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Temporal trends in the retention of BVD+ calves and associated animal and herd-level risk factors during the compulsory eradication programme in Ireland

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ABSTRACT

The national BVD eradication programme in Ireland started on a voluntary basis in 2012, becoming compulsory in 2013. The programme relies on accurate identification and prompt removal of BVD+ calves. However, a minority of herd owners have chosen to retain BVD+ animals (defined as still being alive more than seven weeks after the date of the initial test), typically with a view to fattening them to obtain some salvage value. During each year of the programme, additional measures have been introduced and implemented to encourage prompt removal of BVD+ animals. The objective of this study was to describe temporal trends in the retention of BVD+ calves and associated animal and herd-level risk factors during the first three years of the compulsory eradication programme in Ireland.

The study population included all BVD+ calves born in Ireland in 2013–2015. A parametric survival model was developed to model the time from the initial BVD test until the animal was slaughtered/died on farm or until 31 December 2015 (whichever was earlier). A total of 29,504 BVD+ animals, from 13,917 herds, were included in the study. The proportion of BVD+ animals that were removed from the herd within 7 weeks of the initial test date increased from 43.7% in 2013 to 70.3% in 2015. BVD+ animals born in 2015 had a much lower survival time (median = 33 days) compared to the 2013 birth cohort (median = 62 days), with a year on year reduction in survival of BVD+ calves. In the initial parametric survival models, all interactions with herd type were significant. Therefore, separate models were developed for beef and dairy herds. Overall the results of the survival models were similar, with birth year, BVD+ status, herd size, county of birth and birth month consistently identified as risk factors independent of herd type (beef or dairy) or the numbers of BVD+ animals (single or multiple) in the herd. In addition, the presence of a registered mobile telephone number was identified as a risk factor in all models except for dairy herds with a single BVD+, while the sex of the BVD+ calf was only identified as a risk factor in this model.

Significant progress has been made in addressing the issue of retention of BVD+ calves, however, there is a need for further improvement. A number of risk factors associated with retention have been identified suggesting areas where future efforts can be addressed.

1. Introduction

Bovine viral diarrhoea virus (BVDV) is an economically important pathogen of cattle and is present in many countries worldwide (Anon, 2012a). Transient infection with the virus can result in immunosuppression and a range of reproductive problems including abortion, foetal mummification and a range of teratogenic effects on the central nervous system (Lanyon et al., 2013). In addition, foetal infection with a non-cytopathic biotype of the virus prior to approximately 120 days of gestation will result in the birth of an immunotolerant, persistently infected (PI) calf if it is carried to term (Nettleton and Entrican, 1995; Houe, 1999). Whilst these PI animals typically have a reduced life expectancy relative to their non-PI comrades (Houe, 1993; Taylor et al., 1997; Graham et al., 2015a), they are recognised as playing a key epidemiological role,

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shedding virus in all secretions and excretions. As a result, their identification and removal are central to efforts to control and eradicate the disease at farm, regional or national level (Lindberg and Alenius, 1999; Lindberg et al., 2006).

An industry-led national BVD eradication programme is currently underway in Ireland. This started as a voluntary programme in 2012 (Graham et al., 2014), becoming compulsory on 1st January 2013 (www.animalhealthireland.ie). The programme includes 80,000 breeding herds, of which 73% are beef, 22% are dairy and 5% are dual enterprise herds, with an average overall herd size of 66 animals (beef = 45 animals, dairy = 135 animals and dual = 96 animals). Since 1st January 2013, national legislation (Anon, 2012b, 2014a) requires that a tissue tag sample is collected from all calves within 20 days of birth and submitted by the farmer to one of several laboratories designated to test it for BVD viral antigen or RNA. Calves with a positive or inconclusive result are considered to be PI for the purposes of the programme until shown otherwise. The legislation underpinning the programme provides the option for a confirmatory re-test to be carried out, but this is not mandatory, with some herd owners electing to cull animals on the basis of the initial positive result. Between 2013 and 2015, 71% of calves with an initial positive result were subject to re-test, of which 82% tested positive (unpublished data). A re-test is permitted to differentiate between PI and transiently infected (TI) animals, with a recommended interval of at least three weeks between sample collections. All results are reported to a central database managed by the Irish Cattle Breeding Federation (www.icbf.com) and calves with a positive result are not permitted to move, except to slaughter. The same restriction applies to animals assigned a suspect status, with this most commonly applying to the untested dams of PI calves. The programme database is also used to generate a series of reports to monitor progress at both animal and herd level (http://animalhealthireland.ie/?page_id=220). Significant progress has been made to date, with the animal-level prevalence of PI births showing a two-fold decrease from 0.66% in 2013 to 0.33% in 2015. The prevalence of herds with one or more positive results has shown a similar decline during this period, falling from 11.28% to 5.91%. Results for the first months of 2016 show continued progress. By June 2016, results were available for approximately 1.7 M of the anticipated 2.2 M (77%) annual calf crop, with only 0.15% PI births from 2.52% of herds.

While the legislation underpinning the programme prohibits the sale of PI animals, it does not, in the absence of formal compensation, require their immediate slaughter. The BVD Implementation Group (BVDIG), which oversees the programme, has consistently recommended their prompt removal. However, a minority of herd owners have chosen to retain PI animals (defined in this context as still being alive more than seven weeks after the date of the initial test), typically with a view to fattening them to obtain some salvage value. Studies using national data have demonstrated the impact of the retention of PI animals at animal, herd and ultimately programme level. Consistent with international studies (Houe, 1993; Taylor et al., 1997), PI animals identified in the programme did not survive or thrive as well as their non-PI comrades. Further, herds that retained them were more likely to have additional PI births the following year, particularly if they were retained into the breeding season (Graham et al., 2015a,b), and contiguous herds were also shown to be at greater risk (Graham et al., 2016a). The negative impact of the retention of PI animals on the programme were reinforced by the results of a recent modelling exercise (Thulke et al., 2016), demonstrating a consequential extension of the forecasted time to eradication. In recognition of the challenge posed by retention of PIs, the BVDIG has, in conjunction with the Department of Agriculture, Food and the Marine (DAFM), implemented a number of measures to encourage their removal and minimize their impact. A range of strategies, guided by underpinning research (Graham et al., 2015a,b, 2016a,c), have been used to encourage prompt removal of BVD+ animals. These include an ongoing series of educational messages through a variety of media including the farming press (both print and digital), publications issued by AHI stakeholder organisations, particularly those represented on the cross-industry BVD Implementation Group that oversees the programme, local radio and the AHI website (www.bvdfree.ie). In addition, each herd owner with a BVD+ calf receives several communications from the programme database provided by the Irish Cattle Breeding Federation (www.icbf.com) in relation to both initial and follow-up testing, including SMS messages (where a mobile phone number has been provided) and letters providing details of the positive animal, its results and recommended next steps (including disposal). The BVD Helpdesk also attempts to contact each herdowner following the first positive result for their herd in a given year to reinforce key programme messages, including the need to dispose of BVD+ calves. Finally, limited financial supports up to €140 per animal to encourage removal of PIs within five weeks of the date of first test result, targeted at those most affected economically by the birth and removal of a BVD+ calf have been provided by DAFM during the programme, with these evolving over time based on underpinning research (see Supplementary material for further details or https://www.agriculture.gov.ie/animalhealthwelfare/diseasecontrol/bovineviraldiarrhoeabvd/). Conversely, in 2015 beef herds that were retaining PI animals were excluded from enrolling in the Beef Data Genomics Programme (BDGP) and accessing the financial supports available thereunder, while BDGP members will also have financial supports withheld if they retain PI calves born subsequently (see Supplementary material or http://www.agriculture.gov.ie/media/migration/farmingschemesandpayments/beefdataprogrammebdp/2015/BDGP050515.pdf).

The objective of this study was to describe temporal trends in the retention of BVD+ calves and associated animal and herd-level risk factors during the first three years of the compulsory eradication programme in Ireland.

2. Materials and methods

2.1. Study population

The study population included all BVD+ (BVDPOS and BVDPI) calves born in Ireland from 1st January 2013 to 31 December 2015 (the study period) and tested prior to 1st January 2016. A BVDPI is an animal that was positive for BVDV at both the initial test and a re-test while a BVDPOS is an animal that was positive for BVDV on the initial test but was not re-tested. Animals with an initial inconclusive result and no re-test were excluded from the analysis. Those animals that were born dead (i.e. had a date of death equal to the date of birth) were also excluded from the analysis.

Data for this study were obtained from the Irish Cattle Breeding Federation (ICBF), the Animal Identification and Movement (AIM) database of DAFM and the Land Parcel Information System (LPIS) for herd location in 2015.

2.2. Definition of retention

The length of retention was calculated as the time from the initial test date until removal (either dead on farm due to euthanasia or natural causes or sent to slaughter) or until 31st December 2015, whichever was sooner. A ‘retained’ animal was defined as any BVD+ calf that remained on the farm of birth for more than 7 weeks (49 days) after the date of the initial test. Seven weeks is the period following the date of the initial test within which BVD+ animals

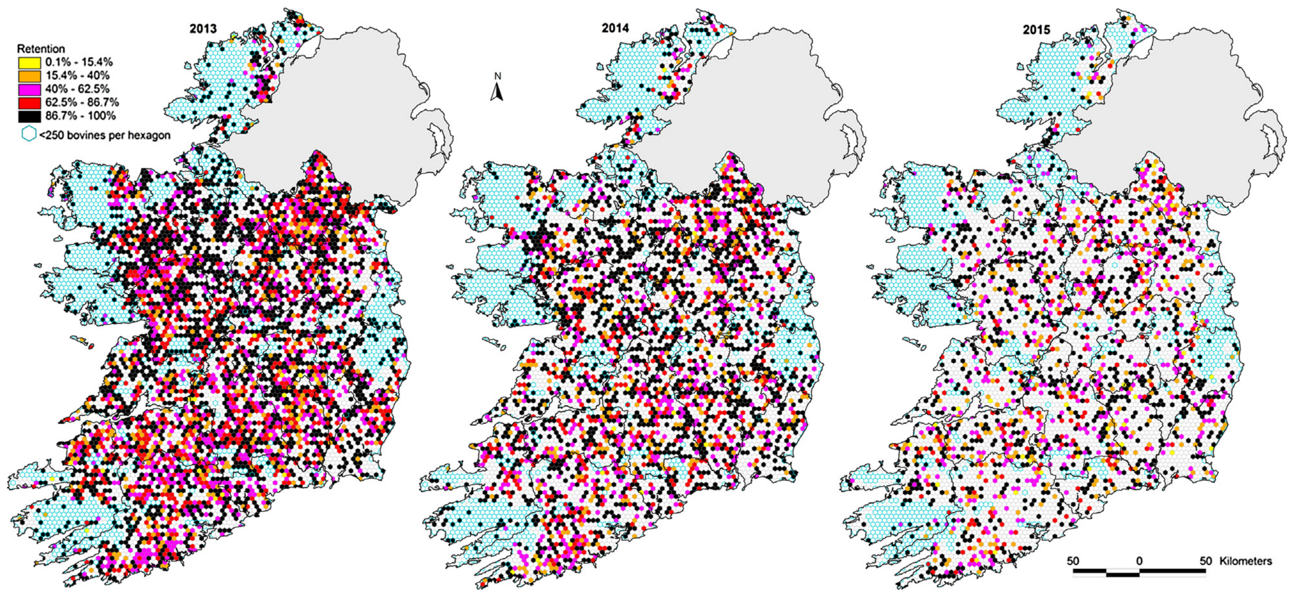

Fig. 1. Geographical distribution of the percentage of BVD+ calves in Ireland retained for more than 7 weeks from the initial test by year of birth. Each hexagon covers an area of 10.0 km^2.

must be removed to qualify for financial supports from DAFM (see Supplementary materials). This period is considered sufficient to allow the herd owner to conduct a re-test, receive the result and act upon it.

2.3. Descriptive analyses

a. Description of the trends in BVD+ retention

Descriptive analyses were conducted to determine:

- The proportion of BVD+ animals by length of retention for each birth cohort (2013, 2014 and 2015).
- The population of BVD+ animals that were alive on the last day of each calendar month across time and by birth cohort.
- The proportion of BVD+ animals alive by time from initial test date, birth cohort and herd type, using Kaplan Meier survival curves.
- The proportion of animals that were retained (for >49 days from the initial test) and the median survival time by the following risk factors: sex, herd type (dairy, beef or dual purpose as categorised by the Irish Cattle Breeding Federation (ICBF)), year of birth, mobile number (presence/absence on database), BVD+ status (BVDPOS or BVDPI), herd size (number of calves registered in year of birth of BVD+ animal), month of birth and county. Whether the proportion of animals retained was independent of each of the risk factors was tested using a chi-square test.

b. Patterns of retention of BVD+ animals within herds over time

Study herds were defined as any herd in which one or more BVD+ calves were born between 2013 and 2015 inclusive. For each study herd, the number of years in which one or more BVD+ calves were born was determined and the number of these birth years during which a study herd retained one or more BVD+ calves (for >49 days since the initial test date) was examined. For example, if a study herd had a BVD+ calf in 2013 and retained it, then had a BVD+ calf in 2014 and also retained it, then this would be counted as having a BVD+ calf in 2 years and retaining BVD+ calves twice. If a herd had a BVD+ calf in 2013 and retained that calf until 2015 then this would be counted as having a BVD+ calf in 1 year and one retention. Similarly, if a herd had a BVD+ calf in 2013 and retained it and a BVD+ calf in 2014 and did not retain it then this would count as a herd having BVD+ calves in 2 years but retention in only one year.

2.4. Multivariable analyses

A parametric survival model was developed, using STATA version 14 (StataCorp LP, College Station, Texas, USA) to model the time from the initial BVD test until the animal was slaughtered/died on farm or until 31 December 2015 (whichever was earlier). To determine the appropriate distribution of the baseline hazard, six distributions were compared including exponential, Weibull, lognormal, log-logistic, generalised gamma and Gompertz. Selection of the appropriate distribution was based on comparing the log-likelihood and AIC from a null model. A model was initially fitted without accounting for clustering within herds then refitted using cluster-adjusted robust standard errors to account for the additional correlation (results are presented in the Supplementary material). This latter method adjusts the standard errors but has no impact on the point estimates. Since more than half of the herds (58%) had only one BVD+ animal during the study period, the sample was also split and two separate models developed, one for herds with only a single BVD+ animal and another for those with multiple BVD+ animals. For the model that included herds with multiple BVD+ animals, a frailty effect was included to account for the clustering of animals within a herd. The frailty distribution can be either Gamma or inverse Gaussian. The appropriate distribution was determined based on the log-likelihood from a null model.

The risk factors considered in the survival models were: month/season of birth, year of birth, herd type, herd size (number of calves within the herd in the birth year), county/province/region, sex, BVD+ status, mobile number (presence/absence on database). A backward selection procedure was used to remove terms from a full model, based on a likelihood ratio test ($p > 0.05$). The choice of the appropriate format for continuous variables was based on comparing the AIC of a univariable model of the variable categorised into 5 groups to the AIC from a univariable model that included just the continuous variable. In addition, a lowess smooth plot of the martingale residuals was used to examine the appropriate functional format of the continuous variable. In order to choose between the location variables (county, province and region) and the variables month and season, the AIC of univariable models were compared.

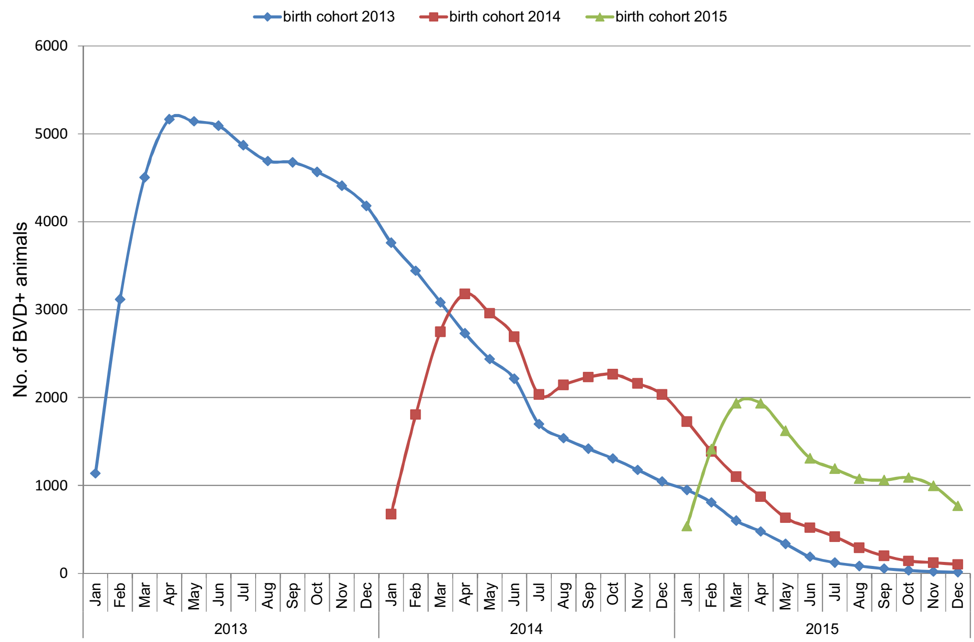

Fig. 2. Number of BVD+ animals in Ireland alive at the end of each month by birth cohort 2013–2015.

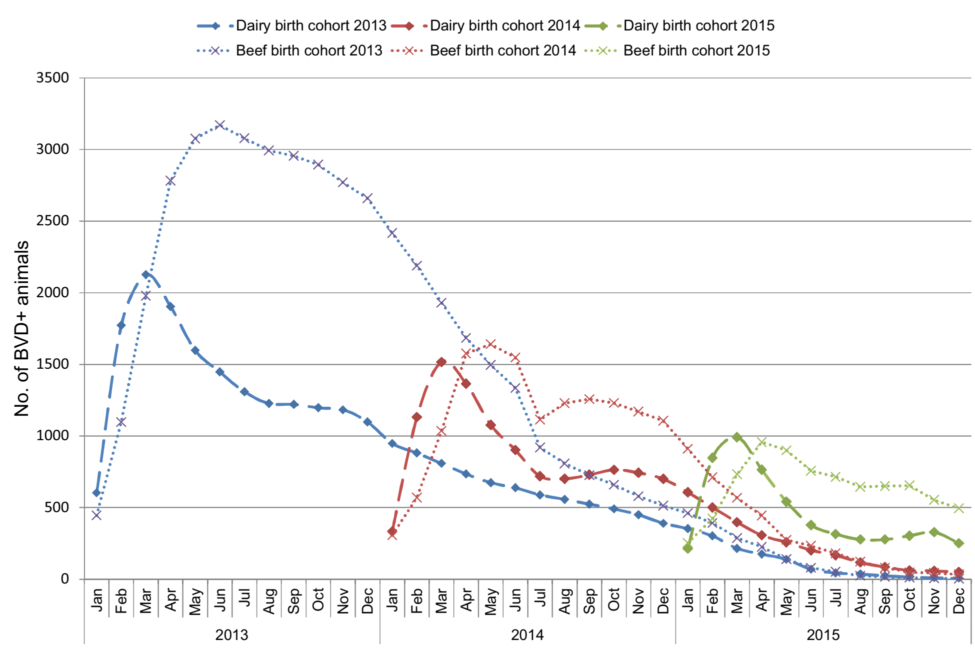

Fig. 3. Number of BVD+ animals in Ireland alive at each month by birth cohort in beef and dairy herds.

Two-way interactions between herd-type and sex, herd-size, location, year and month were tested in the initial full model.

An accelerated failure time metric was used in order to simplify the interpretation of the results when a shared frailty was included in the model and to compare results. Coefficients from the models were expressed as Time Ratios (TRs), which can be interpreted as the relative effect on the mean time to event. A TR < 1 can be interpreted as having a shorter time to event compared to the reference category. The goodness-of-fit of the final model was assessed using plots of cox-snell and deviance residuals.

Herds were assigned a point location based on the centroid of their largest fragment of land. All herds were then spatially assigned to a hexagonal grid with a 2 km radius and an area of 10 km^2. The total number of calves born and the number of BVD+ calves born were summed for each hexagon for 2013, 2014 and 2015 respectively. Maps were created using ArcGIS 10.3 (ESRI, Redlands, California, USA) showing total BVD+ calves born per year, the number of BVD+ calves retained for more than 7 weeks after the initial test date and as the percentage of BVD+ calves retained for more than 7 weeks.

3. Results

The following BVD+ calves were excluded from the study: 660 animals born dead (ie the date of death was the same as the date of birth); 109 animals that had an inconclusive result at the initial test and were not tested again, and a further 46 animals that had died but did not have a recorded date of death. A total of 29,504 BVD+

Table 1
Number of BVD+ animals born in Ireland each year by length of retention until recorded date of death or the number of BVD+ animals still alive at 31 December 2015.

Retention length (days)	Year of birth					
	2013		2014		2015	
	No.	%	No.	%	No.	%
0–49	5755	43.7	5208	55.7	4906	70.3
50–120	2548	19.3	2062	22.1	1016	14.6
121–150	418	3.2	314	3.4	95	1.4
151–180	344	2.6	196	2.1	75	1.1
181–365	1618	12.3	922	9.9	120	1.7
>365	2482	18.8	539	5.8		0.0
Alive	15	0.1	103	1.1	768	11.0
Total	13180		9344		6980	

animals, from 13,917 herds, were included in the study. Of these 8026 herds had only 1 BVD+ animal (62.9% beef herds, 29.5% dairy herds) and 5891 herds had >1 BVD+ animals (51.7% beef herds and 39.3% dairy herds). There was a median number of 1 BVD+ animals per herd per year (interquartile range: 1–2), with a maximum of 56 BVD+ animals per herd (within a year). The median number of BVD+ animals per herd was the same for dairy and beef herds (1 BVD+). However, the interquartile range for dairy herds (1–3 BVD+) was slightly wider than that for beef herds (1–2 BVD+) and the maximum number of BVD+ animals was also greater (55 in dairy herds, 25 in beef herds).

3.1. Description of the trend in BVD+ retention

The proportion of BVD+ animals that were removed from the herd within 7 weeks of the initial test date (49 days) increased from 43.7% in 2013 to 70.3% in 2015 (Table 1). Retention of BVD+ calves occurred across the country, with no clear geographical pattern evident in the percentage of BVD+ calves retained (Fig. 1; see Supplementary material Figs. S1 and S2 for maps showing the distribution of the numbers of BVD+ calves born and retained each year). The proportion of BVD+ animals born each year that were still alive at the end of the study period increased incrementally from 2013 to 2015, reflecting the decreasing time interval available for their removal. Indeed, 242 of the 768 still alive at the end of 2015 were tested in the last two months of the year and had been retained for less than 49 days so far. A higher number of BVD+ calves were born in beef than dairy herds in 2013 (6631 and 5367 respectively) reflecting the higher number of beef herds in Ireland (61,000 beef herds compared to 18,000 dairy herds) with these numbers falling to 3370 BVD+ beef calves and 2888 BVD+ dairy calves in 2015. The number of BVD+ calves remaining alive each month from 2013 to 2015 by birth cohort is shown in Fig. 2, highlighting both the decline in the number of BVD+ animals being born over time and the decrease in their retention. The same figure by herd type is shown in Fig. 3. The peak numbers of BVD+ calves in dairy herds was recorded in the February of each year, reflecting the peak calving month for dairy herds (Anon, 2014b, 2015, 2016). In contrast, the peak numbers of BVD+ calves in beef herds was recorded in June for the 2013 birth cohort, in May for the 2014 birth cohort and in April for the 2015 birth cohort. Peak calving among beef herds falls in March and April, (Anon, 2014b, 2015, 2016) therefore the peak number of BVD+ calves reflects both a peak in calving and retention of BVD+ calves. In 2013 the maximum number of BVD+ calves alive in beef herds exceeded the maximum number alive in dairy herds by approximately 50%, whereas the maximum numbers alive in 2014 and 2015 was similar for both herd types.

There was a significant difference (log-rank test $p < 0.001$) in the survival time from the initial test for BVD by birth cohort (Fig. 4).

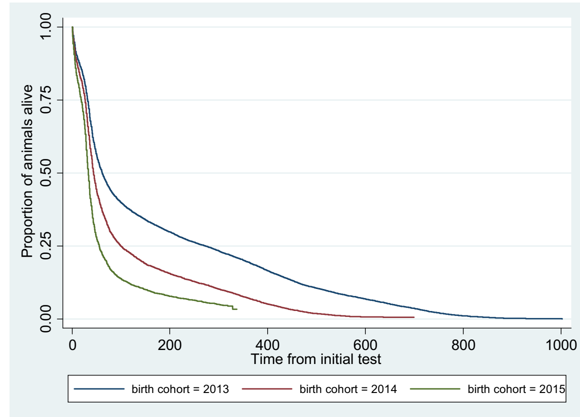

Fig. 4. Survival curves of all BVD+ animals in Ireland from the time of birth by birth cohort.

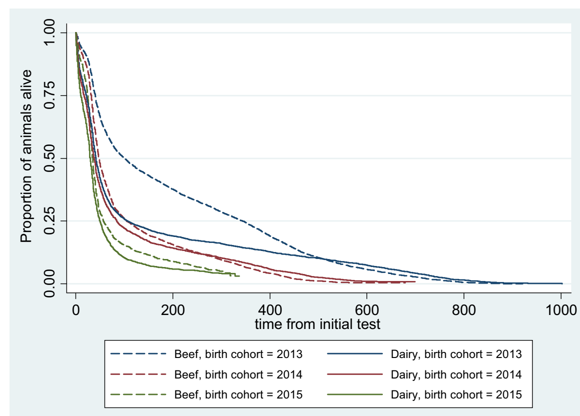

Fig. 5. Survival curves of BVD+ animals in Ireland from the time of birth by birth cohort in beef and dairy herds.

The median survival time for all animals was 45 days. Animals born in 2015 had a much lower survival time (median = 33 days) compared to the 2013 birth cohort (median = 62 days), with a year on year reduction in survival of BVD+ calves (Table 2). Overall, animals in beef and dual type herds had a longer median survival time compared to animals in dairy herds (Table 2). There was a significant difference in the survival rate of beef and dairy herds by birth cohort (log rank test $p < 0.001$). The removal rate was faster for animals in dairy herds compared to beef herds (Fig. 5), with this being particularly evident in 2013. However, for beef herds the removal rate increased for the 2014 and 2015 birth cohorts to levels similar to those for dairy herds.

The proportion of animals retained for more than 49 days since the initial test date by risk factors for retention are shown in Table 2. There were significant differences in the number of animals retained for all the risk factors examined with the exception of sex. A higher proportion of animals in beef herds, animals with a BVDPI status, in herds without a mobile phone number registered on the database, born in earlier years, born in summer months and born in Dublin, Longford and Roscommon were retained.

3.2. Patterns of retention of BVD+ animals within herds over time

Overall of 13917 study herds 22.1% (2691 + 387 = 3078 herds) had one or more BVD+ calves in more than one year (Table 3). Of the 77.9% of herds with BVD+ births in only one year, 48.6% retained a calf or calves. Of 19.3% of herds with BVD+ calves in 2 years, 73.1% (39.4% + 33.7%) retained a calf or calves in 1 or more

Table 2
The proportion of animals that were retained in their birth herd for more than 49 days since the initial test for BVD, for 29,504 BVD+ animals born between 2013 and 2015 in Ireland.

Variable	Class	No. of BVD+ animals	% retained for >49 days[a]	P-value	Median survival time (days)
Sex	Female	14577	45.4	0.917	45
	Male	14927	45.4		45
Herd type	Beef	14642	51.6	<0.001	53
	Dairy	12161	36.4		37
	Dual	2418	51.5		53
	Not provided	283	56.5		60
Birth Year	2013	13180	56.3	<0.001	62
	2014	9344	44.3		44
	2015	6980	26.2		33
Mobile registered	No	656	65.4	<0.001	93
	Yes	28848	44.9		45
BVD+ status	BVDPOS	8569	23.1	<0.001	14
	BVDPI	20935	54.5		56
Herd-size	1–17	6268	54.3	<0.001	58
	18–32	5635	50.9		52
	33–54	5905	46.6		46
	55–90	5803	41.5		41
	>90	5893	33.2		34
Birth Month	January	2478	39.3	<0.001	40
	February	5236	39.3		40
	March	5812	43.2		42
	April	4645	47.7		47
	May	3088	54.8		58
	June	1700	53.1		55
	July	1360	56.7		66
	August	1167	55.9		60
	September	1214	47.6		47
	October	1171	38.4		41
	November	962	36.4		45
	December	671	35.6		42
County	CARLOW	377	50.1	<0.001	52
	CAVAN	1224	43.0		41
	CLARE	1383	46.3		44
	CORK	3920	41.7		42
	DONEGAL	968	42.0		41
	DUBLIN	123	56.1		63
	GALWAY	2250	48.4		48
	KERRY	1669	43.3		44
	KILDARE	574	50.0		52
	KILKENNY	1265	42.6		43
	LAOIS	861	41.2		40
	LEITRIM	415	44.1		45
	LIMERICK	1785	42.2		41
	LONGFORD	496	55.8		61
	LOUTH	373	50.7		53
	MAYO	1442	47.4		48
	MEATH	994	43.2		43
	MONAGHAN	1180	51.3		55
	OFFALY	782	50.5		53
	ROSCOMMON	938	53.3		56
	SLIGO	545	46.2		46
	TIPPERARY	2511	46.8		46
	WATERFORD	830	44.3		43
	WESTMEATH	857	46.0		46
	WEXFORD	1115	40.0		42
	WICKLOW	623	44.9		44
	Missing	4	100.0		98

[a] Animals still alive have been counted as retained or not retained depending on how long they had spent in the herd up to 31st December 2015.

years and of the 2.8% of herds with BVD+ animals in 3 years 87.3% (27.4% + 36.7% + 23.3%) retained a calf or calves in one or more years, with 23.3% of these herds retaining BVD+ calves in all 3 years.

3.3. Survival analysis of BVD+ animals

There were an additional 136 animals excluded from the survival analysis because they had died on or prior to the date that the initial test results were recorded (in other words, their survival time would have been negative).

In the initial parametric survival models, all interactions with herd type were significant. Therefore, in order to simplify interpretation of the results, separate models were developed for beef and dairy herds. Dual enterprise herds were not considered further, however, it would be expected that they would be a mix of

Table 3
Number of years one or more BVD+ calves was born in a study herd in Ireland and the number of years during which one or more BVD+ calves was retained (a retained BVD+ calf was one that remained in the birth herd for more than 49 days after the initial test).

No. of years the herd had a BVD+ birth	Number (%) of times the herd retained one or more BVD+ calves									
	0		1		2		3		Total	% of overall Total
	No.	%	No.	%	No.	%	No.	%		
1	5575	51.4%	5264	48.6%					10839	77.9%
2	724	26.9%	1061	39.4%	906	33.7%			2691	19.3%
3	49	12.7%	106	27.4%	142	36.7%	90	23.3%	387	2.8%
Total	6348	45.6%	6431	46.2%	1048	7.5%	90	0.6%	13917	100%

the beef and dairy results, depending on the actual composition of the individual herd.

a. Beef herds

The models for animals from beef herds were based on 14,606 animals. The quintiles for herd-size categories were based on the distribution of the herd-size within beef herds. The variable: number of BVD+ animals within the herd was excluded from the model because of a significant ($p < 0.001$) association with herd-size when categorised. All of the models included the variables: year of birth, month of birth, herd-size, BVD+ status, county and whether the farmer had registered a mobile phone number. Based on the AIC, a generalised gamma distribution gave the best fit of all the models. For the model based on beef herds with multiple BVD+ animals (i.e. excluding herds with single BVD+ animals), a generalised gamma model with shared frailties was not available within STATA. Instead a log-normal distribution, which gave the next best fit (based on the AIC), was used. In this latter model, the inverse Gaussian frailty was preferred over a gamma frailty, based on the log-likelihood of the two models. The estimated variance of the inverse Gaussian frailty was highly significant ($p < 0.001$) suggesting some herds had shorter intervals to removal than other herds.

For the models based on either one BVD+ or multiple BVD+ animals in the herd (Table 4), animals born in 2014 and 2015 on average had between 32% and 52% shorter time to removal compared to those born in 2013. Further, animals in herds where farmers had registered a mobile phone had a significantly shorter time to removal compared to those without. BVDPI animals had significantly longer time to removal compared to BVDPOS animals in both models (on average the time to removal of a BVDPI animal was 6 times longer than for BVDPOS animals in both models). In the model with just one BVD+ animal per herd, all herd-size categories had a significantly shorter time to removal compared to the smallest herds (1–11 animals). However, in the model with multiple BVD+ animals per herd, only animals in the last herd-size category (44–364 animals) had a significantly shorter time to removal compared to those in the smallest herd-size group. In the model of herds with a single BVD+ animal, those born in May–October, on average, had significantly longer time to removal and animals born in November had the shortest time to removal compared to January. For herds with multiple BVD+ animals there was less variation in the Time Ratio by month of birth, with animals born in June to August having significantly longer time to removal and those born in December having a significantly shorter time to removal. In herds with a single BVD+ animal, those born in Leitrim and Mayo had the shortest time to removal with the longest among animals in Dublin and Monaghan. The relative county differences were slightly different for herds with multiple BVD+ animals per herd, with those in Meath having the shortest time to removal and those in Dublin having the longest time.

b. Dairy herds

The models for animals from dairy herds were based on 12,074 animals. Since there were only 8 BVD+ animals in dairy herds in Dublin, data from this county were combined with those from the neighbouring county of Wicklow. The quintiles for herd-size categories were based on the distribution of the herd-size within dairy herds. The variable: number of BVD+ within the herd was excluded from the model because of a significant ($p < 0.001$) association with herd-size when grouped. All of the models included the variables: year of birth, month of birth, herd-size, BVD+ status and county. The variable sex was significant in all models except when only herds with multiple BVD+ animals were used. The variable: farmer had registered a mobile phone, was significant in all models except the model for herds with a single BVD+ animal. Based on the AIC, a generalised gamma distribution gave the best fitting model for all of the models. For the model based on dairy herds with multiple BVD+ animals, a generalised gamma model with shared frailties was not available within STATA, instead a log-logistic distribution, which gave the next best fit (based on the AIC) was used. In this latter model the inverse Gaussian frailty was preferred over a gamma frailty, based on the log-likelihood of the two models. The estimated variance of the inverse Gaussian frailty was highly significant ($p < 0.001$) which suggests some herds have shorter intervals to removal than others.

For the models based on either one BVD+ or multiple BVD+ animals in the herd (Table 5), the overall parameter values were relatively similar in both the models. For both models animals born in 2014 and 2015 had a significantly shorter time to removal compared to those born in 2013. In herds with a single BVD+ animal, male animals had a significantly shorter time to removal. In models with multiple BVD+ animals differences by sex were not significant. However, farmers with a registered mobile phone number had a significantly shorter time to removal (Time Ratio = 0.7) compared to those without. In both models, BVDPI animals had a significantly longer time to removal compared to BVDPOS animals (on average the time to removal of a BVDPI animal was 9.3 times longer than for BVDPOS animals in herds with just one BVD+ animals and 6.6 times longer in herds with multiple BVD+ animals). All herd-size categories had a significantly shorter time to removal compared to the smallest herds (1–47 animals). In the model of herds with a single BVD+ animal, those born in July and September, on average, had a significantly longer time to removal and animals born in February had the shortest time to removal. Herds with multiple BVD+ animals born in May, June and July had a significantly longer time to removal and those born in December had the shortest time to removal compared to those born in January. In herds with a single BVD+ animal, those born in Kildare and Leitrim had the longest time to removal with the shortest among animals in Louth. The relative county differences were slightly different for herds with multiple BVD+ with those in Kerry, Wicklow and Dublin having the longest time to removal and those in Leitrim having the shortest time.

4. Discussion

Prompt identification and removal of BVD+ calves is critical to ensuring that optimum progress is made in a BVD eradication pro-

Table 4
Parametric generalised Gamma survival model for Irish herds with a single BVD+ and a log-normal shared inverse Gaussian frailty model for herds with multiple BVD+ animals, for time from the initial BVD test until slaughter for animals from beef herds.

Variable	Class	Herds with a single BVD+ (no. of animals = 5048)				Herds with multiple BVD+ animals (no. of animals = 9558)			
		Time Ratio	95% CI		P-value[a]	Time Ratio	95% CI		P-value[a]
			Lower	Upper			Lower	Upper	
Birth Year	2013	Referent				Referent			
	2014	0.68	0.64	0.73	<0.001	0.64	0.62	0.67	<0.001
	2015	0.51	0.48	0.55	<0.001	0.48	0.45	0.50	<0.001
Mobile registered	No	Referent				Referent			
	Yes	0.74	0.65	0.84	<0.001	0.71	0.61	0.82	<0.001
BVD+ status	BVDPOS	Referent				Referent			
	BVDPI	6.20	5.65	6.80	<0.001	6.26	5.95	6.59	<0.001
Herd-size	1–11	Referent				Referent			
	12–19	0.88	0.82	0.95	0.001	1.01	0.94	1.09	0.738
	20–28	0.89	0.83	0.97	0.005	0.95	0.87	1.02	0.165
	29–43	0.82	0.75	0.89	<0.001	0.95	0.88	1.03	0.204
	44–364	0.81	0.73	0.90	<0.001	0.85	0.78	0.93	<0.001
Birth Month	January	Referent				Referent			
	February	1.04	0.91	1.19	0.558	1.00	0.91	1.08	0.907
	March	1.11	0.98	1.25	0.097	1.04	0.97	1.13	0.282
	April	1.17	1.04	1.31	0.008	1.03	0.95	1.12	0.430
	May	1.32	1.16	1.49	<0.001	1.07	0.99	1.17	0.108
	June	1.39	1.21	1.58	<0.001	1.11	1.01	1.22	0.034
	July	1.36	1.17	1.58	<0.001	1.14	1.03	1.25	0.009
	August	1.43	1.21	1.68	<0.001	1.10	0.99	1.21	0.069
	September	1.32	1.11	1.56	0.002	1.03	0.93	1.14	0.552
	October	1.63	1.36	1.96	<0.001	0.97	0.88	1.08	0.611
	November	0.80	0.65	0.98	0.030	0.90	0.80	1.01	0.065
	December	1.08	0.88	1.33	0.454	0.83	0.73	0.93	0.002
County	CARLOW	Referent				Referent			
	CAVAN	0.83	0.65	1.06	0.140	0.89	0.71	1.10	0.283
	CLARE	0.79	0.62	1.00	0.050	0.89	0.72	1.09	0.268
	CORK	0.91	0.71	1.17	0.474	1.01	0.82	1.25	0.890
	DONEGAL	0.85	0.66	1.09	0.195	0.81	0.65	1.01	0.058
	DUBLIN	1.06	0.66	1.72	0.801	1.40	0.83	2.36	0.207
	GALWAY	0.87	0.69	1.09	0.219	0.89	0.72	1.08	0.231
	KERRY	0.82	0.63	1.08	0.157	0.98	0.78	1.22	0.829
	KILDARE	1.00	0.75	1.34	0.983	1.04	0.82	1.31	0.768
	KILKENNY	0.84	0.63	1.10	0.201	0.88	0.70	1.10	0.256
	LAOIS	0.83	0.64	1.08	0.169	0.81	0.63	1.04	0.093
	LEITRIM	0.73	0.57	0.95	0.019	0.98	0.76	1.25	0.864
	LIMERICK	0.98	0.75	1.27	0.878	0.89	0.71	1.11	0.293
	LONGFORD	0.91	0.69	1.20	0.510	1.08	0.85	1.38	0.509
	LOUTH	0.79	0.56	1.11	0.169	0.95	0.71	1.27	0.721
	MAYO	0.74	0.58	0.93	0.010	0.87	0.71	1.07	0.190
	MEATH	1.03	0.79	1.34	0.816	0.78	0.61	0.99	0.041
	MONAGHAN	1.06	0.82	1.37	0.672	0.97	0.77	1.22	0.772
	OFFALY	0.86	0.66	1.12	0.263	0.91	0.72	1.15	0.441
	ROSCOMMON	0.93	0.73	1.18	0.524	0.98	0.79	1.21	0.845
	SLIGO	0.83	0.64	1.07	0.146	0.88	0.70	1.11	0.287
	TIPPERARY	0.88	0.69	1.12	0.304	0.99	0.80	1.22	0.942
	WATERFORD	0.95	0.67	1.33	0.748	1.08	0.82	1.42	0.576
	WESTMEATH	0.99	0.77	1.29	0.963	0.92	0.73	1.15	0.459
	WEXFORD	0.92	0.69	1.21	0.541	0.92	0.74	1.15	0.460
	WICKLOW	0.89	0.66	1.19	0.431	1.08	0.85	1.38	0.514
Variance estimates									
	Kappa[b]	−0.712	−0.800	−0.624					
	Sigma[b]	0.952	0.928	0.978		0.643	0.624	0.663	
	Theta[c]					2.099	1.871	2.355	<0.001

[a] Wald test.
[b] The scale parameter for the generalised gamma distribution indicative of the shape of the distribution.
[c] Variance of the unobserved frailty parameter.

gramme. Peak calving in Irish dairy and beef herds in this study occurred in February and April respectively, with the aim of maximizing production from grass. Compact calving is ideally followed by a compact breeding season, with the mating start date in dairy herds typically falling in late April–early May (Graham et al., 2015a), and somewhat later in beef herds. As a consequence, there is a period early each year when the majority of BVD+ calves have been born but there are few pregnant females carrying foetuses in the first trimester of pregnancy to which these BVD+ calves can transmit infection and establish further PI calves to be born the following season. This profile provides a clear window of opportunity for the Irish programme during which removal of BVD+ calves will have maximum effect on progress to eradication. As has been shown in

Table 5
Parametric generalised Gamma survival model for Irish herds with a single BVD+ and a log-logistic shared inverse Gaussian frailty model for herds with multiple BVD+ animals, for time from the initial BVD test until slaughter for animals from dairy herds.

Variable	Class	Herds with a single BVD+ (no. of animals = 2365)				Herds with multiple BVD+ animals (no. of animals = 9709)			
		Time Ratio	95% CI		P-value[a]	Time Ratio	95% CI		P-value[a]
			Lower	Upper			Lower	Upper	
Sex	Female	Referent							
	Male	0.92	0.86	0.99	0.026				
Birth Year	2013	Referent				Referent			
	2014	0.91	0.83	0.99	0.035	0.86	0.82	0.90	<0.001
	2015	0.72	0.66	0.80	<0.001	0.67	0.63	0.70	<0.001
Mobile registered	No					Referent			
	Yes					0.70	0.50	0.99	0.043
BVD+ status	BVDPOS	Referent				Referent			
	BVDPI	9.34	8.52	10.23	<0.001	6.58	6.29	6.88	<0.001
Herd-size	1–47	Referent				Referent			
	48–66	0.80	0.73	0.89	<0.001	0.82	0.76	0.88	<0.001
	67–90	0.83	0.75	0.92	0.001	0.81	0.75	0.88	<0.001
	91–132	0.76	0.68	0.85	<0.001	0.78	0.72	0.85	<0.001
	133–942	0.80	0.70	0.91	0.001	0.73	0.68	0.80	<0.001
Birth Month	January	Referent				Referent			
	February	0.86	0.75	0.97	0.017	0.98	0.92	1.05	0.597
	March	0.98	0.86	1.11	0.734	1.04	0.98	1.12	0.204
	April	0.96	0.82	1.11	0.563	1.00	0.93	1.08	0.976
	May	1.08	0.90	1.30	0.423	1.10	1.00	1.22	0.042
	June	1.06	0.85	1.32	0.599	1.14	1.00	1.30	0.047
	July	1.62	1.23	2.13	0.001	1.20	1.03	1.40	0.021
	August	1.17	0.84	1.64	0.348	1.09	0.95	1.24	0.213
	September	1.55	1.16	2.08	0.003	1.04	0.93	1.17	0.488
	October	1.17	0.87	1.58	0.301	1.02	0.91	1.14	0.726
	November	1.15	0.81	1.64	0.436	1.04	0.93	1.16	0.541
	December	1.08	0.69	1.67	0.739	0.84	0.73	0.98	0.022
County	CARLOW	Referent				Referent			
	CAVAN	0.77	0.51	1.17	0.222	0.84	0.62	1.13	0.241
	CLARE	0.68	0.44	1.04	0.077	0.85	0.63	1.16	0.300
	CORK	0.88	0.60	1.29	0.526	0.91	0.70	1.18	0.477
	DONEGAL	0.84	0.51	1.39	0.504	0.86	0.63	1.18	0.361
	GALWAY	0.85	0.56	1.29	0.435	0.81	0.61	1.07	0.144
	KERRY	1.12	0.75	1.66	0.579	1.10	0.84	1.43	0.486
	KILDARE	1.32	0.80	2.16	0.277	0.96	0.70	1.33	0.817
	KILKENNY	0.84	0.56	1.26	0.405	0.93	0.71	1.22	0.603
	LAOIS	0.92	0.60	1.41	0.693	0.72	0.54	0.96	0.025
	LEITRIM	1.23	0.42	3.63	0.710	0.52	0.29	0.93	0.028
	LIMERICK	0.78	0.53	1.16	0.215	0.87	0.67	1.14	0.311
	LONGFORD	0.82	0.50	1.33	0.418	0.79	0.52	1.20	0.270
	LOUTH	0.60	0.35	1.02	0.061	1.04	0.73	1.47	0.824
	MAYO	0.78	0.50	1.21	0.263	0.96	0.67	1.38	0.844
	MEATH	0.84	0.54	1.29	0.419	0.86	0.65	1.13	0.267
	MONAGHAN	0.88	0.58	1.34	0.553	0.97	0.73	1.28	0.816
	OFFALY	1.04	0.66	1.63	0.862	0.99	0.72	1.35	0.939
	ROSCOMMON	1.06	0.59	1.89	0.848	0.88	0.57	1.37	0.580
	SLIGO	0.79	0.47	1.35	0.398	0.68	0.39	1.16	0.158
	TIPPERARY	1.02	0.69	1.50	0.916	0.94	0.72	1.22	0.643
	WATERFORD	1.11	0.74	1.67	0.626	1.01	0.77	1.34	0.931
	WESTMEATH	0.69	0.44	1.07	0.097	1.02	0.76	1.37	0.889
	WEXFORD	1.04	0.69	1.58	0.834	0.84	0.63	1.11	0.216
	WICKLOW & DUBLIN	1.12	0.68	1.84	0.653	1.10	0.81	1.50	0.526
Variance estimates									
	Kappa[b]	−0.971	−1.068	−0.875					
	Sigma[b]	0.886	0.854	0.918					
	Gamma					0.414	0.402	0.426	
	Theta[c]					1.223	1.106	1.353	<0.001

[a] Wald test.
[b] The scale parameter for the generalised gamma distribution indicative of the shape of the distribution.
[c] Variance of the unobserved frailty parameter.

a previous study, retention of BVD+ calves into the breeding season increases the likelihood of further PI births (Graham et al., 2015a).

The problem of the retention of BVD+ calves, particularly in beef herds was identified during the voluntary phase of the Irish programme (Graham et al., 2014). This has also been a key challenge for the compulsory phase of the national programme, in the absence of a legal requirement for their disposal and a formal mechanism for full compensation. The current study is the second one examining the disposal of BVD+ calves identified during the Irish eradication programme. The first (Graham et al., 2015b) analysed data from

1953 BVD+ calves born in 1116 herds between 1st January and 15th July 2012 (during the voluntary phase). A key measure analysed in that study was time to involuntary removal (TTIR) due to either death or culling, with risk factors found to be significantly associated with increasing TTIR in beef and dairy herds being BVD status and county (with herd size also significant for beef herds).

The study period for the current analysis covers the first three years of the compulsory programme from 2013 to 2015, during which various measures have been used to encourage the prompt removal of BVD+ calves. The current study expands on the previous analysis in terms of timescale, size (29,504 BVD+ calves in 13,917 herds), risk factors considered and scope (inclusion of voluntary removal through slaughter). It was undertaken to examine risk factors for retention during the compulsory phase of the programme, as well as changes in the pattern of retention over time, possible factors influencing these changes, and to consider whether additional measures are required to address retention. Overall, the study has highlighted the substantial and significant improvement in the timely removal of BVD+ animals, increasing from 44% removal within 7 weeks of the initial test in 2013 to 70% in 2015. Indeed, this latter figure could increase further to 74% if the 242 animals with an initial test date within 7 weeks of the end of 2015 were removed in early 2016. Over this period, the annual prevalence of BVD+ births declined from 0.66% to 0.33%, with a further decrease to 0.15% for the first six months of 2016 (see http://animalhealthireland.ie/?page_id=229 for current figures). The most striking change in the retention figures is the improved removal of BVD+ calves from beef herds from 2014 onwards (Figs. 3 and 5). It is not possible to attribute the improvement in removal of BVD+ calves generally, or for beef calves specifically, to any one of these measures. Collectively, however, their impact is apparent. One important change that is considered to have impacted on removal from beef herds is a revision to the terms and conditions of the financial supports available to beef herds for 2014 relative to 2013. The level of government support provided for removal increased from €100 to €120, but more importantly the restriction of the support to the second and subsequent BVD+ calf removed in 2013 was withdrawn, so that all BVD+ calves became eligible. Given that some 58% of herds had only one BVD+ calf, this revision dramatically increased the number of eligible herds. The introduction of a payment for removal of the second and subsequent dairy breed heifers in 2014 may have had limited impact in dairy herds for the same reason. However, the extension of this payment in 2015 to cover the first and all subsequent dairy breed heifers is considered to have contributed to the ongoing improvement observed between 2014 and 2015 (Fig. 5). Calves with a beef sire, irrespective of their sex, that are born into dairy herds remain ineligible for a support payment. These calves have a significantly (log rank test: $P = 0.003$) higher median retention time (37 days) compared to dairy sire female animals in dairy herds (35 days; unpublished data), which do receive compensation. A further refinement introduced in 2015 for both beef and dairy herds in response to the significantly higher TTIR for BVDPI as opposed to BVDPOS calves in the study by Graham et al. (2015a) was the higher level of support for removal within 5 weeks, as opposed to seven weeks. The inclusion of requirements in relation to BVD in the terms and conditions of the Beef Data Genomics Programme (BDGP; see Supplementary material for further details), in which some 25,500 of 63,000 beef herds are participating, is also considered to have contributed to the continued improvement in removal of BVD+ calves from beef herds.

Those herds that were more likely to retain PI animals for more than 49 days (Table 2) such as beef herds, smaller herds, farmers with no registered mobile and those in certain areas will need to be targeted for future communication programmes. One key message from this study is that herds that did not retain PI animals were less likely to have PIs in more than one year (Table 3).

Overall the results of the survival models were similar, with birth year, BVD+ status, herd size, county of birth and birth month consistently identified as risk factors independent of herd type (beef or dairy) or the numbers of BVD+ animals (single or multiple). In addition, the presence of a registered mobile telephone number was identified as a risk factor in all models except for dairy herds with a single BVD+, while the sex of the BVD+ was only identified as a risk factor in this model.

Consistent with previous findings (Graham et al., 2015b), BVDPI animals had a significantly longer time to removal compared to BVDPOS animals, with Time Ratios ranging from 6.20 to 9.34 (Tables 4 and 5). This may partly reflect the additional time required to conduct a re-test, with the median time to retest after the initial test being 33 days. However, this does not fully explain the difference, with the significantly longer interval to removal of BVDPI animals possibly due to farmers being reluctant to remove a BVDPI animal if it still appears healthy, with them choosing instead to fatten and slaughter the animal. This finding further reinforces the decision to 'front load' support payments to encourage prompt removal. However, the majority of positive animals are subject to a retest. Given a median interval to retest of 33 days, in many cases it will be challenging to remove the calf within 35 days to obtain the higher level of payment, although removal within 7 weeks remains readily attainable. It is therefore important to encourage re-testing 21 days after the initial test or alternatively removal of BVD+ calves without retesting. Recent analysis of test data indicates that both ELISA S-N values and RT-PCR Ct values can be used to predict the outcome of a re-test, allowing practitioners to encourage a re-test only when a negative result is the likely outcome (Graham et al., 2016b).

In all of the models, the smallest herd-size group had the longest time to removal. This was also found by Graham et al. (2015b), who noted that the removal of a BVD+ calf from a smaller herd may be perceived as a relatively greater loss in comparison to removal of a calf from a larger herd. Small beef herds in particular are likely to be run by part-time farmers who may be more difficult to reach with educational messages around BVD+ removal or who may not be as dependent on the herd for income and therefore more likely to accept the risks inherent in retaining a BVD+ calf. Herd-size was measured in terms of the number of calves within the herd. This was considered more influential in guiding calf-level management decisions, such as BVD+ retention, than the number of adult animals within the herd. The rate of retention varied by county, consistent with the previous study by Graham et al. (2015a). The reasons for this remain unclear, but may reflect differences in factors including prevalence, local advisory services and production systems. In dairy herds with a single BVD+ animal, females were retained for significantly longer than male animals. This is a new observation and may reflect the lower intrinsic value of dairy bull calves. The availability or otherwise of a mobile telephone number and seasonal patterns have not previously been explored as risk factors, but both were found to be significant. The reason for the longer retention by herdowners for whom a mobile telephone number was not recorded is not known. In part, it may reflect a reduced level of communication, with the herdowner not receiving text messages with results and a follow up call from the BVD Helpdesk. In addition, it may be a proxy for a particular demographic of farmer in terms of age, awareness of the BVD programme or familiarity with, and receptiveness to, digital communications. While they are associated with only a small proportion of all BVD+ births (656 of 29,504), additional measures to encourage removal of BVD+ calves from these herds appears to be merited.

Seasonal patterns in length of retention were seen in all models, with BVD+ calves born in the summer months being retained significantly longer, with this particularly evident in beef herds. Along with autumn calving in a minority of dairy and suckler herds, this is considered to contribute to the profiles for beef and dairy herds in 2014 and 2015 shown in Fig. 3, where the numbers of BVD+ alive shows a slight increase (or reduced rate of decrease) in the late summer and autumn. Another contributory factor to this profile is the increased incidence of BVD+ births seen in mid-summer (unpublished data) which is considered a consequence of the peak infection pressure earlier in the spring. This period, when the maximum numbers of BVD+ calves are alive, coincides with the 30–120 days of gestation window for creation of BVD+ calves of dams that calve during the summer. The reason why these BVD+ calves are retained for longer is unknown, but may reflect farmers' focus on other activities such as silage making at this time of year. This may also be the explanation for the increased likelihood of retention seen in BVD+ calves born in beef and dairy herds with multiple BVD+ in December (holiday season) and in dairy herds with a single BVD+ in January (onset of calving and lactation).

Less than half of the herds (42%) had multiple BVD+ animals per herd, which caused difficulty when handling clustering within herds. For herds with just one BVD+, it was not possible to create a within herd variance. However, animals within the same herd are likely to have similar risks of retention which needs to be accounted for within the model. Models that were fitted with either no accounting for clustering or by using robust standard errors (Supplementary material) gave relatively similar results. However, these models would have under or over accounted for the clustering. Since we had a large sample size, it was possible to create separate models for herds with a single BVD+ or multiple BVD+ animals which avoids either over or under adjusting for within herd correlation.

While this study shows that significant progress has been made in addressing the issue of retention of BVD+ calves during the study period, it is evident that there is a need for further improvement. Already during 2016 a number of further measures have been introduced. Firstly, herds that retain BVD+ calves are now being subject to restriction, with all movements into and out of the herd prohibited until the retained animal has been removed. This measure began in December 2015 for herds that retained any BVD+ animals born in 2015, resulting in a marked reduction in the numbers retained from 973 in the last week of 2015 to only 244 by week 12 of 2016. Herds retaining 2016-born BVD+ calves are now being restricted in the same way. Data analysis is underway to examine the effectiveness of additional movement restrictions to prevent potential Trojan animals being sold from these herds. Allied to this, herds contiguous to retaining herds are now also being notified of the increased risk (Graham et al., 2016a) posed by their neighbouring infected herd and advised to ensure that the appropriate biosecurity measures to minimize the risk of introduction of infection are in place. Another measure that has been introduced under the Rural Development Plan is the availability to herd owners with BVD+ births of a herd investigation by a trained veterinary practitioner under the Targeted Advisory Service on Animal Health (TASAH; http://animalhealthireland.ie/?page_id=5009). While this is primarily designed to investigate the source of the infection and to review herd biosecurity, it also provides the opportunity for the veterinary practitioner to reinforce the importance of the prompt removal of BVD+ calves. A number of metrics have now been established to monitor patterns of retention of BVD+ calves and changes therein. It is important that these are regularly reviewed and that additional measures, as required, are introduced. In conclusion, the current study demonstrates that significant progress has been made in addressing the retention of BVD+ calves. It is hoped that this work will be of benefit to the Irish programme and also to similar programmes elsewhere by highlighting measures that have collectively contributed to this progress. A number of risk factors associated with retention have been identified (some for the first time), suggesting areas where future efforts can be addressed.

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Appendix A. Supplementary data

Supplementary data associated with this article can be found, in the online version, at http://dx.doi.org/10.1016/j.prevetmed.2016.10.010.

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