Preventive Veterinary Medicine 146 (2017) 103–113

Contents lists available at ScienceDirect

Preventive Veterinary Medicine

journal homepage: www.elsevier.com/locate/prevetmed

A quantitative risk-analysis for introduction of Bovine Viral Diarrhoea Virus in the Netherlands through cattle imports

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ARTICLE INFO

Keywords:
Risk-analysis
Import
Cattle
BVDV
Simulation model

ABSTRACT

Many countries have implemented control programmes aiming to eradicate Bovine Viral Diarrhoea Virus (BVDV). After obtaining the free status, a risk of re-introduction of the virus through import may remain. Therefore the risk of introduction of BVDV through cattle imports in the Netherlands was quantified and the effectiveness of subsequent intervention measures was assessed.

Data, literature and expert opinion were used to estimate values for input parameters to feed a stochastic simulation model. The probability that BVDV was imported was differentiated into persistently infected (PI) cattle, trojan cows that transmitted the virus vertically resulting in a PI foetus (TR) and transient infected cattle (TI). The import risk was stratified to beef, dairy, small scale, suckler, trade, veal and young stock herds. The intervention scenarios that were evaluated consisted of virus testing, a combination of virus testing and antibody testing in pregnant cows, abolishment of imports from high risk countries (i.e. countries with a BVDV prevalence >15%) and a combination of import restrictions and testing prior to import.

Each year, 334 (5th and 95th percentile: 65–902) Dutch cattle herds were estimated to be infected with BVDV through import. Veal herds account for most infections associated with import (87%), whereas in the other herd types, only 9 beef, 6 dairy, 2 small scale, 16 suckler, 10 trade and 2 young stock herds are infected through imports per year. Import of PI cattle is the most important risk for introduction in veal herds, while import of TR cows is the main source of BVDV introduction in dairy, small scale and suckler herds. With the intervention scenarios, the number of BVDV infected herds in the Netherlands could be reduced to 81 and 58 herds per year when respectively virus testing or a combination of virus and antibody testing was applied or to 108 herds when import from high risk countries was abolished. With the scenario in which both import from high risk countries was abolished combined with virus and antibody testing, the number of BVDV infected herds could be reduced to 17 herds per year. The risk assessment showed that BVDV is regularly imported in the Netherlands. The import risk can effectively be reduced by implementing diagnostic testing prior to import and only import cattle with a favourable result, eventually combined with certain trade restrictions.

1. Introduction

Bovine viral diarrhoea virus (BVDV) is an ubiquitous occurring pathogen in cattle. In transiently infected cows, infections with BVDV can remain subclinical but may also lead to severe clinical signs (Evermann and Barrington, 2005; Lindberg, 2003; Waage 2000). In addition, BVDV leads to immunosuppression, which enhances the probability that cattle are secondarily infected by other pathogens (Potgieter, 1995; Wilhelmsen et al., 1990). BVDV can be transmitted both horizontally leading to transiently infected cattle (TI) and vertically. Vertical transmission in early gestation results in a Trojan cow (TR) that carries a persistently infected calf (PI) (Van Oirschot, 1983; McGowan et al., 1993; Houe, 1995). PI cattle are the most important source of virus spread as they continuously shed large amounts of virus and are the main reason of maintaining the infection within a herd (Lindberg and Houe, 2005).

BVDV infections are known to be associated with high economic losses (Hogeveen et al., 2003; Houe 2003; Fourichon et al., 2005; Valle et al., 2005; Lindberg et al., 2006). Therefore, several European countries decided to implement BVDV control and eradication programmes. At this moment, Sweden, Norway, Finland, Denmark, Germany, Austria and Switzerland either obtained BVDV freedom or reached a herd-level

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http://dx.doi.org/10.1016/j.prevetmed.2017.08.003
Received 4 January 2017; Received in revised form 2 August 2017; Accepted 2 August 2017

prevalence below 1.5% (Foddai et al., 2016; Norström et al., 2014; Presi et al., 2011; Rossmanith et al., 2010, Hult and Lindberg, 2005; Rikula et al., 2005; Bitch et al., 2000; Nuotio et al., 1999). Control or eradication programmes are in place in Ireland, Scotland, and parts of France and Italy (Houe et al., 2006; Meier et al., 2016; Barret et al., 2011; Stott et al., 2012; Tavella et al., 2012; Voas, 2012).

In the Netherlands, though a voluntary BVD control programme has been in place for many years, the disease remains endemic. Currently, a national BVDV control programme is discussed with the goal to eradicate BVDV.

Once the BVDV-free status will be achieved, it is important to know the risk of re-introduction of this virus in the cattle population. Purchase of cattle is the major risk factor for (re-)introduction of BVDV (Williams and Winden 2014; Gates et al., 2013; Graham et al., 2013; Presi et al., 2011; Obritzhauser et al., 2005; Van Schaik et al., 2002; Valle et al., 1999; Houe, 1995). In a BVDV-free situation, national cattle trade will no longer pose a risk in contrast to import of cattle from other countries. The exact risk of these imports is unknown and more information is needed to evaluate whether risk mitigating actions for imports are necessary when a national BVDV control programme is implemented. To our knowledge, there is only one study that evaluated the risk of introduction of BVDV through import (Foddai et al., 2014). They investigated the risk of reintroduction of BVDV through import of live animals, semen, embryos or contaminated trucks in Denmark. Nevertheless, the results of this study are not applicable to the Dutch situation because Denmark only imports 246 cattle per year (Foddai et al., 2014) compared to more than 900,000 cattle per year in the Netherlands. Given the large number of annual cattle imports in the Netherlands, the risk of other factors are assumed to be relatively small and were therefore not included in this risk assessment.

The aim of this study was to quantify the risk of cattle imports for introduction of BVDV in cattle herds in the Netherlands in the situation that all Dutch cattle herds are BVDV free. In addition, the effectiveness of four intervention scenarios was evaluated.

Because the import risk differ between different cattle herd types in the Netherlands both the overall risk and the risk stratified to the different cattle herd types in the Netherlands are presented.

2. Material and methods

For the evaluation of the risk of cattle import for introduction of BVDV in the Netherlands, a stochastic simulation model was built in MS Excel (Microsoft Corporation, 2013) and @Risk 6.3.1 (Palisade, 2014). In this study, the 'import risk' and the 'probability of BVDV introduction through import of live cattle' are synonymous. The impact of the subsequent BVDV infection in the receiving herd was not evaluated and is not included in the definition of the import risk.

Input parameters based on data, literature and expert opinion were included in the model to calculate the import risk. Input based on actual data or literature were preferred. Nevertheless, input parameters for which no data or (recent) information in literature were available, were estimated using expert opinion (M.H. Mars DVM, PhD: expert on viral diseases and diagnostic tests, L. Van Duijn DVM: Dutch BVDV expert, and G. van Schaik PhD: Epidemiologist and Professor monitoring and surveillance of farm animal health). Uncertainty in parameter values was incorporated by including probability distributions instead of fixed values (Vose, 2008). In addition, values for input parameters estimated by the experts, were varied in a sensitivity analysis to evaluate the effect of these values on the model outputs.

The robustness of the model outputs was evaluated by varying the number of iterations and was considered stable after 5000 iterations i.e. the mean and variation remained the same. Therefore, outputs that are presented in this paper are based on 5000 iterations. In this paper, the Netherlands is assumed to be BVDV-free and all cattle are susceptible for BVDV infection. Subsequently, each infectious import will result in a newly infected cattle herd.

2.1. Input of the model

2.1.1. BVDV prevalence in source countries

Between 2011 and 2015, the Dutch cattle industry imported cattle from 21 different European countries (EU countries). From these source countries, information of BVDV prevalence and demographic information about the number of cattle and cattle herds was obtained. The herd level virus prevalence was defined as the percentage of herds with an indication of virus circulation. Virus circulation was assumed when either a cohort of young cattle tested seropositive (Houe et al., 2006) or when a herd was classified as status 2 (14–29% of cows test seropositive) or 3 (>29% of the cows are seropositive) based on bulk tank milk evaluation (Niskanen, 1993). Initially, information about the BVDV herd prevalence for each of the countries from which cattle were imported were evaluated based on literature. In addition, more recent information was pursued through personal contacts (either in person or by phone) with BVDV experts from the various countries. The estimated BVDV prevalence in each country and the source of information are presented in more detail in Appendix A.

2.1.2. Number of imported cattle

Data about the number of cattle and herds present in the countries from which cattle are imported was obtained from Eurostat (Eurostat, 2016). Based on this information combined with the prevalence estimations, the number of herds with BVDV virus circulation ($nBVDV\_pos_{herd}$) for each source country (i) was estimated (formula 1).

$$nBVDV\_pos_{herd,i} = Prev_{herd,i} * n_{herd,i} \quad (1)$$

In which $Prev_{herd}$, represent the BVDV prevalence on herd level and $n_{herd,}$ is the number of cattle herds in the respective country.

Between 2011 and 2015, on average 918 thousand cattle were imported in the Netherlands per year (source: Identification and Registration data, RVO The Hague, the Netherlands). Most of the imported cattle originated from Germany (55%), followed by Poland (9%) and Belgium (7%) (Fig. 1).

Within the Dutch cattle industry, seven different cattle herd types are distinguished i.e. dairy, suckler, veal, beef cattle, trade, young stock and small scale herds (definitions are presented in more detail in Santman-Berends et al., 2016). Because the import risk, the risk of subsequent consequences and the probability of transmission to other herds differs per cattle herd type, the import risk was stratified to each of the seven cattle herd types. From the imported cattle, 95% represent calves that are imported for fattening by the Dutch veal industry. Beef farmers import 1.7% of all cattle aged either between 4 and 14 months or >2 years. In addition, a small number of cattle are imported by suckler, dairy and small scale herds (1.2%, 0.6% and 0.2% of all imports, respectively) and these are, in general, adult cows (>2 years of age). Finally, 1.3% of cattle is imported by traders and young stock herds only import small numbers of cattle (0.3% of all imports), which are generally younger than fourteen months of age at import (Fig. 2).

Imports of pregnant cattle are associated with the risk of introducing cows that are carrying a PI foetus because they underwent a BVDV infection during the early stages of pregnancy, which consequently resulted in vertical transmission of the virus to the foetus i.e. trojan cows (TR). To estimate the risk of importing these TR cows, the number of cows that were pregnant at the moment of import and had been at risk of becoming a TR cow either in the herd of origin or during transport were calculated. An imported pregnant cow was defined as a cow that gave birth to a calf within nine months after the date of import as registered in the Dutch identification and registration (I & R) system. In this system, all movements of cattle are registered. Between 2011 and 2015, on average 3051 (0.33%) of the imported cattle per year were pregnant. The imported pregnant cattle were assumed to have been at risk of becoming a TR cow if they were susceptible for a BVDV infection at the moment they became pregnant. Based on previous

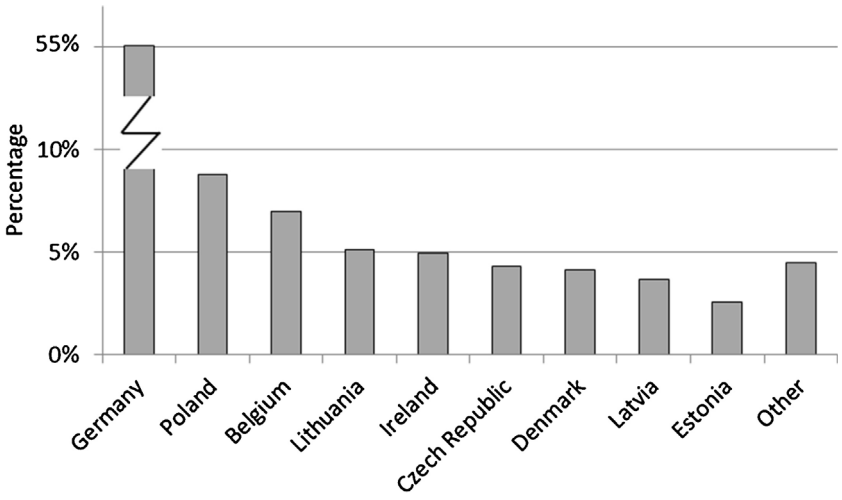

Fig. 1. Percentage of the total number of imported cattle in the Netherlands by country of origin.

research from amongst others McClurkin et al. (1984) and Blanchard et al. (2010), it was assumed that a BVDV infection between 30 and 120 days in gestation results in vertical transmission of the virus to the foetus and subsequently in a persistently infected calf. On average 94% of the imported pregnant cattle were at least one day (mean was 81 days) in the susceptible period of pregnancy in the country of origin and 19% of these (18% of the total amount of pregnant imported cattle) were also at risk of vertical transmission during transport.

2.1.3. Transport

To evaluate the exact number of times BVDV was introduced because of cattle imports, the number of imported cattle was aggregated to the number of import units per importing herd.

It was assumed that one import unit was defined as an import event on a specific date to one specific herd. Subsequently, the number of imported cattle in each import unit was calculated as the total number of imported cattle per importing herd, divided by the number of import units. When the average number of cattle per import unit was below the maximum capacity of the truck as regulated in EC 1/2005 and the national regulation in the Netherlands (EC, 2005; IKB, 2008), it was assumed that all cattle in that specific import unit were transported together. According to the same regulations, each epidemiological unit (such as a truck or trailer) is exclusively allowed to transport cattle to one, or at most two locations. In the model we assumed that a truck had a random probability to deliver cattle to one or two herds and to subsequently infect one or two receiving herds given that at least one BVD infected animal was present in the truck.

2.1.4. Other input parameters

Other input parameters that were included in the simulation model and their source are presented in Table 1.

It was assumed that a PI animal would transmit the BVD virus to all other susceptible cattle in the herd or transport. In the model, all imports were stratified into the age groups <3 months (mo) and >3 mo of age. Imported calves (<3 mo of age) were considered protected by maternal antibodies if the dam was seropostive and the calves received sufficient colostrum (Table 1). Cattle >3 mo of age, calves from seronegative dams and calves that received insufficient colostrum were assumed susceptible for BVDV infection.

Compared to non-PI animals, PI cattle were assumed to have a higher mortality risk. Of these PI cattle, 50% was assumed to die in the first year of life, an additional 40% was assumed to die in the second year of live and the remaining 10% was assumed to have the same life expectancy as non-PI cattle.

2.2. Risk of importing BVD infectious cattle: the model

The risk of cattle imports for introduction of BVDV depended on the number of transports including imported PI, TR and TI cattle. The latter only resulted in additional infected herds when they were infected in the country of origin and imported in the absence of a PI. All input information was combined to calculate the number of imported PI, TR and TI cows per importing herd type in the Netherlands per year.

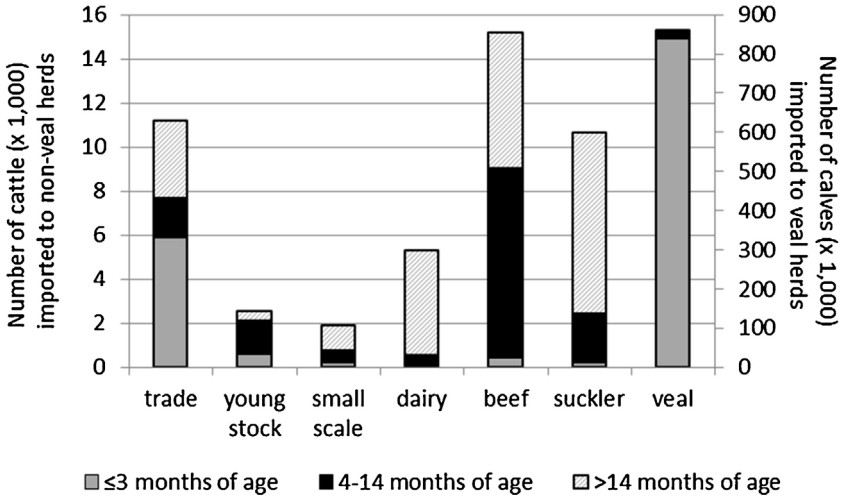

Fig. 2. Number of imported cattle stratified to three age categories that are imported in the Netherlands per cattle herd type per year.

Table 1
Input parameters for the evaluation of the risk introduction of BVDV in the Netherlands through imports of cattle.

Parameter	Mean estimate	Included as	Source
Percentage of PI cattle in a herd with an indication of virus circulation (pPI)	4%	Discrete distribution (2%,4%,4%,10%)	(Houe et al., 2005; Obritzhauser et al., 2005; Graham et al., 2014; Rosmanith et al., 2014)
Mortality rate of PI cattle (pMort)	50% < 1year, 40% 1–2 year, 10% no additional mortality	General distribution	Expert opinion
Percentage calves assume to drink sufficient amounts of colostrum (pCol)	83%	Uniform distribution (67–98%)	Expert opinion and pers. Comm. L. van Wuijckhuise
Protection by maternal antibodies with sufficient colostrum intake	100% in calves < 3mo	Fixed value	Expert opinion
Age at import: veal calves < 1 mo ($A\_imp_{<1m}$)	21 days	Fixed value	I & R data
Age at import: calves 1–3 mo ($A\_imp_{1\text{-}3m}$)	62 days	Uniform distribution 30–93 days of age	I & R data
Age at import: cattle > 3 mo ($A\_imp_{>3\ m}$)	778 days	Uniform distribution 94 days to 4 years of age	I & R data
Age at infection with BVDV when housed in a herd with virus circulation (A_inf)	Mean: 3 months of age	Probability of infection 5% on the first day of life, 50% in the first month, 95% in the first year	Expert opinion
Average infectious period of TI cattle (tTI)	8 days	Pert distribution (1;7;18)	(Sarrazin et al., 2014; Strong et al., 2015; Houe 1999; Lindberg and Alenius 1999; Bolin and Ridpath, 1998; Bruschke et al., 1998)
Percentage susceptible cows (> 2 years) in herds with evidence for BVDV virus circulation (pSpos)	30%[a]	Pert distribution (0%;20%;100%)	Expert opinion
Percentage seropositive cattle in herds with evidence for BVDV virus circulation (pRpos)	70%	1-pSpos	Expert opinion
Percentage susceptible cattle in herds without evidence for BVDV virus circulation (pSneg)	95%[a]	Uniform distribution (90%;100%)	Expert opinion
Probability that a susceptible pregnant cow in an infected herd will be infected during the 90 days at risk (30–120d in gestation) (pr_Cinf)	85%	Uniform distribution (70%;100%)	Expert opinion
R_0 transiently infected animal (R_0 TI)	0.49	Pert distribution (0.01;0.25;1.95)	(Sarrazin et al., 2014)
Probability that import of TI cattle will result in a BVDV outbreak (without presence of PI) (pr_Hinf_{TI})	1.1% per cow[a]	1-1/R_0 TI	formula derived from (Anderson and May, 1991)

[a] Parameter is varied in a sensitivity analysis.

2.2.1. Import of PI cattle

Imported PI cattle are defined as cattle that were infected during their foetal stage and subsequently born persistently infected in the source country.

For each of the countries (*i*) that export cattle to the Netherlands, the probability that a random animal was a PI (*pPI*) was calculated. The number of BVDV positive herds were multiplied with their average herd size and with the assumed prevalence of PI cattle in an infected herd (Table 1) to estimate the number of PI cattle. This number was subsequently extrapolated to the percentage of PI cattle in country *i*.

The probability that a randomly purchased animal was a PI, was stratified per age category between moment of birth and 2 years of age, with one month intervals (pPI_{age}) i.e. calves < 1 month, calves 1–2 months, etc., up to > 24 months of age). This stratification enabled incorporation of a correction factor for the fact that PI calves have a higher risk to die compared to non-PI cattle, which decreases with increasing age (Table 1). Subsequently, the probability that a random imported animal (*pPIcow*) given a certain age (*age*) from country (*i*) was a PI, was estimated.

The total number of imported PI cattle ($nPIimp_i$) per country represented the sum of the number of imported PI cattle per age category. The latter depended on the probability that a random cow in each age category and country was a PI and the number of imports of cattle from the specific age category ($nIMP_{age}$) and country (*i*) (formula 2).

$$nPIimp_i = \sum_{n=1}^{age} (pPIcow_{age,i} * nIMP_{age,i}) \quad (2)$$

For the number of infected transports, the probability that a transport was free from PI cattle ($pTrans\_free_i$) was calculated as the probability that all cattle from country *i* in the transport unit were BVDV free (formula 3).

$$pTransfree_i = (1 - pPIcow_i)^{nTrans} \quad (3)$$

Based on $pTrans\_free_i$, the probability that a transport was infected with at least one PI animal was estimated. A transport containing at least one PI animal was assumed to cause a BVDV outbreak in the receiving herd.

2.2.2. Import of TI cattle

Imported TI cattle were differentiated in 1) cattle that became TI in the country of origin and 2) cattle that were susceptible for a BVDV infection during transport and became TI because they were transported together with a PI. Cattle that became TI during transport were assumed to cause no additional BVDV infected herds as the risk of these transports were already assigned to the PIs.

In the model, it was assumed that a transport containing TI cattle that were imported without the presence of a PI could potentially lead to a BVDV outbreak in the receiving herd. The probability that an animal in a herd with BVDV circulation has already been infected and is seropositive increases with the time the animal is housed in the infected herd. Therefore, it was assumed that the probability that susceptible cattle were infected a few days before the transport in a herd with virus circulation (*A_inf*), declined with age (Table 1).

The number of infected transports with TI cattle was calculated similar to those with PI cattle and was assumed to be transported to one or maximum two different herds per epidemiological unit. The TI cattle were assumed to be infectious at the moment of arrival in the importing herd when they were infected at most eight days before (i.e. the infectious period, Table 1). Based on the basic reproduction number R_0 that was derived from the study of Sarrazin et al. (2014) and the formula described by Anderson and May (1991) ($P_{outbreak}$ = 1-(1/R_0)), the

probability that import of TI cattle would lead to a major outbreak in the receiving herd was estimated to be on average 1.1% per TI animal present in the infected transport (multiple TIs lead to a larger probability of a BVDV outbreak in the receiving herd).

2.2.3. Import of trojan cows

Imported cows with a TR status could either have been infected in the country of origin or during transport.

The number of imported TR cows that became infected in the country of origin (*nTROJ_org*) depended on the number of susceptible and pregnant cows that were at risk for vertical transmission in the source country (*patRisk_org*) (i.e. between 30 and 120 days in gestation) (*pS*), and the probability to be infected during the period at risk (*pr_Cinf*) (formula 4).

$$nTROJ.org_i = npreg*patRisk.org_i*pS*pr.C\,\mathrm{inf} \quad (4)$$

Parameter *patRisk_org*, was calculated based on I & R data, *pS* and *pr_Cinf* were estimated based on expert opinion (Table 1). It was assumed that one transport with a TR cow would infect one receiving herd.

Infection during transport was assumed in 100% of the cases in which susceptible pregnant cattle that were between 30 and 120 days pregnant (estimated based on I & R data) and PI cattle were transported together. In the model it was assumed that transport of TI without the presence of PI cattle would not result in additional TR cows. The probability that susceptible pregnant and PI cattle were transported together was simulated assuming a random distribution of PI cattle and pregnant cows per transport per country. The model assumed that every TR cow that arose from a BVDV infection during transport would lead to an additional infected cattle herd in the Netherlands, assuming a worst-case situation.

2.3. Sensitivity analysis

Sensitivity analyses were carried out on three parameters that were estimated by the experts and were rather uncertain (Table 2). In a first sensitivity analysis, the percentage of susceptible cows in a herd with an indication for virus circulation varied between the most likely value (mean = 30%) used in the default model and a higher value (mean = 70%) or a lower value (mean = 15%). In a second sensitivity analysis, the percentage of susceptible cows in herds without an indication of virus circulation (default value 95%) was decreased to 70%, with minimum and maximum values ranging between 0% to 100% (mean = 63%) or 50% and 100% (mean = 72%). Thirdly, the probability that import of TI cattle that were infected in the country of origin and were transported without the presence of a PI would lead to a BVDV outbreak in the receiving herd in the Netherlands, was changed from 1.1% per TI animal (equal to a R_0 of min. = 0.01; most likely (ML) = 0.25 and max. = 1.95) to a ML value of 5% (equal to a R_0 of 1.05), a ML value of 49% (equal to a R_0 of 1.95) and 0% per transport (equal to a R_0 below 1) (Table 2).

2.4. Scenarios to reduce the import risk of BVDV

2.4.1. Scenario 1: testing all import cattle for BVDV virus prior to import

In this scenario all cattle were tested for BVDV prior to the moment of import and were not imported if they tested virus-positive. Cattle could either be tested by ear notch sampling or blood testing, using a PCR or antigen ELISA. Similar test characteristics were assumed for these tests e.g. a sensitivity of 99% and a specificity of 99.5% (Mars and Van Maanen, 2005).

2.4.2. Scenario 2: testing all import cattle for BVDV and testing pregnant cows for antibodies prior to import

This scenario is equal to scenario 1 with the addition that cows in gestation were also tested for antibodies prior to import in order to prevent TR cows from being imported. Cows with a seropositive test result were not imported. In this scenario, the antibody test was assumed to have a sensitivity and specificity of 98% (Mars and Van Maanen, 2005).

In both scenarios, it was assumed that no errors in the sampling process occurred, which results in an optimal situation. In reality, this might not be the case as errors in the whole sampling process might happen. To evaluate the sensitivity of the model outputs for the probability that sampling errors occurred, both scenarios were also carried out assuming a 20% false-negative rate as a result of errors in the sampling process.

2.4.3. Scenario 3: import is only allowed from countries with a low or medium BVDV prevalence i.e. < 15%

Every country from which cattle were imported was classified in one of three risk categories with respect to their BVDV status. Countries with a herd level virus prevalence below 5% were classified as 'low risk countries'. Countries with a herd level prevalence between 5 and 15% were classified as 'medium risk countries' and countries with a herd level prevalence above 15% were classified as 'high risk countries' (Fig. 3).

In scenario 3, the import of cattle from countries with a high risk status was abolished. This scenario assumed a linear shift of imports towards countries with a low or medium risk for BVDV.

2.4.4. Scenario 4: import is only allowed from countries with a low or medium BVDV prevalence and all imported cattle are tested for BVDV virus and pregnant cows also for antibodies prior to import

In this scenario, the measures of both scenario 2 and 3 are applied. Import of cattle from countries with a high risk status for BVDV (herd level prevalence ≥15%) is prohibited, assuming a linear shift of imported cattle towards countries from which imports remains permitted. Additionally, two sub-scenarios are modelled assuming that a) either all imported cattle from low and medium risk countries are tested prior to import, or b) cattle from medium countries are mandatory tested prior to import whereas imported cattle from low risk countries are exempted from this measure. Analogous to scenario 2, all cattle are tested for BVD virus and pregnant cows are also tested for antibodies prior to import. Similar to the other test scenarios it was assumed that no errors in the sampling process occurred.

Table 2
Parameters that were varied within a sensitivity analyses to evaluate their influence on the import risk for introduction of BVDV in the Netherlands.

	Parameter	Default value	Alternative value
1	Percentage susceptible cows (>2 years) in herds with evidence for BVDV virus circulation	Pert distribution (0%;20%;100%)	Pert distribution (0%;80%;100%) Pert distribution (0%;10%;50%)
2	Percentage susceptible cows (>2 years) in herds without evidence for BVDV virus circulation	Uniform distribution (90%;100%)	Pert distribution (0%;70%;100%) Pert distribution (50%;70%;100%)
3	Probability that import of TI cattle without the presence of PI will result in a BVDV outbreak in the importing herd	1.1% per animal (R_0 Pert distribution (0.01;0.25;1.95)	5% per animal (R_0 1.05) 49% per animal (R_0 1.95) 0% per animal (R_0 <1)

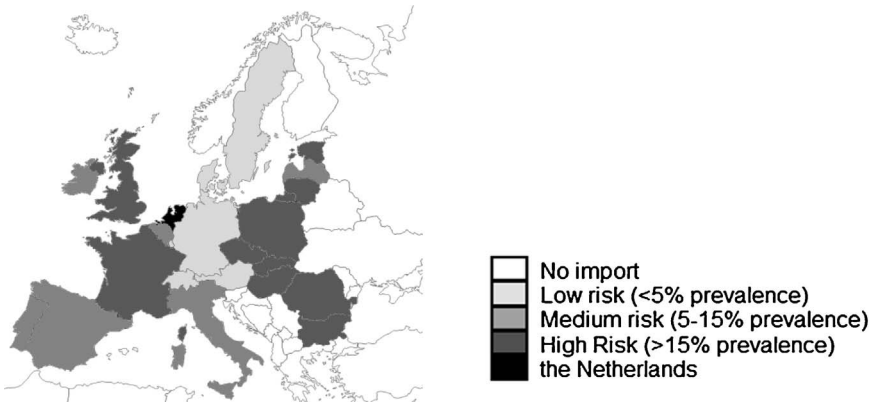

Fig. 3. Risk classification based on BVDV prevalence of European countries that trade cattle to the Netherlands.

3. Results

3.1. BVDV infected herds associated with cattle imports

Each year, 744 (5th and 95th percentile: 270–1579) of the imported cattle are infectious because they are either PI (mean 465), TR (mean 37), or TI (mean 242). These 744 cattle are imported by farmers of 334 Dutch cattle herds (5th and 95th percentile: 65–902). Of these, PI cattle are imported to 252 (75%) herds, TR cows are imported to 27 (8%) herds and 56 herds (17%) import TI cattle that were infected in the country of origin (Fig. 4). Veal herds account for most BVDV infections associated with import (87%). Only few herds from other herd types were estimated to import infectious cattle i.e. 16, 10, 9, 6, 2 and 2 suckler cow, trade, beef, dairy, small scale and young stock herds, respectively (Fig. 4).

The source of the BVDV infections differ between cattle herd types. Import of PI cattle is the major risk for introduction of BVDV in veal and beef herds, while import of TR cows was the main source of BVDV infection in trade, dairy, small scale and suckler herds (Fig. 4). TI cattle were mainly imported by veal herds and were associated with 55 infected veal herds each year (Fig. 4).

3.2. Sensitivity analysis

The proportion of susceptible cattle in source herds with virus circulation, mainly influenced the number of imported TR cows (Fig. 5). A higher proportion of susceptible cows in herds with virus circulation resulted in more cows at risk to become a TR, leading to a slight increase in TR cows. Increasing the number of susceptible cattle in these herds, from on average 30% to 70%, increased the number of infected Dutch cattle herds from 334 to 367. Decreasing this parameter to an average of 15%, decreased the number of infected cattle herds to 323.

The proportion of susceptible cattle in herds without virus circulation only influenced the number of cattle that were infected during transport. TI cattle (not being TR) transported with PI cattle, would not cause additional infected herds and varying this parameter had a negligible effect on the model outputs (Fig. 5).

The model outputs were most sensitive for alterations in the probability that a transport with TI cattle without the presence of a PI would cause a new BVDV outbreak in receiving herds (Fig. 5). Changing this probability to ML 49% (equal to a worst case R_0 value of 1.95) per TI, resulted in an additional 720 BVDV infected receiving herds (increase from 334 to 1054). This high probability of infection for a TI, resulted in 100% infected importing veal herds in most iterations, which led to a reduced variation around the mean.

Changing the probability that import of TI cattle without the presence of a PI would lead to a new BVDV outbreak in the receiving herd to ML 5% (equal to a R_0 value of 1.05) per cow, resulted in an increase in BVDV infected herds from 334 in the default model to 520 infected herds. Again, most effect was observed in veal herds (Fig. 5). When it was assumed that the R_0 value of TI cattle was always below 1, import of TI cattle would not result in additional BVDV infected herds. In this

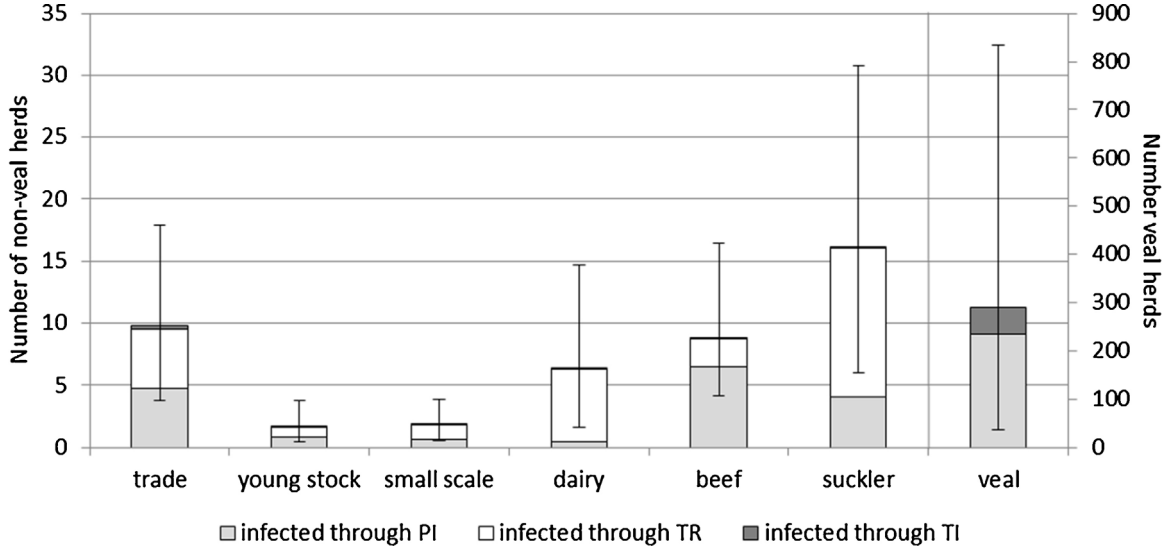

Fig. 4. The mean number (5th and 95th percentile) of herds infected with BVDV per year through import of cattle in a situation in which the Netherlands is BVDV free. The results are stratified to the source of the infection (PI: persistent infected cattle, TR: Trojan cows, TI: transiently infected cattle) and to seven cattle herd types.

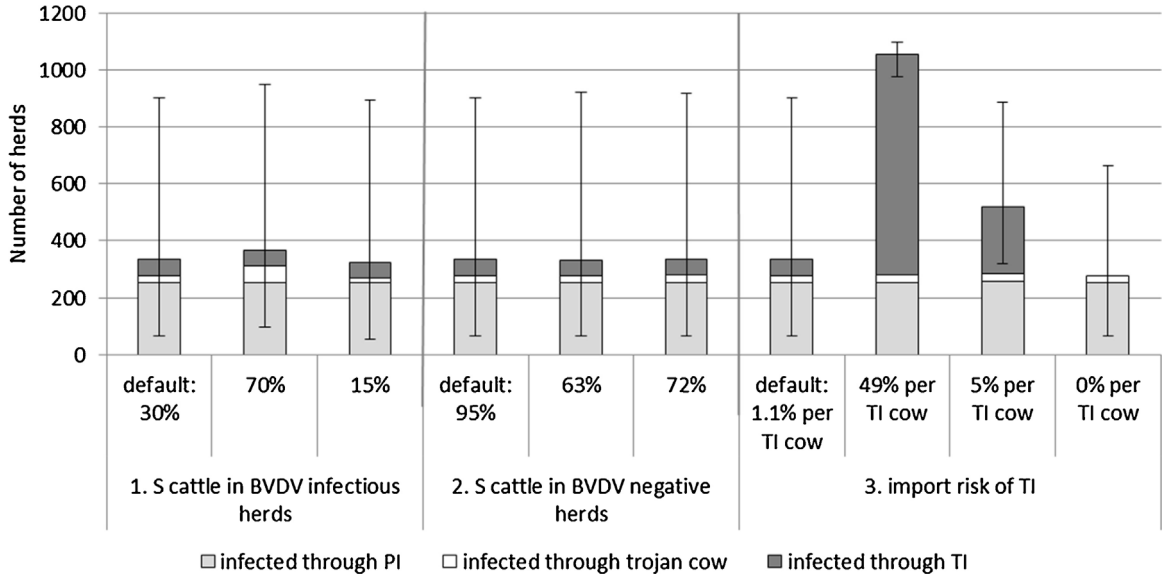

Fig. 5. The mean number (5th and 95th percentile) of herds infected with BVDV associated with import of cattle per year given that the Netherlands is BVDV free, when the values of three uncertain parameters were varied in a sensitivity analysis.

case, the number of infected herds through cattle import decreased to 279 herds per year.

3.3. Risk mitigating scenarios

The number of cattle herds that were infected through import of BVDV infected cattle, decreased from 334 when no risk mitigating actions were applied, to 81 (5th and 95th percentile: 6–476), 58 (5th and 95th percentile: 1–432) and 88 (5th and 95th percentile: 12–309) in scenario 1, 2 and 3, respectively (Table 3). When it was assumed that 20% errors were made in the sampling process (a worst case scenario), the number of BVDV infected herds associated with import was estimated at 131 (5th and 95th percentile: 22–516) and 115 (5th and 95th percentile: 14–494) herds in scenario 1 and 2.

Scenario 2 was the most effective test scenario because it reduced both the number of imported PI and TR cattle while scenario 1 mainly reduced the risk of imported PI cattle (Table 3). With the second scenario, only one non-veal cattle herd got infected per year (Table 3). The risk intervention scenarios which involved testing did not influence the risk of infections associated with TI cattle, because in the model, these cattle were infected a few days prior to import before antibodies may be detected with diagnostic tests. With scenario 3, the number of BVD infected herds through import of TI cattle was reduced to 16 herds per year. In countries with a lower BVDV prevalence the probability that cattle come in contact with the virus within eight days before transport is lower than in countries with a high (>15%) BVDV prevalence. This resulted in a lower number of infections associated with import of TI and a lower 95th percentile. Scenario 4a reduced the number of BVD infected herds to the lowest value i.e. 17 herds per year of which 16 herds were infected because of import of TI cattle. With scenario 4b, which was similar to 4a with the exemption that cattle from low risk countries did not have to be tested, reduced the number of BVD infected herds through import to 24 herds per year (Table 3). Again, the most important risk that remained was the risk of importing TI cattle. Imports of these cattle account for 17 out of 24 infected herds. With both scenario 4a and 4b the risk of reintroduction of BVD in non-veal herds were reduced to at most two herds (Table 3).

4. Discussion

When the Netherlands was assumed BVDV free and import levels remain as they currently are, the model estimated that 334 cattle herds would become infected through import of BVDV infectious cattle per year. The majority of these infected herds were veal herds, from which the virus would not, or hardly spread to other herd types because veal calves are housed indoors and are only moved off farm to go to slaughter. In the other herd types, only a limited number of herds are infected with BVDV through cattle imports.

In our model, the impact of a BVDV introduction, which may be large (Moerman et al., 1994; Lindberg, 2003), was not assessed. Our quantitative risk analysis showed that the import risk greatly differed between herd types. Veal calf herds had the largest probability to import BVDV, while other herd types only imported BVDV sporadically. When BVDV is introduced through cattle import, the probability of

Table 3
The mean, 5th and 95th percentile of the total number of BVDV infected cattle herds per year for each type of infectious import in the Netherlands.

Scenario	Type of infection*			Total (5th and 95th percentile)	Number of BVD infected non-veal herds
	PI	TR	TI		
Default	252	27	56	334 (65–903)	45 (12–96)
Sc1: virus testing prior to import	3	22	56	81 (6–476)	23 (5–50)
Sc2: sc1 combined with antibody testing of pregnant cattle	3	0	55	58 (1–432)	1 (0–4)
Sc3: Import is only allowed from countries with a low or medium BVDV prevalence i.e. <15%	57	14	16	88 (12–309)	26 (4–64)
Sc4a: sc3 combined with sc2 for all cattle	1	0	16	17 (0–125)	0.6 (0–2)
Sc4b: sc3 combined with sc2 for cattle originating from medium risk countries	6	1	17	24 (1–144)	2 (0–8)

* PI: BVDV persistently infected, TR: BVDV trojan cow, TI: BVDV transiently infected.

transmission to other cattle herds will be higher in herds with calvings (Gates et al., 2014), herds that graze their cattle and herds that trade (Valle et al., 1999; Ersbøll and Stryhn, 2000; Van Schaik et al., 2002; Bedekovic et al., 2013Bedeković et al., 2013). The risk of spread of the virus from veal herds to other cattle herds is considered low as veal herds do not have either of these risk factors. In addition, professional visitors such as veterinarians and advisors, generally differ between veal herds and other cattle herd types, which also limits indirect transmission routes. In order to minimise the probability that BVDV will spread from veal herds to other herds, enhanced biosecurity measures could be implemented in order to reduce the probability of transmission of virus both within and between herds (Lindberg and Houe, 2005; Laanen et al., 2013).

The 334 BVDV infected cattle herds per year in a BVDV-free situation are probably a worst-case scenario. Because many of the countries from which cattle are imported are currently conducting BVDV eradication programmes, the prevalence in these source countries will probably decrease. This will result in a lower import risk for the Dutch cattle population when freedom of BVDV infection is achieved. Additionally, in the model we assumed that all animals that were transported together with a PI were infected, assuming to result in additional infected receiving herds when susceptible contact animals evolved to the TR status. This represents a worst-case situation, because in reality many transports have a limited duration in which not all cattle may be infected by the PI. However, the model estimated that each year, only four herds became infected with BVD because of import of TR cows that originated from infection during transport whereas the rest of the infections were due to import of TR cows that were already infected in the country of origin (results not presented). Therefore, this assumption only leads to a very limited overestimation of the import risk.

The risk of infections with BVDV through other import routes such as import of semen, embryos or contaminated trucks, was not included in this risk assessment as they were hypothesized to play a minor role compared to import of live cattle. This hypothesis was supported by the study of Foddai et al. (2014), who concluded that the risk of introduction of BVDV in Denmark through import of semen, embryos or contaminated trucks was very low. In their risk analysis, import of cattle was also estimated to be a low risk. However, Denmark imports less than 250 heads of cattle per year compared to more than 900,000 heads in the Netherlands. Although exclusion of the import risk of other means than cattle may have resulted in a slight underestimation of the total import risk, this underestimation is assumed to be small given the strict requirements for imported sperm and embryos with regard to BVDV.

The outputs of the model seemed fairly robust and were most sensitive to the R_0 value of TI cattle. In general TI cattle are assumed to play only a minor role in the transmission of BVDV (Sarrazin et al., 2014). This is supported by the results of our risk analysis which showed an unlikely high number of infected veal herds when the R_0 of TI cattle was assumed to be higher. The results of the default model were according to the expectations of the BVDV experts. The percentage of infected veal herds estimated by the default model was quite similar to the percentage of infected veal herds that could be observed in herds that exclusively fatten imported calves (based on Dutch prevalence data, results not shown).

Four intervention scenarios were included in the model: virus testing prior to import, a combination of virus and antibody testing prior to import, prohibiting cattle imports from high risk countries and a scenario in which import restrictions were combined with testing. The antibody testing was only applicable to pregnant cows while the virus testing was applicable to all imported cattle. With the intervention scenarios, the import risk of BVDV could be reduced with 74% (sc3) to 95% (sc4a). In the test scenarios, scenario 1 and 2, import of TI cattle by veal herds would remain the most important risk for introduction of BVDV. In the model it was assumed that these TI calves were not yet detectable at the moment of sampling, to represent a worst-case scenario. In our model, the cow had to test virus negative but it may be more efficient to also consider the herd status for BVDV rather than the status of the animal alone. Taking the BVDV status of the source herds into account, will result in a further reduction of the import risk of TI cattle. The effectiveness of the diagnostic intervention scenarios decreased when it was assumed that the sampling process would be imperfect (with 20% sampling errors). In those cases, the import risk would be reduced by 61% and 66% in scenario 1 and 2, respectively.

Scenario 4a in which import restrictions were combined with testing, was estimated to be most effective in reducing the BVD import risk (from 334 to 17 infected herds per year). Nevertheless, this scenario may not be costs effective because of the extraordinarily high additional costs for both import limitations and testing. With scenario 4b we quantified the increased risk when an exemption from the test obligation would be implemented for cattle that originated from low risk countries. The output showed that scenario 4b would lead to seven additional infected herds per year compared to scenario 4a. Yet, the costs of this scenario would be much lower given that cattle imported from e.g. Germany (involving the far majority of cattle imports) would not have to be tested. Whether the costs for the risk mitigating actions in the scenarios outweigh the losses associated with BVDV infections, was not investigated in our study. Given the fact that introduction of BVDV in a (partly) naïve cattle herd can cause major economic losses and may lead to additional outbreaks (Hogeveen et al., 2003; Houe 2003; Fourichon et al., 2005; Valle et al., 2005; Lindberg et al., 2006), implementing risk mitigating scenarios are expected to be cost effective. Nevertheless, an economic evaluation is needed to determine which of the possible risk mitigating scenarios would be optimal. This optimal scenario should be feasible to implement for all herd types, should lead to a considerable reduction in import risk and should be cost-efficient.

For BVD, import of infected cattle in non-veal herds are assumed to cause a higher risk for further transmission than import of these cattle in veal herds because of the structure of the veal industry. With scenario 2, 4a and 4b, the majority of the remaining risk was assigned to veal herds. The remaining risk of reintroduction of BVD in non-veal herds reduced to respectively 1, 0.6 and 2 herds per year, which was deemed acceptable. After reintroduction of the virus, it is very important that the virus is detected as soon as possible. The time between introduction of the virus through import and subsequent detection in the Netherlands was not included in our study. It is recommended to evaluate the potential spread of BVD after re-introduction and to assess the effectiveness of surveillance measures implemented for early detection of re-incursion of the virus in the Netherlands. Given our results, it appears advisable to implement surveillance that aims to detect new introductions of BVD before the virus is transmitted to other herds.

Initially, also intervention scenarios in which all imported cattle were vaccinated prior to import or channelling of veal calves to a limited number of veal herds were considered. It was decided not to include these scenarios in the model. The type of vaccine used in each of the EU countries and the quality of administrating the exact moment at which vaccination was applied, was unknown. Furthermore, vaccination does not reduce the infectiousness of PI cattle and in order to gain protection for vertical transmission, the cow has to be vaccinated before gestation which is difficult to maintain. Although, vaccination would protect cattle from becoming TI, protection of a TI status during transport would not influence the probability of infection of an importing herd given that a PI would be present in the same transport. The majority of imported TI that were infected in the country of origin involve young calves. These calves were infected because of lack of maternal antibodies and were too young to be effectively vaccinated. A vaccination scenario in the country of origin was therefore considered not feasible. The scenario in which channelling of imported calves would be applied would be effective in reducing the import risk. However, because the veal sector already applies channelling which

was included in the default model, additional channelling would only result in a slight decrease in risk.

The assumptions and inputs used in the model were valid for BVDV type 1 as this is the most common BVDV type occurring in Europe (Couvreur et al., 2002; Liebler-Tenorio et al., 2006). The results might not be valid for other, more virulent strains of BVDV. However, given that import of PI and TR in our model was assumed to cause infections in all importing herds, this risk would be similar for more virulent BVDV strains. Whether the import risk TI cattle is similar between different BVDV strains is unknown.

Our import risk analysis only considered the risk of introduction of BVDV into the Netherlands in a BVDV free situation. Currently, BVDV is still endemic in the Netherlands. Given the current BVDV prevalence, the model estimated that cattle imports were causing 182 newly infected cattle herds per year.

Although this study was conducted for the Netherlands which import high numbers of cattle, the applied methodology can also be used for quantitative risk assessments for other diseases, other import risks and in other countries.

5. Conclusions

The import risk analysis showed that BVDV is regularly imported into the Netherlands. However, the majority of herds that are infected through import are veal herds, in which calves are housed indoors and are only moved off farm to go to slaughter. The number of infected cattle herds through cattle imports in each of the other herd types was limited. The import risk can effectively be reduced by testing imported cattle for BVDV virus (all cattle) and antibodies (pregnant cattle only), abolishing imports from countries with a high BVDV herd prevalence (>15%) or through a combination of both.

Acknowledgements

This study was commissioned and funded by the Ministry of Economic Affairs, within the framework of Policy Support Research, One Health For Food. We acknowledge the input from Prof. M. Nielen (Utrecht University), Dr. M. Mourits (Wageningen University) and Dr. H. Saatkamp (Wageningen University).

Appendix A. Estimated BVD virus herd prevalence in European countries

Country	Virus herd prevalence	Year of estimation	Included as	Source
Belgium	10%	2014	fixed value	Diergezondheidszorg Vlaanderen, Lier Belgium
Bulgaria	70% (56–82%)	2006–2008	binomial distribution	Assumed equal to Hungary
Denmark	0.0%	2015	fixed value	Pers. Comm. SEGES, Aarhus, Denmark and University of Copenhagen, Copenhagen, Denmark
Germany	0.3% (0.3–0.3%)	2015	binomial distribution	Pers. Comm. Friedrich Loeffler institute, Riems, Germany
Estonia	17.0% (9.4–24.6%)	2007	pert distribution	(Lassen et al., 2012)
France	21.5 (20.9–22.0%)	2004	binomial distribution	(Joly et al., 2005)
United Kingdom	58.6 to 75%	2007–2010	discrete distribution	(Bishop et al., 2010; Humphry et al., 2012; Williams and Winden, 2014)
Hungary	70% (56–82%)	2006–2008	binomial distribution	(Kovago et al., 2015Kövágó et al., 2015)
Ireland	5.7% 5.6–5.8%)	2015	binomial distribution	Pers. Comm. Animal Health Ireland, Dublin, Ireland
Italy	12.7% (10.3–15.5%)	2014	binomial distribution	Pers. Comm. Italian health authority and research organization for animal health and food safety (IZSVe), Legnaro, Italy and National reference laboratory for Asfivirus, Pestivirus and ruminants retroviruses, Perugia, Italy
Latvia	11.4% (10.6–12.2%)	2007–2008	binomial distribution	Pers. Comm. Institute of Food Safety, Animal Health and Environment (BIOR), Riga, Latvia
Lithuania	54.4% (46.0–62.6%)	1997–2001	binomial distribution	(Mockeliuniene et al., 2004Mockeliüniene et al., 2004)
Luxembourg	0.14%	2015	fixed value	Pers. Comm. Ministry of Agriculture, Luxembourg, Luxembourg
Austria	0.2% (0.1–0.3%)	2008	binomial distribution	(Rossmanith et al., 2010)
Poland	50.5% (40.3–60.7%)	2010–2013	binomial distribution	(Kuta et al., 2013)
Portugal	9.7% (5.1–16.3%)	2003	binomial distribution	(Niza-Ribeiro et al., 2005)
Romania	70% (56–82%)	2006–2008	binomial distribution	Assumed equal to Hungary
Slovakia	70–75%	2016	Uniform distribution	Assumed equal to Chech Republic
Spain	10–58%	2003–2008	Discrete distribution	Extrapolated from France and Portugal
Czech Republic	70–75%	2016	Uniform distribution	Pers. Comm. Zoetis, Prague, Chech Republic
Sweden	0.8%	2005	pert	(Hult and Lindberg, 2005)

	(0–2.7%)		distribution	
Switzerland	1.1% (0.9–1.2%)	2010	binomial distribution	(Presi and Heim, 2010)

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