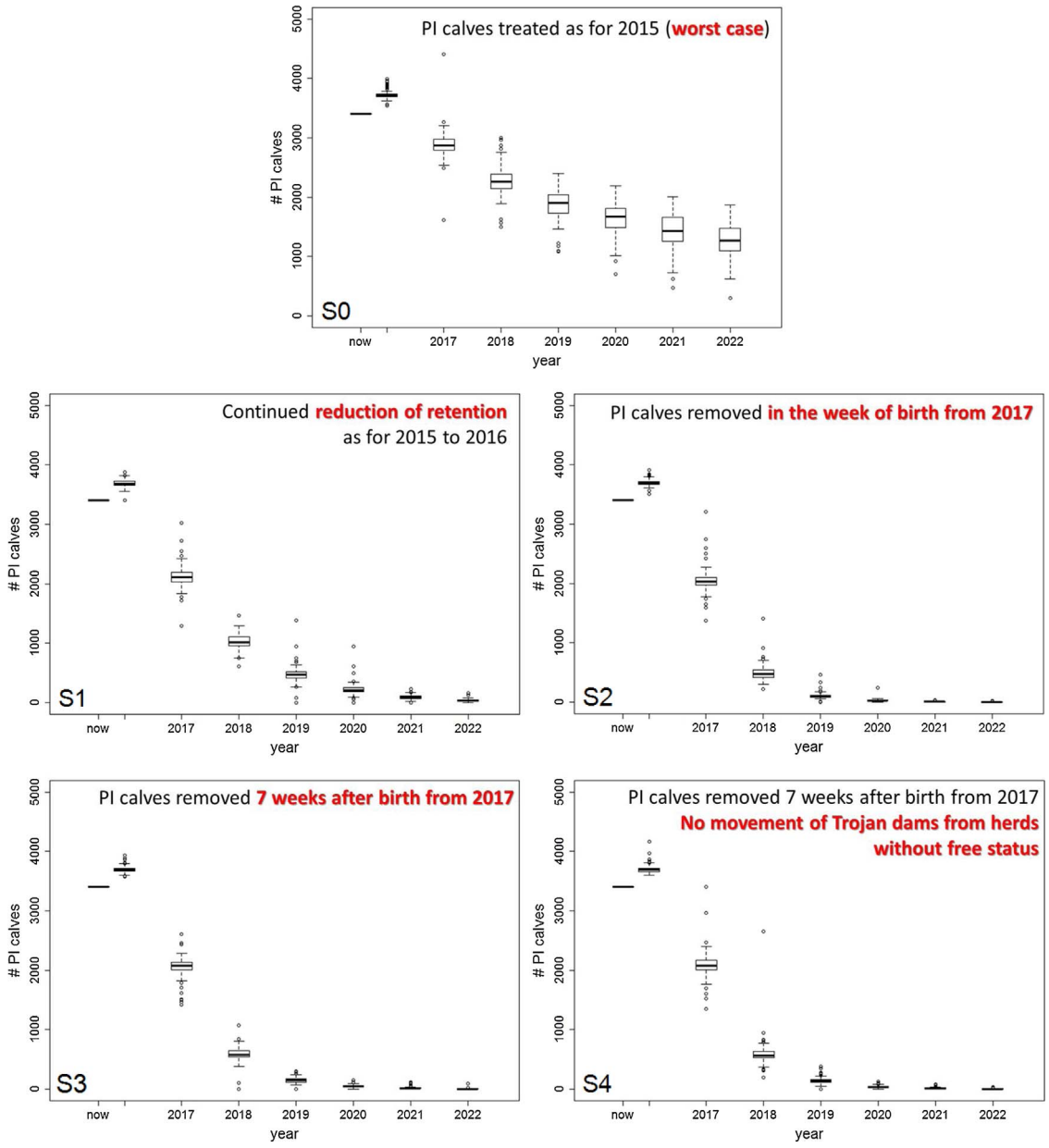

Fig. 3. Model prediction of the number of newborn PI animals in the Irish cattle population from August 2016 onwards (label "now"), based on simulations that account for control measures as applied in the Irish BVD eradication programme between 2013 and 2015 but considering alternative enforcement scenarios of measures for 2016 onwards (S0–S4). Predicted absolute numbers refer to newly detected calves per annum. Variability was introduced by testing disease and transmission related parameters for their sensitivity with regards to the annual dynamics of PI decline. Box-whisker plots are constructed from the median (bold line in box), interquartile range (IQR, box), whiskers representing least value within 1.5*IQR, and outlier values (small circles).

Our herd-level examination of costs saved by changing from tissue-tag testing of the new-born calves to young stock serological sampling was conducted using estimated animal-level costs of EUR 7.66 for serology versus EUR 2.50 for tissue-tag testing in herds with NHS status, which would be needed to allow the herd to switch to serology. Only herds breeding more than 30 calves per year would save money when changing to serological testing, i.e. 10 blood samples would equate to approximately EUR 76 annually, which would be exceeded if tissue-tag testing were used on 31 calves at a cost of EUR 77.50. However, even amongst herds producing > 30 calves a year, not all would have a large enough sample of young stock remaining on the farm for long enough to allow for young stock serology. Including both these criteria would leave about 25% of all 78,380 breeding Irish herds able to use serology to reduce costs (14% in beef and 78% in dairy breeders; Fig. 4).

On the basis of actual stock levels, we calculated the total testing costs which would be saved if these 25% of herds switched from tissue tag testing to serology (Fig. 5, top row). First, herd-level savings were calculated (right panel) and then divided by the number of breeding cows present, giving the animal-level savings per individual herd. The median value of savings was EUR 73.40 per herd (right panel) and EUR 1.22 per cow in the herd (left panel). Half of these 25% of herds would save less than EUR 73.40 in total and EUR 1.22 per cow in the herd. On the optimistic end of the distribution of savings from switching to serology, 99.95% of all Irish breeding herds would reduce annual costs by less than EUR 3.60 per cow (0.05% percentile equals EUR 3.59).

In Ireland and elsewhere, large herds are often not managed as one group, but rather as a number of smaller age-related management groups. Therefore, each management group of young stock needs to be tested independently due to the risk of limited BVDV transmission, and hence seropositivity, in situations where cohorts are reared separately.

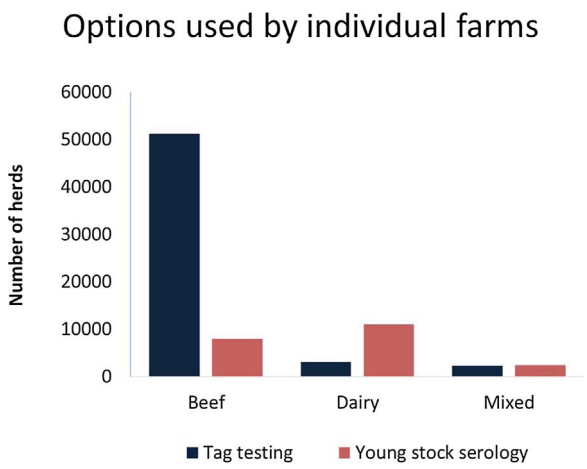

Fig. 4. Histogram of Irish herds as of 2015 for which a change in testing strategy from tissue tag testing to serology would be economically beneficial, by production type (blue – herd would continue tissue tag testing; red – herd would change to young stock serology). The reasons for herds not opting to change testing protocol are either because the herd size is too small (annual calf numbers are less than 31, this being the threshold at which the minimum cost level for serology is cheaper), or limited young stock are available in the month of testing (that is, a large numbers of young stock are traded from the herd). (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article.)

In this context, and assuming 50 breeding cows as the maximum size of a single management group, the savings which can be made from changing from tissue-tag testing of every calf born (at EUR 2.50 per calf) to serological sampling of 10 animals (at EUR 7.66 per sample) per management group, rather than per herd, are reduced. Under this assumption concerning management groups, half of the 25% of herds potentially participating in the strategy change would save less than EUR 33.60 per herd and EUR 0.56 per cow in the herd. Of all Irish breeding herds, 99.95% would – by switching test procedure – reduce annual costs by less than EUR 2.96 per cow (0.05% percentile equals EUR 2.95).

4. Discussion

Should there be a change in control measures during an active, ongoing BVD eradication programme with successful reduction in disease incidence? To answer this question, we reviewed literature, programme data from the compulsory Irish BVD eradication programme, and predictions from a dedicated BVD expert system model (FarmNet-BVD). This question was answered in the context of the Irish situation, however, lessons learnt from this example may stimulate a comparable evaluation of other national BVD eradication programmes, or indeed of control/eradication plans for different production diseases. Here, we consider available epidemiological information, contributing to the ongoing debate with respect to implementation of the current BVD eradication programme in Ireland (see animalhealthireland.ie/?page_id = 220).

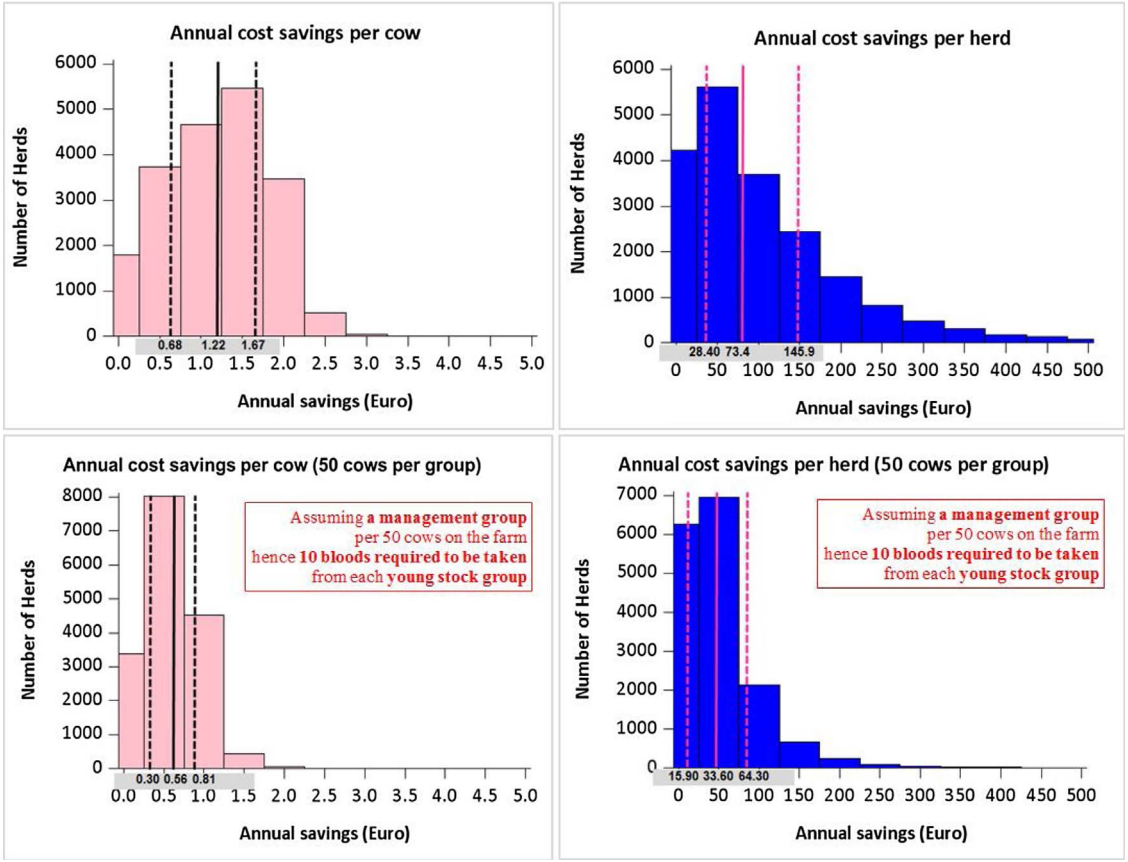

Fig. 5. Distribution, median (bold line) and quartiles (dotted lines) of expected annual savings shown per herd (right) and per individual cow (left column) for those 25% out of all 78,380 Irish breeding herds that could reasonably opt for changing the testing strategy from tissue-tag to serological tests (same herds as in Fig. 4). Data about herd structure, size of breeding cow cohort and the movements of breeding herds in Ireland 2015 were used to determine the expected savings from changing BVD control measures from tag testing to serology. The x-axis shows the savings realised for the herd, right: total saving for the herd, left: saving per cow in the herd. Upper panels: assuming all cows to be reared in one management group independent of herd size, lower panels: one epidemiologically independent management group for every 50 cows, with each group requiring its own set of test samples.

In line with other national programmes (Presi and Heim, 2010; Schwermer et al., 2012), the Irish BVD eradication programme applied compulsory ear tissue tag testing of every newborn calf. At the time of writing, four years of tissue tag testing had been performed, since the start of the compulsory phase in 2013. The steep decline of herd-level prevalence (about 75%, Fig. 2A) coupled with the ongoing annual costs of tissue tag testing (for approximately 2.2 million calves annually) formed the basis for reflections about the possibility, and appropriate timing, for a change to an alternative testing strategy. In this context, sample-based serological testing was proposed as an equally effective, but less costly, testing strategy as the programme moved towards eradication. A similar approach has been taken in the later stages of other national BVD eradication programmes, supported by cost-benefit calculations (Häsler et al., 2012; Thomann, 2016) or implemented once eradication had been achieved in individual herds, i.e. for demonstration of continued freedom in expectedly free herds (Greiser-Wilke et al., 2003; Houe et al., 2006). At the time of this discussion, there was sector-wide participation in compulsory use of tissue tag testing, and annual tagging of newborn calves had already been integrated into routine farm practice. Further, the current measures were universally recognised as effective, the programme (and industry-agreed) target was towards final eradication of the virus, and there was an acceptance of the need for disease management without compulsory preventive vaccination. Therefore, in the current study, the key issues did not relate to effectiveness or acceptance, but rather practical implications, improved insights in herd-level savings, and other options to address the likely difficulties faced during the final stages of a disease eradication programme (Del Rio Vilas et al., 2017).

4.1. Practical implications of implementing sample-based serology

Tissue tag testing is seen as an easy and effective method to eradicate BVD from a cattle population (Schwermer et al., 2012), and is readily understood by the farming community. This is reasonable as the regulations, the logistics and the diagnostic principles are straight forward, given the widespread use of these approaches internationally (Houe et al., 2006; Barrett et al., 2011; Presi et al., 2011; Duncan et al., 2016; Quinet et al., 2016; Wernike et al., 2017). Further, with this approach, it is possible to accumulate extremely detailed, animal-level epidemiological data (Table 1). The compulsory testing of all newborn animals contributes to a detailed understanding of the role of individual animals, which in the longer term allows for a detailed epidemiological understanding of the entire national population. With the rapid turnover of bovine animals in modern cattle management systems, it is possible to achieve a near-perfect understanding of the host population within 3–4 years, as documented e.g. in the Irish programme (Table 1). The importance of such data for epidemiological outbreak investigations and breakdown tracing is recognised in disease contingency measures (Caporale et al., 2001). In the Irish BVD programme, the added value of these data became apparent when quantifying acknowledged risk factors, e.g. transmission between contiguous herds (Graham et al., 2016) and the role of movement-based *in utero* introduction of PIs (Reardon et al., 2016).

Given this background, a transition to a sample-based investigation of serological status using animal bloods will result in the replacement of an approach that is easily communicated to one that is more complicated. Further, several testing approaches will need to be simultaneously applied in different herds depending on their herd status, the outcomes of which will then need to be integrated (Fig. 4). In addition to cost considerations, there is a need to consider logistical issues associated with the required mixing of serosurveillance, follow-up tag testing after detection, and milk and bulk tank screening during the mandatory programme aiming at fixed time-limit for eradication. Herds may also need to change their testing approach year by year reflecting the local BVD situation. These concerns would be less problematic if serosurveillance were established at the start of a programme or during post eradication surveillance. In these situations, with all stakeholders informed, programme implementation is guided by the serological status of the cattle population with respect to age and purpose (Schwermer et al., 2012). However, as long as the measures taken target the eradication of the virus, the animal-level data are of value (Kroschewski et al., 2006) and these will be diluted in their completeness due to the sample-based approach of serology. The Irish animal data on BVD status are the result of a four-year investment in tagging efforts, and any change would need to be considered with care, given the benefits that accrue with such data. In particular, there is no evidence that eradication would be achieved more quickly using serology (Thulke et al., 2017). Nonetheless, eradication has not yet been achieved, and epidemiological investigations will become increasingly relevant as the programme moves towards this final target (Del Rio Vilas et al., 2017).

4.2. Testing cost implications of implementing sample-based serology

The BVD eradication programme in Ireland is being implemented effectively using tissue tag testing. Therefore, considerations must be given to more than just strategic and logistic issues when considering a possible shift in national testing strategy. Therefore we reviewed the monetary aspects relating to the implementation of the alternative test approach, but under the assumption that funds required for implementation are covered and hence do not impact our discussion. The most striking insight was found during the in depth analysis of herd-level test options and associated savings per breeding cow. The following discussion refers to herds without BVD (i.e. NHS herds) as this is the prerequisite of applying the alternative testing strategy. Therefore, testing efforts are the relevant herd-level contribution to the national costs of BVD eradication. There is only a small share of herds that potentially gain from any monetary benefits of changing the programme strategy (i.e. 25% of Irish farms, respective 14% of beef and 78% of dairy farms; Fig. 4); therefore, three quarters of the sector will have no interests in the debate at all. We note that the actual percentage (here 25%) will change, depending on the number of young stock that would be required per herd for serosurveillance. Countries with either smaller or larger herds than Ireland will likely have a different percentage of herds that would benefit from a change in programme strategy. Most important, however, was the recognition after changing to serology that the herd-level savings of testing costs do not increase greatly. Considering the optimistic scenario of unstructured management (Fig. 5, top row), 75% of these herds would have saved less than EUR 150 per annum (Fig. 5, top right, Q1 EUR 145.90). In other words, 50% of potentially participating herds save at most EUR 1.22 per cow (Fig. 5, top left). What does this value imply? With the example of a dairy herd with an average annual milk yield per cow of 5000 L (IFA, 2014) and the equivalent to farm gate milk price of EUR 0.32 per litre (Dairy Market Blog, 2017), the annual saving per cow would correspond to 0.08% increase in milk production value of the cow, or, if these farms would instead continue tissue tag testing, a loss equivalent to farm gate milk price of 4 l milk per year (or 11.2 l using 0.05% percentile value of savings). These figures may vary slightly depending on assumptions regarding serology test price, season of blood sampling and sample size per herd (Tratalos et al., submitted). The benefits would be even less if young stock were managed as more than one management groups e.g. saving 1.75 l per cow per year instead of 4 (Fig. 5, bottom left).

Although the benefit from changing the testing protocol was found to vary substantially between Irish herds (including 70% with zero savings), effective BVD eradication is recognised as a challenge facing the whole sector rather than individual herds, a view confirmed by the economic literature (Hult and Lindberg, 2005; Schwermer et al., 2012; Graham et al., 2014; Sayers et al., 2015). Calculating the BVD on-farm losses separately for herds with and those without PI animals, Stott et al. (2012) found only small differences in their cost burdens caused by BVD circulating in the national cattle sector.

In the countries that have introduced eradication campaigns, the programmes have been shown to be cost effective (Houe, 2003). A population perspective is generally taken when conducting an economic evaluation of eradication or control programme. Similar literature also exists with respect to the economic evaluation of national BVD eradication programmes (Gunn et al., 2005; Valle et al., 2005; Häsler et al., 2012; Stott et al., 2012; Thomann, 2016; Pinior et al., 2017). In a detailed review of studies estimating economic losses and effects of control strategies both locally and nationally, Houe (2003) highlighted national losses of between EUR 9 and 36 million per million calves born. With about 2.2 million Irish calves born, the expected range would therefore have been EUR 20–80 million. The proposed figure for the losses due to BVD in the Irish cattle sector not accounting for vaccination was estimated about EUR 100 million (Stott et al., 2012). Indeed, the evaluation confirms the need for thorough epidemiological investigations conducted under the same conditions in which the programme is going to be applied (Houe, 2003). In the compulsory Irish BVD programme, tissue tag testing costs were estimated to be approximately EUR 9 million per year (Stott et al., 2012) which is likely overestimating the actual burden to the farming sector under existent prevalence levels. Equivalent annual figures with the alternative use of sample-based serological testing are not available. However, in the context of this study, the cost-effectiveness of the current testing strategy, in place since 2013, is not under scrutiny (Stott et al., 2012). Rather, the more pressing figure to understand is the direct costs of testing. There are testing costs regardless of approaches taken in the future to achieve virus eradication. Direct costs of applied diagnostic tests can be evaluated on the national scale and for the total future programme. Model-based research into this direction was undertaken for the Irish programme (Thulke et al., 2017), suggesting only a subtle difference between the two gross values due to the substantial price difference in the two tests in favour of the tissue tag testing. This difference was not sufficient to suggest a change in the testing approach from the one applied from the start of the programme. Rather, it was suggested that there may be potential benefits when analysing the programme testing costs dependent on the individual herd's characteristics i.e. size, production focus, calving patterns or BVD status with the results now available and shown in Figs. 4 and 5.

An additional argument became apparent when comparing national-level cost estimates of BVD (i.e.) EUR 100 million; Stott et al. (2012) to the estimate of annual eradication effort (i.e. EUR 9 million) in combination with the programme performance (Fig. 2A). In fact, 75% of herds harbouring PI animals at the start of the measures no longer suffer losses after four years into the programme (Fig. 2A). One may reasonably argue that the 75% reduction in PI herds does not directly convert to a reduction of losses by about EUR 75 million (i.e. 75% reduction in the EUR 100 million pre-programme BVD burden). Nevertheless, assuming that the pre-programme costs would have continued in the absence of the national programme, then the current annual costs of BVD will be substantially lower, even after accounting for the EUR 9 million programme costs that incur annually. The aim of the programme is to eradicate the virus. Logically, and after virus eradication, the aim of possible measures to monitor BVD free populations may be considered with the altered objectives of surveillance (Houe et al., 2006; Thulke et al., 2009).

4.3. Enforce BVD eradication using tissue tag testing

Following a review of the Irish programme data, including a clearer understanding of the cost implications of the change from complete tissue tag testing to sample-based blood tests, we conclude that the evidence for a changed national testing strategy is not compelling.

In these last paragraphs, we therefore take a different viewpoint, namely addressing the uncertainty associated with an expected timeline to eradication through continued tissue-tag testing. Uncertainty can be the reason why the sector's investment into BVD eradication is repeatedly reviewed and also why the industry has effectively decoupled annual expenses from losses prevented. In particular, if the current approach lacks useful indicators of successful achievement of the objectives, positive results may turn into struggles with fatigue and compliance.

It can be very difficult to gain a robust understanding of future events in systems that are influenced by human decisions and behaviours (Kopéc et al., 2010). The only feasible approach is rigorous evaluation of data and expert understanding and projection of this system thinking into the future. Indeed, an approach combining explicit process-modelling and scenario analysis is now well established for animal health decision issues and contingency planning of exotic diseases (Dijkhuizen et al., 1991; Hurd and Kaneene, 1993; Garner and Hamilton, 2011; Thulke, 2011; Webb et al., 2017). The forecasting technique, with all its acknowledged limitations, was applied to reduce uncertainty in the context of continuation of the Irish eradication programme.

In our study, the simulated scenarios represent an increasingly stringent implementation of PI removal. Indeed, if less optimal efforts are implemented from the start, the ultimate objective can still be achieved, if the programme allows for flexibility of the regulations (Hult and Lindberg, 2005). Rather than strategy change, these amendments target programme improvement to meet the final aim of BVD eradication.

It is well acknowledged that the detection and removal of PI animals facilitates effective BVD eradication on farm and on the national scale (Houe et al., 2006; Lindberg et al., 2006; Schefers et al., 2009; Lanyon and Reichel, 2013; Laureyns, 2014). There is less research available regarding the temporal dynamic of PI decline during an effective eradication programme. However, an understanding of this latter issue may allow programme progress to be monitored, thereby limiting the uncertainty regarding future investments towards final eradication. Expert system modelling has addressed the comparative performance of the main testing alternatives with regards to the impact on the national PI subpopulation (Thulke et al., 2017). The study also highlights the negative impact of PI retention on the expected time to eradication, highlighting non-compliance with PI removal as the major drawback in the early years of the Irish programme. With the simulation of alternative enforcement scenarios of PI removal, we seek to establish indicative figures about the PI decline that could be tested against recordings in the future of the programme. For discussion, we summarise key aspects of the model results shown in Fig. 3 by plotting the median line of the five panels therein (Fig. 6).

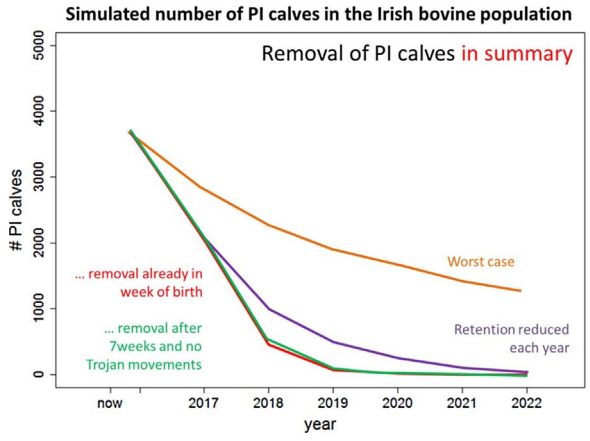

Fig. 6. Model prediction of the number of newborn PI animals in the Irish cattle population from August 2016 onwards, based on simulations that account for control measures as applied in the Irish BVD eradication programme between 2013 and 2015 but considering alternative enforcement scenarios of measures for 2016 onwards. Here only the median data of Fig. 3 are shown (bold lines within boxes of Fig. 3). Each line graph corresponds to one panel of Fig. 3.

The worst case scenario implies future PI removal with the same characteristics as during 2015; that is, an ongoing, serious problem of PI retention, preventing finalisation of the eradication programme. Retention in the Irish data is not an artificial phenomenon, despite a clear understanding by stakeholders of its adverse effects on the whole programme (Clegg et al., 2016). Although rare, there are examples of herds with PIs surviving for more than 100 weeks (Fig. 2B). Efforts at enforcing PI decline should take these retention characteristics into account. The proof of concept can be seen in the Irish 2016 data on PI reduction (Fig. 2A). In the third year of the programme, the awareness of stakeholders was reinforced following the analysis of PI retention data, and model-based predictions of time to eradication dependent on PI retention levels. As a consequence, there was an observed increase in annual PI incidence reduction (from approximately 2k to approximately 4k fewer PIs), leading to the highest efficiency (50% rather than 30% decline) seen in any year of the programme (Fig. 2A). In Scenario S1 (retention reduction), the same performance (i.e. 50% reduction of retention herds) was put forward, with eradication following 10 years of tissue tag testing (2013–2022). Further reductions in PI retention would likely shorten the time to successful eradication (Laureyns, 2014).

Subsequent scenarios sought to address these transitions by excluding the retention of PI calves. Further, two scenarios (S2 & S3; Fig. 3) addressed the impact of an imposed early removal. While S2 is considered optimistic, S3 implements PI removal within seven weeks of birth. Theoretically, PIs that were identified within three weeks of age, in accordance with Irish regulations, could be immediately disposed (S2). With such stringent measures, there is a fall in PI incidence, and eradication is achieved two years earlier. We accept that 'instantaneous disposal' cannot be easily implemented e.g. due to logistics. With Scenario S3, where we sought to be both optimistic and practical, near eradication is achieved in the ninth year of tissue tag testing. Hence other stringent measure may be necessary to enforce reduced PI incidence. The literature suggests that BVDV perpetuation on the national scale is dominantly driven by animal movement into unaffected herds (Courcoul and Ezanno, 2010). Programme data further demonstrates the importance of Trojan incursions, i.e. the introduction of *in utero* PIs (Reardon et al., 2016). Hence, in scenario S4 (forced removal & movement restrictions) we suppressed untagged PI calves and *in utero* PIs being moved off herds with a BVD risk status (non-NHS). Based on model results, the impact is similar to the theoretic optimum (scenario S2), with eradication levels being achieved after eight years of tissue tag testing.

As outlined by Laureyns (2014), programme rules should be concise and simple to explain at the start of an eradication programme, gradually becoming more stringent and detailed during later programme stages. As illustrated in the modelled scenarios (i.e. dramatic increase in PI removal following detection, prevention of movement of PI from non-status herds), the Irish measures may need to go beyond existing rules. This, hopefully, will be the right answer to the observed compliance and awareness issues. With support from industry stakeholders, these more stringent measures are reflected in the 2017 regulations of the Irish national BVD programme.

It is well acknowledged that predictions towards future consequences of decision, efforts and regulations may not necessarily be realised. Nonetheless, there is much value in hypothetical considerations driven by programme data and model-based forecasting in response to hypothetic argumentations. First, the range of adequate expectations of near-term programme outcome is settled down to manageable variability; and second, decisions towards less purposeful programme changes may be prevented to the benefit of the investment made in the past. To be explicit, the multi-approach analysis presented here does not seek to be used for comparison with other national BVD eradication programmes based on either tissue tag testing or blood sample serology. The focus was rather an epidemiologically driven approach to address issues internal to an effective disease programme. There are many options for serological testing, using blood or either individual or bulk milk, in BVD management and strategies for incorporating these into an eradication programme beyond the approach considered in this paper. Further, there are many particularities in different national control or eradication programmes, including sample size, sample type and sampling time that need to be considered. It was not the intention of this work to provide an overarching assessment of the conditions where serology may be as good as tag testing − the latter indeed could also be performed differently from that proposed here, for Ireland. Rather, we were interested to assess the consequences of changes from an existing to an alternative procedure, within the practical context of the Irish eradication programme.

5. Conclusions

Without logical and quantitatively convincing reasons, the principle of not changing a working system may be seen as pivotal in questioning any efforts to bring into effect a change in animal health strategy. A decreasing efficiency of control measures towards the end of programmes addressing animal health issues is well recognised. We conclude that continuing an approved approach but with some refined implementation is an option to consider i.e. as it might stand to reason for the Irish BVD eradication programme using tissue tag testing. Aiming at BVDV eradication, we did not find compelling quantitative arguments in favour of a strategy change under Irish programme conditions. Budgetary benefits were limited for the individual beneficiary and highly skewed between them. Options to enforce PI removal and safeguarding non-compliance are straight to superimpose to a running protocol and predictive of shortening the programme. We further conclude that structured monitoring of the Irish BVD programme allowed critical stakeholder concerns to be addressed, and consequences to be quantified. The assembled information provides scientific arguments, contributing to an informed debate of the pros and cons of a change in eradication strategy in Ireland. Finally, we conclude that rumours, attitudes and expectations can influence anticipated future outcomes and hence decisions taken into the future. The less that prediction is grounded in quantitative assessment methods and the less transparent accepted uncertainties are, the more that a good strategy may become vulnerable to misguided calls for action.

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Appendix A. Supplementary data

Supplementary data associated with this article can be found, in the online version, at https://doi.org/10.1016/j.prevetmed.2017.11.017.

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