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Quantification of the probability of reintroduction of IBR in the Netherlands through cattle imports

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ABSTRACT

In the Netherlands, the feasibility of a national control program for infectious bovine rhinotracheitis (IBR) is discussed. The aim of this program would be to achieve freedom from BoHV1 circulation (the causal agent of IBR), in the Dutch cattle population. When IBR would be eradicated, maintaining the free status is essential and insight in the probability of introduction of IBR through cattle imports is crucial. Values for input parameters such as the number of imports per country of origin, herd level prevalence and probability that a random imported animal per age category was either acutely or latently infected with IBR were quantified. A stochastic simulation model was built to predict the basic risk and the efficacy of four risk mitigating scenarios were evaluated. These scenarios involved testing prior to import, import restrictions and vaccination. The model output predicted that IBR infected animals are imported regularly. In an IBR free situation, 571 (5th and 95th percentile: 431–781) cattle herds will be newly infected. Latent infections account for most newly infected herds (77%). When the virus in the imported latently infected animal does not reactivate, subsequent impact of such infections remains limited. The model predicted that most of the herds infected by introduction of acutely infected animals would be veal herds. The scenario in which imports were only allowed from status 9 or 10 countries combined with testing cattle that originated from status 9 countries was most effective in reduction of the import risk to 70 herds per year. The scenario in which vaccination of calves was combined with testing of older cattle was estimated to reduce the number of newly infected herds to 82 per year. The stakeholders classified the latter scenario as most realistic because this scenario was deemed both feasible and rather effective. This study did not evaluate the impact of introduction of IBR in the cattle population, which might differ depending on the type of infection (acute vs. latent) and the herd type in which the virus is introduced. Moreover, when making the final decision about the optimal intervention, the economic perspective should also be taken into account. This study predicted that introduction of IBR will remain a risk for the Dutch cattle population after virus circulation is eliminated from the Netherlands. The import risk is reduced most in scenarios in which testing and vaccination are combined.

1. Introduction

An accepted method to evaluate the risk and uncertainty associated with animal health, involves risk assessment (Vose, 2008). Quantitative risk analyses are frequently used to evaluate the risk of import of infectious diseases (De Vos et al., 2015). Because import of animals is frequent in the Netherlands, it is vital to gain insight in the probability of introduction of infectious diseases of which we are either free or that occur sporadically.

Currently, the feasibility of a national control program for infectious bovine rhinotracheitis (IBR) is discussed with the goal to eradicate this cattle virus from the Netherlands. IBR is caused by bovine herpes virus type 1 (BoHV1). After infection with BoHV1, an animal will shed the virus during a short period of approximately 10 days after which it becomes seropositive (Bosch et al., 1996; Kaashoek et al., 1996a, 1996b; Kaashoek and Van Oirschot, 1996). Seropositive cattle remain latently infected for the rest of their lives and stress can induce reactivation and intermittent excretion of the virus (Kaashoek et al., 1996a; Muylkens et al., 2007).

Purchase of cattle and direct contacts between cattle from different herds are the major risk factors for reintroduction of IBR (Van Schaik et al., 2002; Vonk Noordegraaf et al., 2004; Boelaert et al., 2005). When

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the Netherlands will be free from IBR, national trade will no longer pose a risk and import of cattle becomes the largest threat for reintroduction of the virus. In the Netherlands, more than 900,000 cattle are imported annually, of which the far majority (> 94%) are veal calves that are fattened for a few months and are send to slaughter thereafter. About 50,000 heads of cattle are imported by dairy herds, young stock rearing herds, traders or beef herds. Most imported cattle originate from countries that are either free or nearly free from IBR. Nevertheless, a substantial part of the cattle are imported from countries in which the virus is still endemic. The extent of the import risk is unknown and more information is required to decide whether risk mitigating actions will be necessary and which intervention measures will be most effective in reduction of the risk.

The objectives of this study were to 1) quantify the risk for reintroduction of IBR caused by cattle imports using stochastic simulation modeling in a situation where the Dutch cattle population is free from BoHV1 circulation, and 2) assess a number of risk mitigation scenarios in their ability to reduce the import risk.

2. Materials and methods

Based on the conceptual framework of quantitative risk assessments, a risk release pathway was drawn to qualitatively describe the possible risk of introduction of IBR when cattle are imported (Fig. 1). A stochastic simulation model was built to evaluate the import risk using MS Excel (Microsoft Corp., 2013) and @Risk 6.2.0 (Palisade, 2014). In this model, the risk of cattle imports was quantified based on available data, information originating from literature and expert opinion. Uncertainty in parameter values was incorporated by including probability distributions instead of fixed values (Vose, 2008).

2.1. Imports

The information about cattle imports on animal level were derived from Identification and Registration data (I & R; RVO Assen, the Netherlands). In this database, all imported cattle are registered on animal level with the country of origin, the birth date of the imported animal, the import date and the unique herd number of the receiving herd. The cattle that are imported in the Netherlands originate from 21 different European member states (EU MS) (I & R data from 2011 until 2015). Most imported cattle were calves < 4 months of age that were imported from Germany (55%), Poland (9%) and Belgium (7%) (Appendix A). In the model, import of calves and older cattle were distinguished from each other to enable inclusion of age specific risks. Furthermore, for calves it was possible to determine the origin at regional level (within countries) based on the ear tag number because imported calves were assumed to originate from their birth region. For older cattle, the region from which the cattle were imported was unknown because there was no information available about the trade history of these animals prior to import. Thus, for imported calves we used regional differences in import risk within the country of origin, if available. For older cattle we evaluated the risk on country level

The probability of importing IBR was estimated, based among others on the number of imports and disease status of the region or country of origin combined with demographic information of the country of origin (i.e. number of cattle herds and total number of cattle).

2.2. Disease specific information

For IBR, all herds with seropositive cattle were assumed a risk and

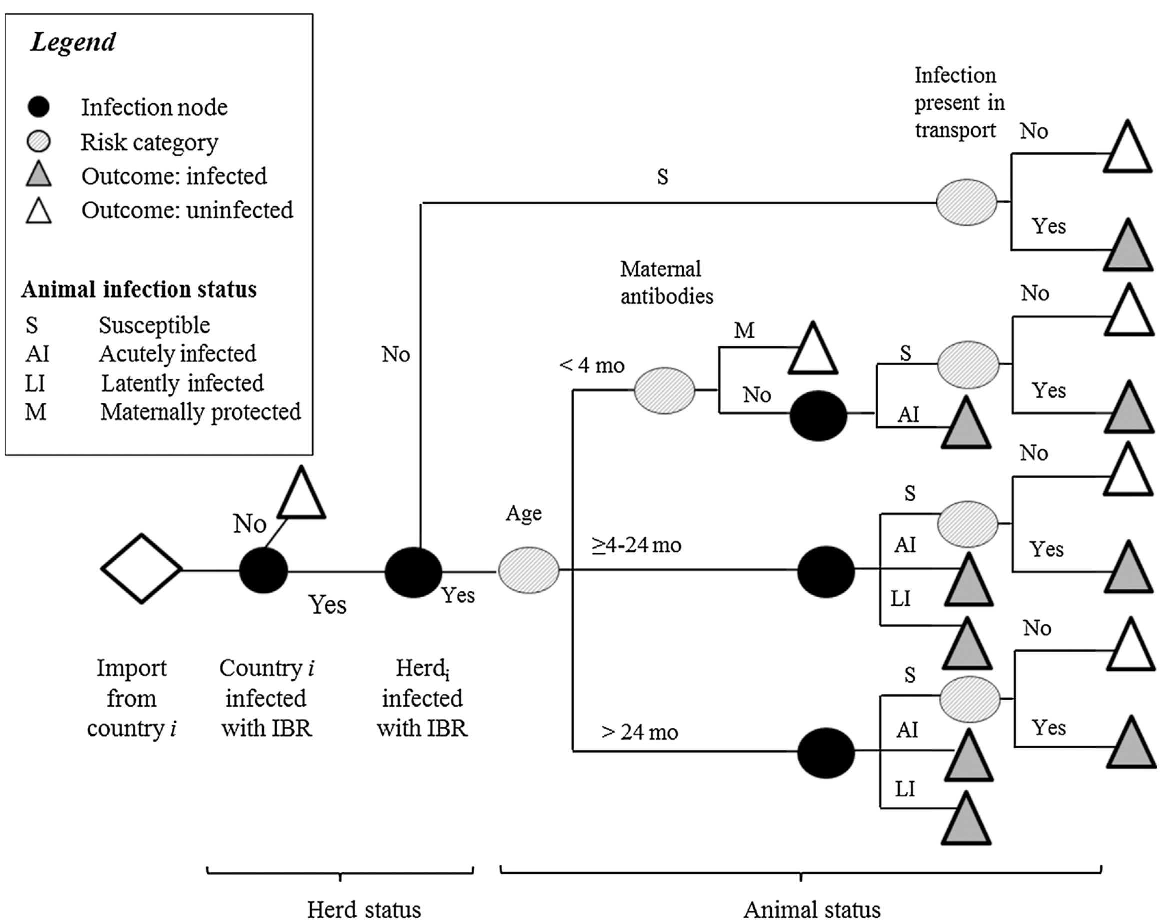

Fig. 1. IBR import risk pathway for cattle that imported to the Netherlands.

the seroprevalence at herd level was obtained for each of the source countries. Initially, information about the IBR herd prevalence was evaluated based on literature. However, given all current initiatives in place in EU member states to control and eradicate IBR, part of the literature was outdated and experts about the epidemiology of IBR from the source countries were contacted (either in person or by phone) to obtain more recent information. The goal was to obtain recent prevalence estimations for both beef and dairy herds, preferably on a regional level. For most countries regional level prevalences were not available but good estimates were present for the whole cattle population. Eventually, it was decided to evaluate the import risk from Germany on regional level (good prevalence information on regional level and high numbers of imported calves) and to evaluate the import risk from all other countries on national level.

For IBR, cattle from infected herds could have one of four infection statuses i.e. Susceptible (S), Maternally protected (M), acutely infected (AI) or latently infected (LI). Acutely infected cows are a higher risk for further transmission compared to latently infected cattle because the latter will not result in spread of IBR if the virus does not reactivate. Nevertheless, import of a single animal of either type of infection was assumed to result in loss of the IBR free status.

The percentage of infected cattle (either acute or latent) in infected herds is known to differ between age categories and was estimated at on average 55% in adult cows (Mars et al., 2001; Lassen et al., 2012) and 18% in young stock between 4 and 24 months (Mars et al., 2001; Sayers et al., 2015) (Table 1). The probability that calves < 4 months were infected with BoHV1 prior to import when they were born in an IBR infected herd and were not maternally protected, was very uncertain and could not be determined based on literature. We tried to estimate this parameter based on diagnostic results for IBR in young breeding bulls that were available at GD Animal Health. In IBR infected herds, potential breeding bulls are separated from their dams at birth and are fed colostrum from IBR seronegative cows. These calves do not have maternally derived antibodies and are susceptible to an IBR infection. Before these calves are moved to an breeding center, they are tested for antibodies against BoHV1. The results of 130 of such calves that were tested between 2009 and 2015 and that were younger than 21 days were used to estimate a value for the probability that calves < 4 months are infected with IBR prior to import. Of these, 4 calves tested positive (3.1%; 95% CI: 0.8–7.7%). This percentage was assumed to be the maximum prevalence in the first three weeks because tracking and tracing indicated that part of these seropositive calves accidentally received colostrum from seropositive cows and thus were probably not infected (Personal communication). Therefore, the probability that calves < 4 months were infected, was modelled as a uniform distribution with a minimum of 0 and a maximum of 3.1 (Table 1). Because of the uncertainty in the value of this parameter, we varied it in a sensitivity analysis. Given that 67–98% (expert opinion) of the new born calves are assumed to receive sufficient amounts of colostrum, the probability that imported calves < 4 months of age originating from IBR positive herds are infected with IBR was estimated to be 0.8% (calves with seropositive dams * insufficient colostrum intake * P infection prior to import + calves with seronegative dams * P infection prior to import) (Table 1). Assumptions were also included for the ratio acutely versus latently infected cattle which was assumed to differ depending on age (Table 1). The infectious period of an acute IBR infection was estimated to be 10 days based on earlier studies (Table 1).

2.3. Risk associated with transport

To evaluate the number of times that IBR was introduced through cattle imports, the number of imported cattle were aggregated to the number of trucks that transported import cattle per year. Although, the exact annual number of cattle transports with import cattle was unknown, it was possible to obtain a rough estimate using information from the Dutch I & R system. To estimate the average number of transports with import cattle per year, first, the number of import occasions were extracted from the I & R data (Table 2). One import occasion was defined as an import event on a specific day to one specific herd. Secondly, we calculated the average number of imported cattle per import occasion by dividing the total number of imported cattle per herd per year by the number of import occasions. When the average number of cattle per import occasion was less than the maximum allowed number of animals per transport according to EU and national regulations (EC, 2005; IKB, 2008), it was assumed that these cattle were transported together (Table 2). According to the same regulations it was assumed that a transport unit (such as a truck or trailer) is allowed to transport cattle to one, or at most two locations.

In the model, latently infected cattle in which the virus reactivated during transport, were assumed equally infectious as acutely infected cattle. In addition, cattle that became infected during transport, could not yet lead to secondary infectious animals prior to arrival in the receiving herd because most transports were assumed to have a duration of less than 8 h. This period is rather short to become both infected and evolve to the subsequent infectious status. These assumptions had a negligible effect on model outputs because, in both situations, the

Table 1
Input parameters for the cattle import risk analysis for IBR in the Netherlands.

Parameter	Most likely value or point estimate (%)	Distribution	Source
Percentage seropositive cattle > 24 months in IBR infected herds	**55**	Discrete distribution 53; 54%; 55%; 58%	Mars et al. (1999); Lassen et al. (2012); Pers. Comm. Belgium, 2016
Percentage seropositive young stock 4–24 months in infected herds	18	Uniform distribution 15%–20%	Mars et al. (1999); Sayers et al. (2015); Pers. Comm. Belgium, 2016
Probability that calves < 4 months are infected with IBR prior to import provided that they are housed in an IBR infected herd and are not maternally protected	1.5[a]	Uniform distribution 0%–3.1%	GD data from screening of bull calves for AI companies
Total probability that import calves < 4 months are infected with IBR	0.8	25th–75th percentile 0.29%–1.24%	Result of the first three parameters in this table
Percentage calves assume to drink sufficient amounts of colostrum (pCol)	83	Uniform distribution 67%–98	Expert opinion[b]
Ratio acute versus latent IBR infections (calves < 4 months)	100 acute[a] 0 latent[a]		Expert opinion[b]
Ratio acute versus latent IBR infections (young stock 4–24 months)	1 acute[a] 99 latent[a]		Expert opinion[b]
Ratio acute versus latent IBR infections (cows > 24 months)	1 acute[a] 99 latent[a]		Expert opinion[b]
Average infectious period of acute infected cattle (tI)	10 days	Discrete distribution 9.8;10.3;10.5;10;9.5	Bosch et al. (1996); Kaashoek et al., (1996a, 1996b); Kaashoek and Van Oirschot (1996); Kaashoek et al. (1998)

[a] Varied in a sensitivity analysis.
[b] M.H. Mars, H.W.F. Waldeck, L. van Duijn, P. Wever and G. van Schaik.

Table 2
Average number of imports and transports that occurred for import of cattle per year in the period 2011–2015.

	Average annual number of import occasions[a]	% herds per herd type that import cattle	Average number of imports per importing herd per year	Average number of cattle imported at each import occasion	Average assumed number of transports per import occasion[b]
Dairy	514	2%	1.6	13	1
Veal	4691	47%	4.8	185	2
Young stock	111	2%	2.3	24	1
Suckler cows	842	7%	3.6	9	1
Beef	985	36%	4.1	17	1
Traders	438	20%	7.1	32	1
Small scale	280	2%	1.5	7	1

[a] Assumed that one import on one day to one herd equals one import occasion.
[b] Assumed that the minimum allowed number of transports (according to regulations) were applied.

transport was already infected with IBR and would always result in import of IBR infected cattle in a herd.

2.4. The stochastic simulation model

The risk of IBR introductions through cattle imports, depends on the number of transports with the presence of at least one acutely or latently infected imported animal. Imported cattle with an acute IBR infection at arrival in the receiving herd were defined as cattle that were infected within 10 days prior to the date of import and that were infectious during transport. For each of the EU MS (*i*) from which cattle are imported, the probability that a random animal was either acutely or latently infected with IBR ($pINF_c$) was determined based on the between ($Hprev$) and within herd IBR prevalence ($INFprev_c$) combined with the probability that an IBR positive animal was in the acute or latent phase of the infection at the moment of import ($pIBR_{c,age}$). The subscript letter *c* represents the infection status which could be either acute (*a*) or latent (*l*). The within herd prevalence differed between each of the age categories (age) in the model and thus *pINF* was calculated per specific age class (formula 1).

$$pINF_{c,age,i} = Hprev_i * INFprev_{c,age} * pIBR_{c,age} \quad (1)$$

Imported cattle that were latently infected were defined as cattle that were infected more than 10 days prior to the date of import and that were antibody positive. The probability that a random imported animal was either acutely or latently infected with IBR, was multiplied with the total number of imported cattle ($nIMP$) for each of the stratified age categories (*age*) and EU MS (*i*). The number of imported cattle that were infected was summed over the age categories and subsequently resulted in the number of acutely and latently infected imported cattle ($nimp_c$) per age category (formula 2).

$$nimp_{c,i} = \sum_{n=1}^{age} (pINF_{c,age,i} * nIMP_{age,i}) \quad (2)$$

To translate the number of imported cattle that were infected with IBR into the number of infected transports, the probability that a transport was free from IBR infected animals ($pTrans\_free_i$) was calculated as the probability that all cattle in the transport unit (*nTrans*) were not infected with IBR (1-pinf) (formula 3).

$$pTransfree_{c,age,i} = (1 - p\,\mathrm{inf}_{c,age,i})^{nTrans} \quad (3)$$

Based on $pTrans\_free_i$, the probability that a transport was infected with at least one BoHV1 infected animal was estimated. It was assumed that each transport unit would infect most likely one and at most two importing herds. Cattle that became infected with IBR during transport did, in general, not lead to any additional infected herds because the receiving herd would already have become infected due to the initial infected animal present in the transport.

The stability of the model output was evaluated by comparing the output of different numbers of iterations and was determined stable after 5000 iterations when the mean and variation of the output were stable.

In the model, the Netherlands was assumed free from IBR and every import of infectious cattle led to newly infected herds. In addition, seven different cattle herd types were distinguished i.e. dairy, suckler, veal, beef, trade, young stock and small scale herds because both the risk of import and the risk of subsequent spread to other herds differed per cattle herd type.

2.5. Sensitivity analysis

Sensitivity analyses were conducted for two parameters that could not be estimated based on data or literature and of which the experts were rather uncertain. In a first sensitivity analysis, the ratio of acutely versus latently IBR infected cattle ≥4 months in a source herd was varied between a ratio of 5% versus 95% and 10% versus 90%, respectively (default 1% versus 99%). In a second sensitivity analysis, the estimated percentage of IBR infected calves born in IBR infected herds that were assumed to be acutely infected at arrival in the Netherlands was varied. In the basic model this percentage was estimated to fluctuate between 0% and 3.1%. In the sensitivity analysis this percentage was set at a fixed value of 1% (expert opinion) or was assumed to fluctuate around 5.2%. The latter percentage was based on two studies that evaluated the IBR prevalence in calves. Sayers et al. (2015) found an IBR prevalence of 6.7% in young stock between 3 and 18 months (average 9 months). In Belgium, an IBR prevalence of 14% in calves between 6 and 12 months was found (personal communication). Because the calves that were evaluated in these studies were much older than the veal calves that are imported in the Netherlands (average age at import of 21 days), the average of these two studies (10.4%) was included as maximum value. This parameter was included as a uniform distribution in the model with 0% as minimum.

2.6. Risk mitigation scenarios

When the Netherlands will be free from BoHV1 circulation, there will remain a risk of reintroduction of the virus due to cattle imports. Therefore, a number of possible risk mitigation scenarios were evaluated that could include disallowance import of cattle from high risk countries for IBR, testing of cattle prior to import and prohibit import of IBR positive cattle and vaccination of import cattle with gE deleted DIVA vaccines prior to transport. In the scenarios in which testing prior to import was evaluated, two different tests could be applied i.e. a gE ELISA or a gB ELISA. With gE ELISA wild type BoHV1 antibodies will be detected with a sensitivity of 87% (Wellenberg et al., 1998a). The gB ELISA is a conventional test and will detect all BoHV1 antibodies, with a sensitivity of 98% (Wellenberg et al., 1998b) and can only be used in unvaccinated populations. In the first scenario, imported cattle were tested with a gE ELISA prior to import and if tested positive, not imported (gE test scenario). In a second scenario, import animals were tested with a gB ELISA prior to transport (gB test scenario). In a third scenario, import from high risk countries would be prohibited (import restrictions scenario). In the European Union, two official acknowledged IBR statuses can be obtained for IBR: article 9 i.e. an EU approved control program is in place or article 10 i.e. an IBR free status. In this scenario, only imports from countries with an article 9 or 10 status would be allowed and cattle originating from countries with an EU article 9 status were additionally screened with a gE test. A fourth scenario was included in which export calves would be vaccinated prior to transport and preferably as soon as possible after the calf was born. Additionally, older cattle ≥4 months are tested with a gB test prior to import (test and vaccination scenario).

Finally, in an additional scenario, the remaining import risk was evaluated assuming that both Belgium and Germany achieved the article 10 status at the moment the Netherlands would be free from BoHV1 circulation.

3. Results

3.1. Basic model

The model predicted that IBR infected animals are regularly imported in Dutch cattle herds. These cattle would lead to 571 newly infected herds (5th and 95th percentile: 431–781) per year. From these 571 newly infected cattle herds, 437 (77%) import cattle that are latently infected and 134 (23%) import cattle that are acutely infected with IBR (Fig. 2). Veal herds import the majority of acutely infected cattle. The non-veal herds account for the far majority of reintroductions of IBR through import of latently infected cattle (n = 418 herds per year) (Fig. 2).

3.2. Sensitivity analysis

The model output appeared not very sensitive for the ratio acutely versus latently infected cattle in IBR positive source herds (Fig. 3). The model output appeared sensitive for the probability that a young calf became infected with IBR prior to the date of import. The total number of newly infected herds due to imports reduced from 571 to 532 (5th and 95th percentile: 431–781) when the probability that susceptible calves became infected was changed to a fixed value of 1%. Increasing this probability to an average of 5.2% (uniform distribution between 0 and 10.4%), resulted in an increase from 571 to 819 infected herds (Fig. 3).

3.3. Risk mitigating scenario's

When the test scenarios were applied, the number of cattle herds that were infected because of import of IBR infected cattle, decreased from 571 to 194 or 143 per year with the gE or gB test scenario, respectively (Table 3). The scenario in which import from countries without an official EU status would be prohibited combined with additional testing of cattle from countries with an article 9 status, resulted in a risk reduction from 571 to 70 newly infected herds per year (Table 3). The scenario in which calves would be vaccinated prior to import and imported cattle ≥4 months would be tested with a gB test followed by the subsequent action of not importing test positive animals, reduced the number of newly infected cattle herds in the Netherlands to 82 per year (Table 3).

The import risk of IBR would decrease from 571 to 341 newly infected herds (decrease of 40%) when Belgium and Germany would be IBR free and no intervention measures would be taken in Dutch cattle herds (Fig. 4).

4. Discussion

The model with input parameters based on the current situation estimated that in an IBR free situation, cattle imports would lead to 571 newly infected cattle herds per year. From these, 77% would be caused by import of latently infected cattle and 23% would be due to import of acutely infected cattle. In the model we assumed that import of a single IBR infected animal would always result in an infected receiving herd. Thus, we did not apply differentiation between the risk of importing acutely or latently infected cattle. Nevertheless, there might be a major difference in the consequences. Import of an animal that is acutely infected with IBR and that is still infectious at arrival, will probably result in a major IBR outbreak in a susceptible receiving herd. A latently infected animal first needs to reactivate before it is able to transmit the virus. Without reactivation the latently infected animal will remain a single reactor in the receiving herd. However, because latently infected cattle can reactivate throughout their lives and stress (because of for example transport) is known to enhance the probability of the virus to reactivate, they are assumed to pose a similar risk compared to acutely infected animals.

Each year, approximately 900,000 cattle are imported into the Netherlands. Although it was possible to differentiate the number of imports between countries, and for Germany even between regions of origin, it was not possible to correct for clustering within herds of origin because it was unknown which imported cattle came from the same herd. However, we do believe that the clustering within herds is limited because the majority of imported animals are veal calves that are randomly clustered together in groups of similar calves. Clustering within in herds of origin is more likely with older cattle import because these animals are more often coming from the same source. Therefore, assuming a random probability of infection per animal may have resulted in a slight overestimation of the import risk.

The model did not include the risk of collection of cattle prior to transport. This may have resulted in an underestimation of the total import risk. Nevertheless, given the R_0 value of 2.1 for IBR (Mars et al., 2001), the average infectious period of 10 days (Kaashoek et al., 1996a) and the short stay at a collection center, it was assumed that the effect of exclusion of this factor would be limited. In addition, we assumed that acutely infected animals would not be diagnostically detectable just prior to transport. Although an acute infection with IBR might evolve subclinically, part of the acutely infected animals may be

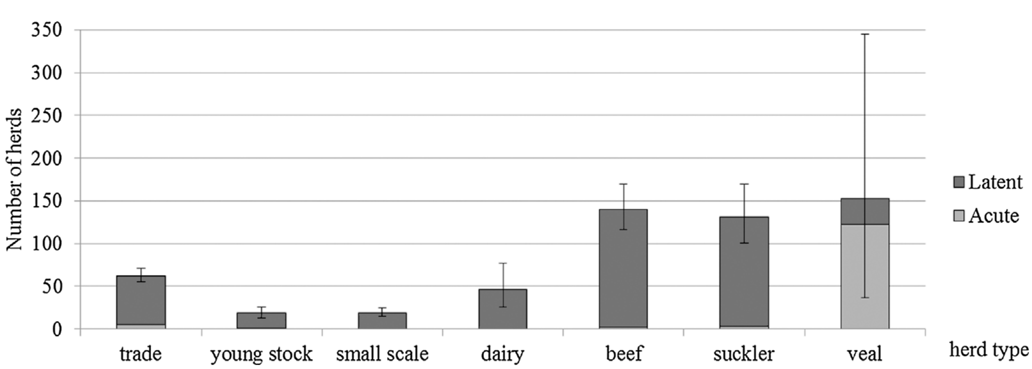

Fig. 2. The estimated average number of cattle herds newly infected with IBR per year (5th and 95th percentile presented with the error bars) in a situation in which the Dutch cattle sector is free from IBR.

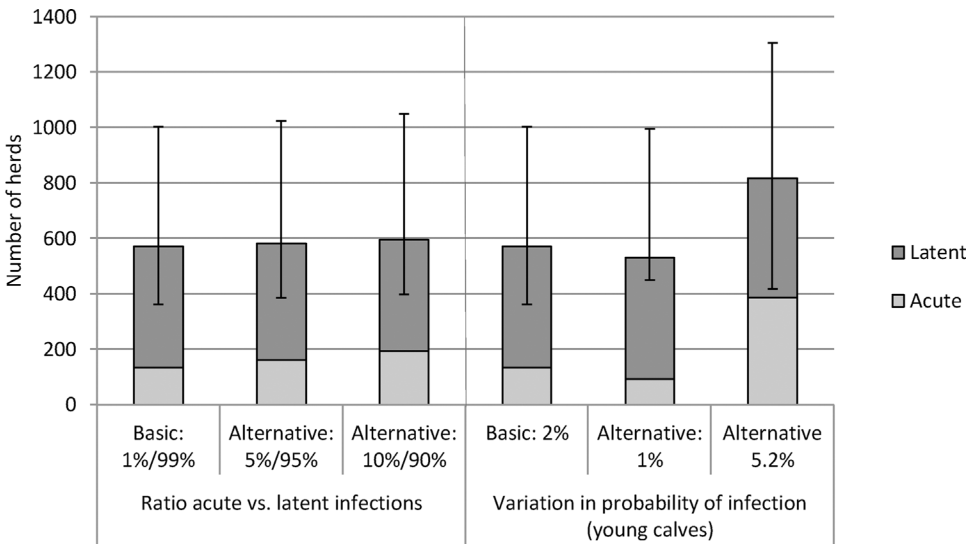

Fig. 3. The average number (5th and 95th percentile presented with the error bars) of herds newly infected with IBR associated with import of cattle per year in the Netherlands, when the values of uncertain parameters were varied within a sensitivity analysis.

detected during the standard clinical export examination and will be excluded from import.

This import risk assessment only considered the risk of introduction of IBR into the Netherlands. The consequences of an introduction, which may be substantial because of direct losses and trade restrictions, was not assessed. When IBR is introduced through import, the risk of spread to other cattle herds will be higher in herds that graze their cattle and herds that trade cattle (Van Schaik et al., 2002). The risk of transmission of the virus from veal herds to other cattle herds is considered limited as veal herds do not graze their cattle and only move the calves off-farm to go to slaughter at an age of 6–8 months of age. In order to minimize the probability that IBR will spread from veal herds to other herds, additional management measures such as enhanced biosecurity measures and movement restrictions could be implemented.

The risk of infection with IBR through other routes such as import of semen, embryos or contaminated trucks, were not included in this risk assessment. Given the regulations in place for import of genetic material and biosecurity measures concerning trucks, they were hypothesized to play a small role as compared to the large number of imported cattle in the Netherlands. In earlier risk assessments, semen, embryo's or contaminated trucks were found to be associated with a risk of introduction of BVD of once per nine years for import of BVD in Denmark (Foddai et al., 2014). Given the fact that the Netherlands trades internationally and extensively, the risk of these other introduction routes may become more important when the risk of importing cattle is diminished.

Almost 95% of all imported cattle are calves that are imported by the veal industry at an average age of 21 days. To estimate the risk of the calves being infected with IBR, information was needed about the probability that a young calf born in an IBR infected herd would be infected prior to import. Based on limited data, the percentage of calves without maternal antibodies against BoHV1 that were housed in IBR infected herds and assumed to be infected with IBR prior to import was estimated to be 1.5%. The value of this parameter was based on screening results of 130 young bull calves by breeding organizations in the Netherlands. Nevertheless, because the amount of data was limited and do not represent a random sample, the value of this parameter was varied in a sensitivity analysis. Although, the model output appeared sensitive for alterations in this parameter, the experts believed that the probability that calves without maternal antibodies in IBR infected herds were infected with BoHV1 during the first 21 days of their lives would be lower rather than higher than the 1.5% default value. It was therefore expected that the results of the sensitivity analysis would have overestimated the import risk of IBR in veal herds.

Four risk mitigating scenarios were included in the model: gE ELISA test, gB ELISA test, import restrictions and test and vaccination scenarios. In the first two scenarios, the risk of importing IBR in the Dutch cattle industry reduced with 66% (gE ELISA) or 74% (gB ELISA). When only unvaccinated cattle are imported, gE testing is less effective than testing with a gB ELISA given the lower test sensitivity. However, as long as part of the cattle are vaccinated, only a gE test can be used to detect IBR infected cattle. Although both test scenarios were very effective in reducing the import risk of latently infected cattle, the number of newly infected herds remained substantial because imported calves were not tested as maternal antibodies would hamper the diagnostic results. Thus, both scenarios exclusively decreased the import risk for non-veal herds given that the import risk for veal calves was mainly caused by import of acutely infected animals. The scenario in which only imports from countries with an article 9 or 10 status were allowed combined with testing cattle from article 9 countries, was most

Table 3
The average, 5th and 95th percentile of the total number of IBR infected cattle herds associated with cattle imports per year in the basic model and with the risk mitigation scenarios in the Netherlands.

Scenario	Type of infection		Total (5th and 95th percentile)
	Acute	Latent	
Basic model	134	437	571 (431–781)
1. testing imported cattle ≥4 months with a gE test prior to import (87% sensitive)	134	60	194 (74–402)
2. testing imported cattle ≥4 months with a gB test prior to import (98% sensitive)	134	9	143 (24–344)
3. imports are only allowed from countries with an article 9 or 10 status, and cattle ≥4 months from countries with an article 9 status are tested prior to import.	34	36	70 (41–119)
4. imported calves < 4 months are vaccinated with live vaccine, reducing the risk of infection with 50%, imported cattle ≥4 months are tested prior to import	73	9	82 (21–184)

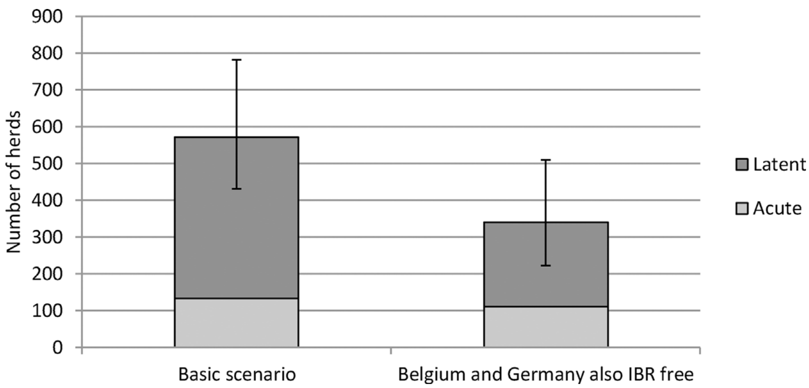

Fig. 4. The average number (5th and 95th percentile presented with the error bars) of herds newly infected with IBR associated with import of cattle per year in the Netherlands, assuming imports only from countries with no or few herds with IBR.

effective in reducing the IBR import risk. However, considering the international market for veal calves, this scenario may not be a realistic option, given that the total number of calves that are required by the veal industry exceeds the number of calves that are available from countries with an article 9 or 10 status at this moment. The fourth scenario seemed more feasible and was also rather effective in reducing the number of infected herds associated with cattle imports. In this scenario, a combination of testing cattle ≥4 months and vaccinating calves < 4 months prior to import was simulated. The model output predicted that this scenario could reduce the risk of importing IBR with 86%, from 571 to 82 newly infected herds per year. For the stakeholders from the cattle industry this would be the preferred scenario because it was a realistic option and was rather effective in reducing the risk. The import restrictions and test and vaccination scenarios, reduced the import risk in both veal and non-veal herds. Although, the scenario with import restrictions are at present not a realistic option, it may be a reasonable option in the future given that several countries are currently applying control and eradication programs for IBR.

In the scenario in which calves were vaccinated, we assumed that intranasal vaccination of calves prior to import would reduce the risk of importing acutely infected cattle by 50%. However, from the study of Kaashoek and Van Oirschot (1996), it was concluded that the efficacy of protection induced by vaccination highly depended on the moment of vaccination relative to the moment of infection. The sooner calves were vaccinated the more effective the vaccination. Vaccinating several days prior to the moment the calves were challenged with the IBR virus, resulted in a higher protection rate than 50%. In contrast, if vaccination and infection occurred on the same day, the vaccination was less effective. Thus, although our study assumed a 50% risk reduction, this percentage might be higher when calves are vaccinated earlier in live and might be lower if the calves are not vaccinated until they are collected.

Our risk assessment did not include the economic aspects of implementation of the risk mitigating scenarios. These scenarios are associated with additional costs, but will decrease the probability of introduction and transmission of IBR and the subsequent losses in the Netherlands, which is important to gain support of the cattle industry for the eradication program. Although the losses related to clinical signs of IBR appear to be limited (Nandi et al., 2009; Van Schaik et al., 1999; Hage et al., 1998), the economic losses associated with restrictions of livestock trade may be substantial. To evaluate whether implementation of the risk mitigating scenarios will be cost-effective, and which of the scenarios is financially most attractive, an economic evaluation based on the results of this study is required. Additionally, efficient surveillance should be developed and implemented to enable early detection of new IBR introductions.

The model and subsequent output represent the situation in 2016 and include Dutch field data, literature and expert opinion about for example herd prevalence per country of origin. At this moment, IBR is still endemic in the Netherlands and it will take several years to achieve the free status. Many EU countries are currently conducting control and eradication programs for IBR, which results in a tendency towards a decreasing herd prevalence in the EU. It is therefore likely that the risk that was estimated in this study will overestimate the true import risk at the time the Netherlands will be actually free from IBR. According to our results (BE and DE are free scenario), the true import risk might be 20%–40% lower compared to the current situation.

The quantitative risk assessment of IBR was conducted simultaneously with a quantitative risk assessment of the risk of introducing BVD through cattle imports (Santman-Berends et al., 2017). Modeling both viruses at the same time appeared very efficient because synergies could be obtained with regard to the selection of risk factors (i.e. age, maternal protection), quantification of import movements and the stochastic framework. In addition, countries had to be contacted only once to acquire the most recent herd prevalence estimations for both infections. The definition of an infected herd and animal differed tremendously between both viruses and thus in the models. For BVD a herd was considered infectious if there was an indication of virus circulation i.e. presence of a persistently infected animal. Herds with antibodies but without indication of a persistently infected animal were considered no risk (Santman-Berends et al., 2017). For IBR this was different because all cattle with antibodies can reactivate and spread BoHV1, which meant that all herds with at least one seropositive animal were considered infected. Therefore, the models diverted from the step in the model where the disease specific characteristics were taken into account. The quantitative risk assessment of introduction of IBR through cattle imports showed that the import risk of IBR differed from the import risk of BVD (Santman-Berends et al., 2017). For IBR, veal, beef and suckler herds had a large and quite similar risk of reintroduction while for BVD, the risk for veal herds was much higher than for other herd types (Santman-Berends et al., 2017). This difference is a consequence of the fact that for BVD import of calves (> 94% of all imported cattle) is a higher risk than import of older cattle while for IBR this is the other way around.

This risk assessment showed that the Netherlands has a substantial risk that IBR is reintroduced through cattle imports in an IBR free situation. If risk mitigating measures are implemented, the import risk can be reduced, but additional measures are needed to further reduce the risk. Before a final decision can be made on the enactment of risk mitigating actions, an economic evaluation might be necessary to assess which scenario is most cost-effective. Even though this study was conducted for the Netherlands, in which a lot of cattle is imported, the applied methodology can also be used for quantitative risk assessments of other diseases and in other countries.

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Appendix A. Average annual number of imported cattle (total and < 4 months) in the Netherlands, by country of origin in the period from 2011 until 2015

Country	Total N imported cattle	N < 4 mo
Austria	448	282
Belgium	63,951	42,242
Bulgaria	15	15
Czech Republic	39,405	37,094
Denmark	37,449	35,730
Estonia	23,464	22,980
France	6074	497
Germany	495,328	487,071
Hungary	157	83
Ireland	45,409	45,218
Italy	8690	7873
Latvia	33,787	33,575
Lithuania	48,226	48,008
Luxembourg	10,809	10,362
Poland	76,267	75,632
Portugal	8	3
Romania	1608	1540
Slovakia	10,851	10,736
Spain	72	22
Sweden	18	0
United Kingdom	38	1
Total	**902,074**	**858,964**

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