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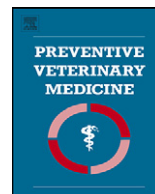
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A nation-wide epidemiological study of acute bovine respiratory disease in France

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ABSTRACT

Acute bovine respiratory disease (ABRD) is a respiratory syndrome caused by various infectious agents, and represents a major economic and health problem in cattle herds worldwide. The aim of the study was to present how we can describe the epidemiological characteristics of ABRD in France, including risk factor analysis and spatio-temporal pattern investigation.

The data were collected by specialized surveyors during the 2001 animal survey conducted by the French Ministry for Agriculture and Fisheries, from a representative sample of cattle herds. The health questionnaire concerned farm characteristics, practice of BRD vaccination, presence of ABRD, time of occurrence and number of affected animals for the period November 2000–October 2001. After a descriptive analysis of the syndrome, a space–time scan statistic was performed to detect potential clusters, and a logistic regression model was used for analysis of risk factors.

The study sample included 16,581 cattle herds as representative of the 260,000 French herds. The ABRD cumulative incidence at farm level was 9.8%, the cumulative incidence at animal level was 2.1%, the cumulative mortality 0.1% and the lethality proportion 6.5%. ABRD occurred mainly during cold months with an epidemic peak in December. Spatial repartition of the syndrome showed that the whole territory was affected, with a higher number of cases in the north-east region, the main bovine production area in France. Three space–time clusters were identified in the period November 2000–February 2001. ABRD was significantly associated with production type, herd size, and BRD vaccination. Beef herds were less affected than dairy herds, and increased herd size increased the risk of ABRD.

The outbreak was clustered in space and time, suggesting a common infectious agent for the epidemic in the detected areas. The influence of production type and herd size on syndrome occurrence highlighted the importance of management practices, human movement and animal density.

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1. Introduction

Bovine respiratory disease (BRD) is a major health problem in cattle herds worldwide (Callan and Garry, 2002). BRD can cause high morbidity and mortality rates and lead to heavy economic consequences in terms of drug

and veterinary costs, extra labour and production losses (Hage et al., 1998; Hurd et al., 1995; van der Fels-Klerx et al., 2001).

Acute BRD (ABRD) is a respiratory syndrome linked to presence of infectious agents, but also to management, environment, stress and immunity factors (Callan and Garry, 2002). A wide range of pathogens, essentially viruses and bacteria, can cause ABRD, separately or simultaneously (Autio et al., 2007). Nevertheless, the main agents involved are viruses (Caldow et al., 1993), the most

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frequent being bovine herpesvirus 1 (the agent of infectious bovine rhinotracheitis) (Hage et al., 1998), bovine respiratory syncytial virus (BRSV) (Elvander, 1996), bovine viral diarrhoea virus (BVDV) (Van Reeth and Adair, 1997), and parainfluenza-3 virus (PIV-3) (Hartel et al., 2004). Some other viruses have been identified during BRD outbreaks, such as bovine coronavirus (BCV) and adenovirus (BAV) (Hartel et al., 2004; Storz et al., 1996), and even influenza A virus (Brown et al., 1998; Graham et al., 2002; Jones-Lang et al., 1998). Most of these pathogens are ubiquitous and ABRD is enzootic with outbreaks occurring regularly, especially during the autumn–winter season (Jones-Lang et al., 1998; van der Fels-Klerx et al., 2001). In addition to a seasonal pattern, ABRD has a strong spatial heterogeneity and dynamic (Elvander, 1996) caused by epidemics clustered in space and time (Norstrom et al., 1999).

Several risk factors for ABRD have been highlighted through epidemiological studies (Norstrom et al., 2000; Sivula et al., 1996) or expert consensus (van der Fels-Klerx et al., 2000). At the herd level, the main risk factors concern type of production, herd size, housing characteristics (housing system, ventilation, animal density) and management practices (animal movement, hygiene, BRD vaccination) (van der Fels-Klerx et al., 2000). Main animal characteristics associated with ABRD occurrence concern age, body condition and immune status (Callan and Garry, 2002). The noticeable health and economic consequences and the high variability in space and time of ABRD would require a nation-wide surveillance of the syndrome in order to improve its control. Moreover, a better knowledge of past years ABRD spread could help to better prevent the infection the following years.

The aim of the present study was to describe ABRD epidemiological characteristics highlighted from retrospective interviews of a representative set of French bovine farmers through risk factor analysis and spatio-temporal pattern investigation.

2. Material and methods

2.1. Data

Data were collected from a cohort of French cattle herds through the 2001 animal survey conducted by the Central Service for Survey and Statistical Studies (“Service Central des Enquêtes et Etudes Statistiques” or SCEES: <http://www.agreste.agriculture.gouv.fr/>) of the French Ministry of Agriculture and Fisheries (MAF). The purpose of the survey was to provide representative information at a national level of indicators of farm management. The retrospective cohort was made up by a stratified random sampling with unequal probabilities among the 282,553 cattle herds in France (bovine population census in 2000). The stratification was based on the administrative region (department), type of production and herd size. Twenty-one strata in each department were created (Fig. 1), in which a random sample of farms was selected using a random numbers generator. An extrapolation coefficient (EC) was calculated to ensure sample representativeness, i.e. $EC = \text{population size in the stratum} / \text{sample size in the stratum}$. The sample

size in each stratum depended on the number of farms and on the heterogeneity of the farms in the stratum: the higher the heterogeneity of location, breed and housing type, the higher the sample size was, and the lower the EC of each sampled farm was. Hence a region with many farms of the same type close to each other was represented by only a small amount of farms as each one was very representative of the others, in terms of farm characteristics but also inter-farms contagious diseases. Seventy-three out of the 96 French departments were areas of bovine production with a total of 271,963 farms from which 17,462 farms were selected for the sample.

The data covered the period from November 2000 to October 2001 and were collected by trained SCEES surveyors in November 2001. A health questionnaire concerning ABRD was added as a supplement to the ‘2001 animal survey’ questionnaire, and included identification of farms, total herd size, number of animals by category (dairy cows and heifers, beef cows and heifers, calves, steers, bulls), whether vaccinated against BRD or not, ABRD occurrence or not and peak month(s), and number of affected animals (ill and dead). The case definition was: clinical episode with respiratory symptoms (nasal discharge, cough, respiratory distress), fever and depressed general condition, often affecting several animals and developing in 7–10 days, with possible mortality. The geographic coordinates of the town (centroid) the farm was belonging to, were obtained via the National Institute for Statistics and Economic Studies. The database was created using Microsoft Excel.

2.2. Statistical analysis

Descriptive analysis and risk factor analysis were conducted using the software SAS 9.1 for Windows (SAS Institute Inc., Cary, NC, USA, 2002–2003), and space–time cluster analysis was performed with SaTScan™ (Kulldorff and Information Management Services Inc., 2006).

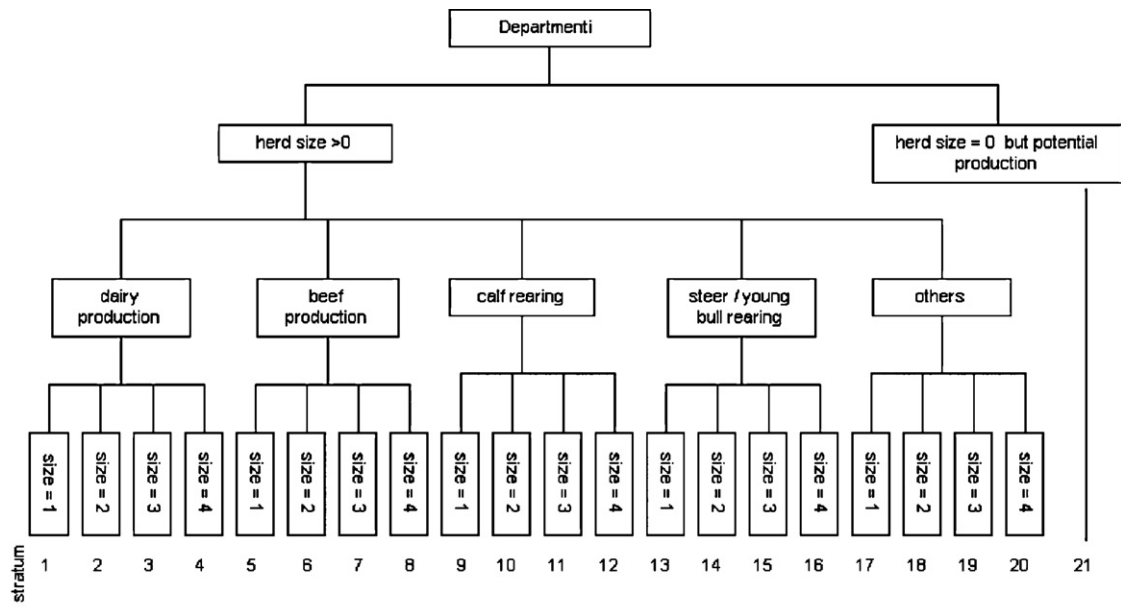
2.2.1. Descriptive analysis

Descriptive analyses were weighted, multiplying each observation by the EC to provide results at population level. After a descriptive analysis of the herd characteristics, we calculated the following parameters:

- cumulative incidence at farm level: number of new farms affected by ABRD over the time period (1 year)/total number of farms;
- cumulative incidence at animal level: number of new cases of ABRD (statistical unit = animal) over the time period/total number of animals;
- cumulative mortality: number of deaths due to ABRD over the time period/total number of animals;
- lethality proportion: number of deaths due to ABRD over the time period/number of new cases of ABRD over the time period.

2.2.2. Space–time analysis

We explored spatial and temporal patterns of ABRD using the geographical information system software ArcView 8.2 (ESRI, USA, 2002) for a geographic representation



Herd size:	Type of production				
	dairy herds	beef herds	calf	steer/young bull	others
1	<20	<20	<100	<40	<30
2	20 to 39	20 to 49	100 to 199	40 to 79	30 to 59
3	40 to 79	50 to 99	200 to 399	80 to 159	60 to 119
4	>79	>99	>399	>159	>119

Fig. 1. Stratification method used to sample the 17,462 bovine farms (stratified random sample with unequal probabilities) to study acute bovine respiratory disease in France (ABRD), November 2000–October 2001.

of cumulative incidence at farm level by department, a key territorial division in France. In order to study the spatial and temporal dynamic of ABRD, we then performed a space–time cluster analysis, using the retrospective space–time scan statistic for point data (Kulldorff et al., 1998). This method tests whether the spatial and temporal locations of all cases were independent of each other by performing a comparison of the risk of being a case within a moving cylinder (the base of the cylinder representing space and the height representing time) to the risk of being a case outside the cylinder, and estimates the relative risk. The most likely cluster is the cylinder with the maximum likelihood of representing the observed data. Secondary clusters can also be detected, the criteria being no overlap with the most likely cluster. ABRD-affected farms were defined as cases with the corresponding date of occurrence (if a farm was affected more than once, it appeared several time in the case file). Non-affected herds were defined as controls, and were given a random date within the time span of the study period. We used the Bernoulli model to detect clusters with high rates, using month as time precision, and 999 Monte Carlo replications. Several parameters were tested for maximum spatial cluster size (20%, 30% 40% and 50% of the total population) and maximum temporal cluster size (30%, 40% and 50% of the study period).

2.2.3. Risk factors analysis

We performed a weighted multivariable logistic regression (Collett, 1991) to model the binary variable of ABRD occurrence in a farm during the period November 2000–October 2001. The weighting process was performed by modification of model dependent estimators (Pfeffermann, 1993). The explanatory variables examined were production type, herd size, and the practice of vaccination against ABRD. The department was added as a random effect to account for geographic variations. The production type was a qualitative variable whose categories were defined as dairy, beef, calf rearing, steer/young bull rearing, and other forms of production, according to the dominant animal category of the farm. Dummy variables were created, with beef production as the reference group. The herd size was the total number of animals in the herd on the date of the survey. We used successively both continuous and categorical variables for herd size and evaluated log-linearity. The practice of vaccination against BRD was a binary variable. We first performed a univariable analysis with a risk alpha = 30% to select the explanatory variables to be included in the multivariable analysis. We then used the stepwise procedure of Hosmer and Lemeshow during the multivariable analysis to obtain the final model. We also tested two by two interactions terms and kept only the significant ones in the final model.

Table 1

Main characteristics of French bovine dairy herds, November 2001 (stratified random sampling with $n = 16,581$ herds, representative sample of the 260,064 French herds): production type, herd size and acute bovine respiratory disease (ABRD) epidemiological parameters.

	All herds	Beef production	Dairy production	Steer/young bull production	Calf-rearing farms	Other production type
<i>N</i> (%)	260064 (100)	126288 (48.56)	106757 (41.05)	20649 (7.94)	3319 (1.28)	3052 (1.17)
Median herd size (range)	60 (1–1700)	46 (1–1090)	75 (1–960)	11 (1–1683)	199 (1–1700)	63 (1–950)
ABRD vaccination (%)	34593 (13.30)	21842 (17.30)	9720 (9.10)	1919 (9.29)	355 (10.69)	757 (24.81)
ABRD-affected farms (cumulative incidence at herd level) (%)	25390 (9.76)	11318 (8.96)	12387 (11.60)	910 (4.41)	207 (6.24)	569 (18.64)
ABRD cumulative incidence (animal level) (%)	2.06	1.31	3.06	0.96	2.32	5.28
ABRD cumulative mortality (%)	0.06	0.06	0.04	0.04	0.03	0.21
ABRD lethality proportion (%)	6.46	9.67	3.40	8.77	2.90	7.24

3. Results

3.1. Descriptive analysis

Among the 17,462 farms of the cohort, 879 had a herd size of zero, corresponding to farms no longer existing or to existing farms that no longer kept cattle. Two other farms had no valid geographical coordinates. Consequently, the final study population consisted of 16,581 cattle herds representing the sampled 73 French administrative regions with a total of 260,064 cattle herds. The proportion of missing values in the study sample was less than 1% and 99.7% of the affected farms provided the number of animals affected with ABRD.

The production type was distributed as follows (Table 1): 49% beef herds, 41% dairy herds, 8% steer/young

bull production farms, 1% calf-rearing farm, and 1% other types. The median herd size was 60 animals (range = 1–1700), and varied according to production type. The BRD vaccination coverage was 13.3%. ABRD cumulative incidence in farms was 9.8%, while the cumulative incidence at animal level was 2.1%, the cumulative mortality 0.1%, and the lethality proportion 6.5%.

3.2. Space–time analysis

The geographic representation of ABRD cumulative incidence at farm level by department (Fig. 2) showed that the whole country was affected. Nevertheless, the central west, the north-west and a small area in the south of France had higher ABRD cumulative incidence at farm level

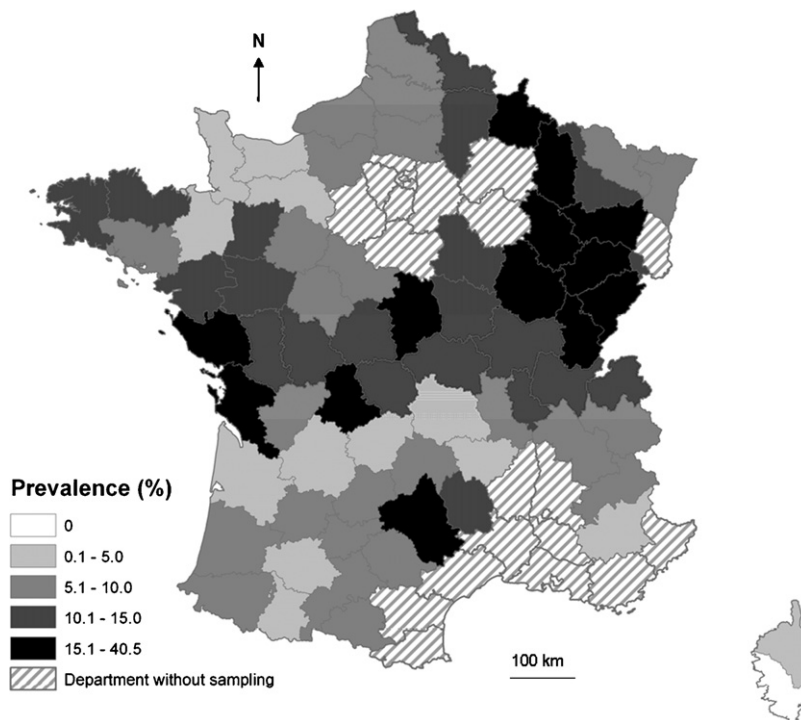


Fig. 2. Spatial distribution of cumulative incidence at herd level of acute bovine respiratory disease (ABRD) in France by department (French administrative division), November 2000–October 2001 (stratified random sample with $n = 16,581$ herds).

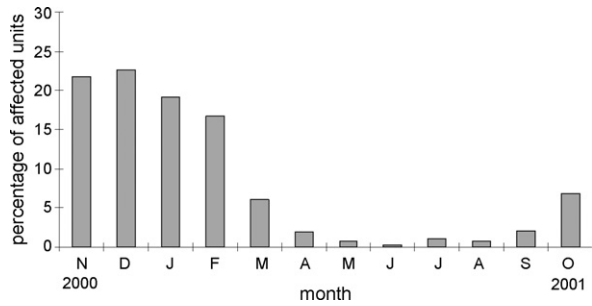


Fig. 3. Temporal distribution of acute bovine respiratory disease (ABRD) in France, November 2000–October 2001 (stratified random sample with $n = 16,581$ herds).

than other areas. Temporal distribution of the syndrome (Fig. 3) highlighted the occurrence of ABRD mainly during cold months, with 80% of the farms affected between November 2000 and February 2001 and an epidemic peak in December 2000.

The space-time cluster analysis of ABRD (20% as maximum spatial cluster size and 50% as maximum temporal cluster size) identified the most likely cluster in north-eastern France, around the city of Nancy (Fig. 4), during the period November 2000–February 2001. The relative risk (RR) associated with this cluster was 3.57 ($p = 0.001$) comparing to the surrounding areas and time periods. Two secondary clusters were identified, the first one in the central west around the city of Poitiers (RR = 3.44, $p = 0.001$), and the second one close to the city of Albi in the south (RR = 2.61, $p = 0.001$), during the same time-period as the most likely cluster.

3.3. Risk factors analysis

In the final logistic model, the type of production, herd size and practice of ABRD vaccination were all significantly associated with ABRD occurrence during the period November 2000–October 2001 (Table 2). Compared to beef herds – the reference group – dairy herds were at higher risk of ABRD (OR = 1.85), while steer/young bull and calf-rearing farms were at lower risk (OR = 0.66 and 0.32 respectively). The herd size was used as a continuous variable as the assumption of log-linearity was checked by the categorical variable. Herd size was positively associated with ABRD occurrence, with an OR equal to 1.34 for a herd size increase of 50 animals. ABRD vaccination was

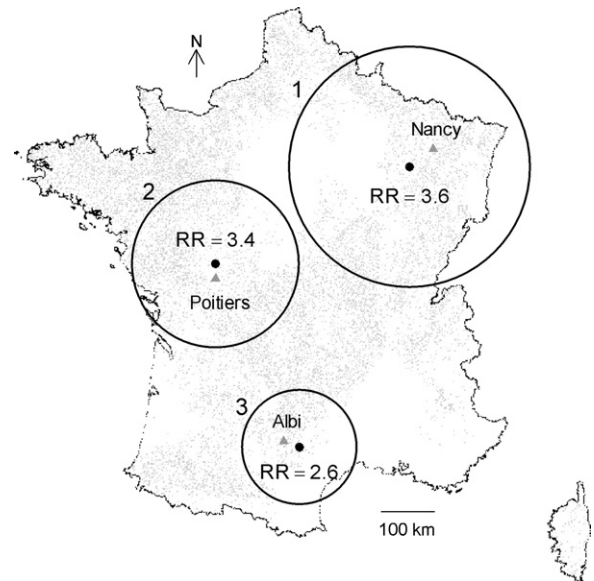


Fig. 4. Farm location (grey background) and clusters of acute bovine respiratory disease (ABRD) detected by the space-time scan statistic in France, November 2000–October 2001 (stratified random sample with $n = 16,581$ herds). 1: Most likely cluster, 2 and 3: secondary non-overlapping clusters, ●: cluster centre, ▲: main cities close to the clusters, RR: relative risk associated with the cluster.

positively associated with ABRD occurrence (OR = 4.45). The department as a random variable had a significant effect.

4. Discussion

4.1. Biological results

ABRD is a fairly frequent syndrome in cattle herds, as nearly 10% of the farms were affected at least once during the period November 2000–October 2001. The herd-level incidence of ABRD was 35% in the study of Norstrom et al. (2000), but in Norway no specific ABRD virus occurs endemically, consequently the susceptible population is larger than in France where ABRD outbreaks occur annually. According to our study, ABRD was clustered in space and time, with clusters corresponding to the areas with the highest ABRD cumulative incidence at farm level. These clusters were not explained by the risk factors herd

Table 2

Logistic regression model for acute bovine respiratory disease (ABRD) occurrence in French bovine herds, November 2000–October 2001 (stratified random sample with $n = 16,581$ herds).

Variable	Odds ratio		p value	
	Estimate	95% CI		
Production type (reference = beef production)	Dairy	1.85	1.78–1.91	<0.0001
	Steer/young bull	0.66	0.61–0.72	<0.0001
	Calf rearing	0.32	0.27–0.38	<0.0001
	Others	1.82	1.63–2.03	<0.0001
Herd size (steps of 50 animals)	1.34	1.33–1.35	<0.0001	
BRD vaccination	4.45	4.30–4.60	<0.0001	

Department as random effect: $p < 0.0001$. Intercept = -3.41 .

size or type of production as these risk factors varied in space but had no space–time interaction. ABRD clustering suggested a common infectious agent in the epidemic of those specific regions, but since no serological tests were performed, it was not possible to determine which agents were involved. As ABRD is multifactorial and its causative agents ubiquitous, no specific reporting or control measure is required in France when a farm is affected. Consequently the infection can easily spread to the surroundings farms. ABRD mainly occurred during the colder months, suggesting the influence of conditions like low temperatures, high humidity, and high population densities (Callan and Garry, 2002).

The risk of ABRD was significantly associated with production type. Dairy herds presented a higher risk than beef herds, this outcome being consistent with previously published results (Norstrom et al., 2000). Steer/young bull rearing and calf-rearing farms were less affected than beef herds, but as these types of production were usually considered separately in other studies, the between-studies comparison was not easy. The influence of production type could be explained by different management practices, and especially by the housing system, as beef cattle are more frequently raised in open-range conditions, with a lower burden of respiratory pathogens and airborne contaminants such as dust particles, ammonia and endotoxins (Callan and Garry, 2002). Herd size was also involved in ABRD occurrence, larger herds having a higher risk, in accordance with previously published results (Norstrom et al., 2000; van der Fels-Klerx et al., 2000). This effect could be due to more numerous animal-to-animal contacts, increase in inter-farm human traffic, and potential higher animal densities, all these characteristics being important risk factors for the infection (Callan and Garry, 2002). BRD vaccination was associated with syndrome occurrence, and farms with a higher use of vaccination were more affected. But this relation should probably be explained in a converse way, i.e. the farmers having experienced an outbreak of ABRD were more prone to practice BRD vaccination. As we did not collect the date of vaccination with our survey, this hypothesis could not be demonstrated.

4.2. Data quality and methodology

With this study, it was only the second time that the SCEES, a MAF division usually dealing with economic issues, have collaborated on animal health management issues (Barnouin and Berger, 1988). Such a collaboration gave the study an advantage in terms of a representative sample of bovine herds, a high response rate to the state survey, and the skills of trained professional surveyors.

One of the main concerns in such types of study is the ability of farmers to correctly diagnose the syndrome. In France, many diagnoses and treatments are performed and implemented by farmers alone, veterinarians intervening only for serious cases. Therefore farmers were the only observers able to report ABRD outbreaks occurring in their herds. Moreover, they were provided with a case definition by the surveyors. Sivula et al. (1996) demonstrated that farmer diagnosis of calf mortality due to pneumonia had a

sensitivity of 56% and a specificity of 100%. Consequently, relying on farmers' reports could have led to some underestimation of the cumulative incidence of ABRD at farm level.

Another concern about this retrospective study was the recall biases. ABRD is important enough in terms of economic consequences in the herds to be noticed by the farmers who would not consider the event as commonplace and unimportant and would remember it. Consequently, recall bias in reporting the occurrence of the ABRD was expected to be low, but it may have been higher in reporting date information. However, even if the month could have been approximate, the general period was considered to be reliable, and the seasonal trend unaffected by the potential for recall biases.

4.3. Usefulness of the results

The study intended to propose a nation-wide scheme on how to describe epidemiological characteristics of ABRD. The use of the MAF animal survey to collect and analyze health data, a new concept in France, showed its ability to provide useful information concerning ABRD and potentially other diseases (Barnouin and Berger, 1988). Moreover, the cost of the performed survey was quite low as it used a pre-existing study scheme and only consisted in adding a very small number of questions to a farm questionnaire dealing with general herd characteristics. Nevertheless, the survey we performed should be conducted regularly for a dynamic and more accurate vision of disease trends, the present preliminary work aiming to build baseline data to evaluate annual risk of ABRD. The spatial and temporal patterns of the respiratory syndrome evolve every winter, but a significant amount of information could be learnt from the past years to better deal with the epidemic in the following years.

5. Conclusion

The epidemiological study of ABRD conducted in France through retrospective interviews from a nation-representative sample of farmers highlighted important epidemiological characteristics of the respiratory syndrome: cumulative incidence at farm level around 10%, occurrence mainly during cold months, and trend to cluster in space and time suggesting a common infectious agent involved. Moreover, production type and herd size were identified as ABRD risk factors in French breeding conditions.

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