Exploring the importance of mixed autogenous vaccines as a potential determinant of lung consolidation in lambs using Bayesian networks.

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Highlights

- A Bayesian network has been developed to evaluate the effect of autogenous vaccines on lung consolidation
- An experiment with 460 fattening lambs has been performed by applying four autogenous vaccines

- Mixed autogenous vaccines could be considered as an effective control tool against ovine respiratory complex
- Bayesian networks may be used to help in the prevention of lung consolidation

Abstract

Bayesian networks are used to evaluate the effectiveness of mixed autogenous vaccines in fattening lambs to prevent the ovine respiratory syndrome. An experiment was performed with 460 fattening lambs, which were clustered into four groups according to the kind of vaccine received (*Pasteurella spp*., *Mycoplasma spp.,* Mixed *Mycoplasma-Pasteurella* or placebo). After slaughtering, lungs were collected, and macroscopic and microscopic studies were performed. A microbiological study was carried out to evaluate the presence of *Mycoplasma* spp. and *Pasteurellaceae* by conventional culture and identification by nested polymerase chain reaction. To the best of the authors' knowledge, Bayesian networks have not been used to evaluate the effect of vaccines on the absence/presence of lung consolidation. Our results revealed that the use of mixed autogenous vaccines can decrease lung consolidation from 15.75% (12.42-19.08) to 9.24% (6.59-11.89). Therefore, the use of these autogenous vaccines in farms could be considered an effective control tool against ovine respiratory syndrome.

Keywords

Autogenous vaccines; Bayesian networks; Risk factor; Ovine respiratory syndrome; Preventive medicine.

Introduction

Ovine respiratory syndrome in lambs is responsible for great economic losses worldwide. Pneumonia produces important economic losses in the sheep industry in Spain. They are particularly relevant in Extremadura (south-western Spain), where 94% of the municipalities have sheep herds (López, 2002). This condition may result in sudden death or in a protracted illness causing suffering to the affected animals (Nicholas et al., 2008).

The most common cause of pneumonia is pasteurellosis, which occurs worldwide (Nicholas et al., 2008). *Pasteurella* spp. is highly prevalent among animal populations, where it is often found as part of the normal microbiota of the oral, nasopharyngeal, and upper respiratory tracts. *M. haemolytica* is the most obvious cause of pneumonic pasteurellosis, but the role of mycoplasmas is often overlooked (Nicholas et al., 2008; Fernández et al., 2016). Their role as a primary pathogen in different respiratory disease complexes of livestock has been previously described (Nicholas et al., 2008). *M. ovipneumoniae* is a cause of a non-progressive (atypical) pneumonia, which may enable the invasion of *M. haemolytica* with far more serious results. In addition, *M. arginini* is a ubiquitous microorganism frequently isolated from the respiratory tracts of sick lambs (Fernández et al., 2016). This pathogen is sometimes present in mixed culture with *M. ovipneumoniae* (Azizi et al., 2011).

Treatment with effective antimicrobials against Mycoplasma species often produces immediate respite, which may be enough for the animal to recover and may be the result of secondary bacterial elimination (Nicholas et al., 2008). Thus far, in the international market, there are no vaccines against *M. ovipneumoniae,* but only against contagious agalactia. Selected antimicrobials for treating affected animals should be based on correct diagnosis and accurate information about the effectiveness of this antimicrobial agent (Nicholas et al., 2008).

The outbreaks of pneumonia presented in pasteurella-vaccinated flocks suggest that incorporating a mixed selection of *M. ovipneumoniae* strains into these vaccines should be considered to provide greater protection against respiratory diseases (McAuliffe et al., 2003).

Autogenous vaccines can be used to treat ongoing chronic infection and can therefore be considered as therapeutic vaccines. Autogenous vaccines are strain-specific, permitting control of infections caused by bacteria for which no classical preventive vaccine has been available (Rizzo et al., 2006).

Bayesian Networks (BNs) have been extensively developed in statistical research and can address risk assessment and decision analysis problems as causal models using both knowledge and data (Fenton and Neil, 2012). BNs have been applied in many disciplines, such as health (Marvin et al., 2017), industry (Zarei et al., 2017), transportation (Zhang et al., 2016), and cybersecurity (Shin et al., 2015), among others. The have also been used in veterinary science. McKendrick et al. (2000) used them to aid in the differential diagnosis of tropical bovine diseases by including expert knowledge. Geenen and Van der Gaag (2005) identified patterns for the early

detection of swine fever in herds, and later Van der Gaag et al. (2010) applied a similar solution for individual pigs. Wilson et al. (2013) identified factors associated with the presence of the tick *Ornithodoros erraticus* on pig farms. Ge et al. (2014) observed the main factors related to antibiotic use and inferred incentive mechanisms to reduce its use in livestock production. Finally, Galapero et al. (2016) identified risk factors, including environmental conditions, for the presence of ovine lung consolidation. However, to the best of the authors' knowledge, BNs have not previously been used to relate vaccination against these microorganisms with the presence/absence of pulmonary consolidation.

The purpose of this study was to compare the effects of autogenous vaccines (*Pasteurella multocida* and *Mannheimia haemolytica*, *Mycoplasma ovipneumoniae* and *M. arginini* and both mixed) on lung consolidation , and determine which is the most effective to protect lambs during production time. By using a BN-based approach, it is possible to analyze risky scenarios to elucidate the possible effects of complex vaccination in lung consolidation.

Materials and methods

Experimental design

Fattening lambs were obtained from five farms in Extremadura (south-western Spain). These animals were controlled from birth, when the vaccination protocol was applied. Animals were grouped in a pen at a density of 0.5 m^2 per animal (high density) or more than 0.5 m^2 per animal (low density).

Four groups of animals were established: lambs vaccinated with a vaccine composed of Pasteurellaceae family (114 animals); lambs vaccinated with a vaccine composed of *M. ovipneumoniae* and *M. arginini* (114 animals); lambs vaccinated with both autogenous vaccines (113 animals) and the last group, a control group of animals vaccinated with an adjuvant vaccine (117 control animals).

Two autogenous vaccines of pasteuralleceae strains were applied at an interval of 21 days. For the Mycoplasma spp. vaccine, the animals only received one application, and the animals in both autogenous vaccine groups received a dose of Mycoplasmas on day 21 coinciding with revaccination with Pasteurella.

This study was approved by the Experimental Animal Ethical Committee of the University of Extremadura (Approval number 29/2010).

Microbiology

The microbiology study was carried out with samples of lungs that were inoculated in selective media for each studied microorganism.

Mycoplasma spp.: A 5 cm piece of lung was sliced from the cranial lobe for each examined animal. Two approaches were taken to examine the lung tissue. In the first, a 0.3-cm-long section with a visible airway (i.e., bronchi or bronchiole) was inoculated in 2.5 ml of Eaton's broth (Nicholas and Baker, 1998). The other approach used cotton swabs to vigorously swab the exposed lung surface in the previous step. From 1.5 ml of broth cultures, the genomic DNA was extracted and purified using a silica-membrane-based spin kit (GenEluteTM Bacterial Genomic DNA Kit, Sigma-Aldrich®, Vienna, Austria) according to the manufacturer's instructions. PCR of the 16S–23S intergenic

spacer sequence differentiated the cultured *Mycoplasma* species by their amplicon size as described by Tang et al. (2000).

Pasteurellaceae: All samples were inoculated onto 10% Sheep Blood Agar and incubated at 37 ºC overnight. Colonies were identified by an automatic system identification Phoenix® (Becton Dickinson Diagnostics, Franklin Lakes, NJ USA), according to the manufacturer's instructions. Molecular identification of *P. multocida* was carried out using PCR to amplify the specific fragment of gene kmt1 (PM-PCR) using the primers KMT1SP6 and KMT1T7 described by Townsend et al. (1998). The resulting PCR products were electrophoresed on 2% agarose gels, stained with ethidium bromide and photographed. Distilled water without any DNA was used as a negative control. Electrophoresis conditions were 90V for 60 min. NCTC 10322 strain was used as a positive control for *P. multocida. M. haemolytica* isolated were further characterized by an indirect hemagglutination technique.

Vaccines

Autogenous vaccines were produced in the Unit of Infectious Disease of the University of Extremadura. For the *Mycoplasma* spp. vaccine, the microbes were isolated and subsequently processed according to a standardized procedure from the Mycoplasma Group of Veterinary Laboratories Agency (Weybridge). To inactivate the pathogen, the samples were kept at 4 °C for 16 hours with saponin, then heat-inactivated at 56 °C for 30 minutes (Nicholas et al., 2002). Using a spectrophotometer measuring at 450 nm, the optical density was 0.1 McFarland.

Vaccine capsules were administered subcutaneously at 21 days with 1 milliliter per animal. For the Pasteurella spp. vaccine, the microbes were isolated, and each

serotype was individually processed, inactivated at 5 °C for 24 hours with formalin and the optical density was measured at 0.5 McFarland with a spectrophotometer at 450 nm. The vaccine capsules were administered subcutaneously at 7 days with 2 milliliters per animal followed by another application at 21 days with three milliliters per animal.

The different periods of administration of these autogenous vaccines were based on our clinical experience and following the indications proposed by other authors such as Aulley et al. (1999) and McAuliffe et al. (2003).

Macroscopic and microscopic study

Lungs were photographed on each side. The percentage of lesion compared to the size of the lung was calculated using the computer program Adobe Photoshop cs5®. Digital images of ventral and dorsal sides of the lungs were taken. They were classified into two groups depending on whether consolidation was found or not, i.e., presence of consolidation (greater than 0%) or absence (equal to 0%). Lesional areas and total area were delimited using Adobe Photoshop cs5® software. The percentage of affected lung was calculated by the ratio of affected area/total area. Figure 1 represents how the area of consolidation was delimited.

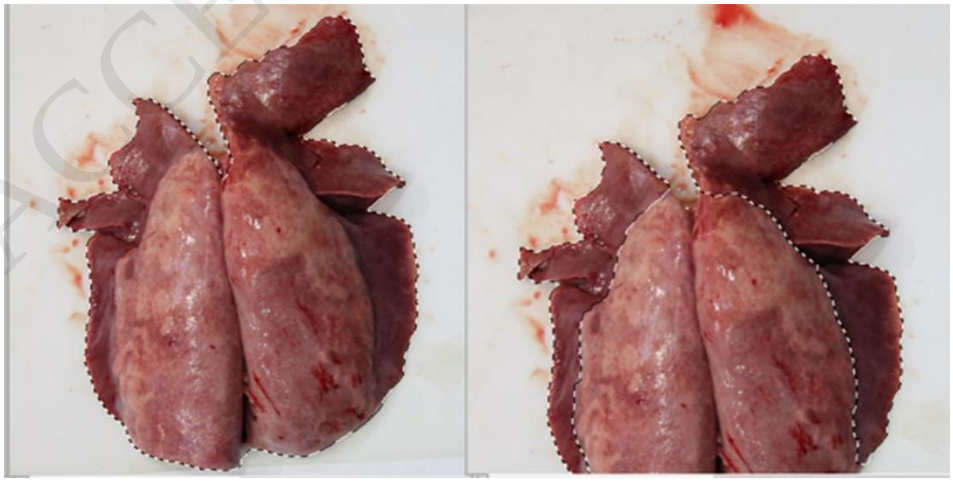

Figure 1. Delimitation of the lung (left) and delimitation of the lung consolidation (right).

For the histological study, samples were fixed in neutral buffered formalin (3.5%, 0.1 M, and pH 7.2), routinely processed, and embedded in paraffin. Sections of 5 µm. were stained with hematoxylin and eosin. Four histological groups were established following the classification of (Maxie, 2015), i.e.: diffuse alveolar damage, interstitial pneumonia, suppurative bronchopneumonia and bronchointerstitial pneumonia.

Microphotographs were taken using a microscope (Eclipse 80i, NIKON®, Tokyo, Japan) with a digital video camera (DXMI200F, NIKON®, Tokyo, Japan).

Statistical analysis

BNs (also known as Bayesian Belief Networks) are Directed Acyclic Graphs (DAG) that define a joint probability distribution for a set of variables (see, e.g., Nielsen and Jensen, 2009). Each node represents a variable and the arcs represent causal dependence between nodes. For each node, the distribution of its variable conditioned on its predecessors in the net is defined and is called conditional probability distribution. The complete network defines a joint probability distribution, based on the conditional probability distribution and the relationships observed in the network. This joint probability distribution is given by the product of the probabilities of each node conditioned on the value of its predecessors. BNs are specifically defined for modeling uncertain and complex risk domains. As they are defined strictly in terms of probabilities and conditional independence statements, their main use is to analyze different conditional probabilities scenarios (see Donald et al., 2009). They can also be applied to prediction problems (see Marcot et al., 2006). One of the main advantages

of their use is that they provides both a causal and probabilistic model; thus, they are ideal for providing information supported by expert knowledge combined with conditional probabilities, resulting in a human-interpretable decision tool (Heckerman, 2008).

Five categorical variables (density, vaccination, microorganisms, histopathology and lung consolidation) were used to build a Bayesian network using GeNie/SMILE software (Druzdzel, 1999). For this task, the Greedy Thick Thinning algorithm (Dash and Cooper, 2004) was considered after a model selection framework implemented in Genie (Druzdel, 1999).

The graph-structure learning algorithm searches for a DAG that maximizes the scoring function in the search space of all DAGs containing the finite set of variables. For structure learning, a scoring function measures how good a given network matches the data set. The score was calculated using the Bayesian Dirichlet equivalent uniform criterion (BDeu), which is based on a Dirichlet distribution with a weakly informative uniform prior (see Cooper and Herskovits, 1992 and Silander et al., 2008). The Greedy Thick Thinning algorithm starts with an empty graph at a specific point in the structure space. To maximize the Bayesian score, it continues adding neighboring arcs until no additional arc improves the score. It then starts to remove arcs until a local optimum is achieved. The first process is known as thickening, and the second as thinning. The result is the model that best fits the given data. The used algorithm provided the best results for model selection among a total of 6 different algorithms.

The performance of the algorithm was tested using a 10-fold cross-validation (Kim, 2009). The accuracy and the Area Under the Receiver Operating Characteristic (ROC)

curve were considered as goodness-of-fit measures. The ROC curve presents sensitivity in the *y* coordinate versus 1-specificity or false positive rate in the *x* coordinate. The Area Under Curve (AUC) is a measure of model performance used for classification models that varies in the range [0,1]. When it is close to 1, it means that the algorithm is able to adequately identify the risky cases in which the animals could have lung consolidation. AUC is one of the most widely used performance metrics combined with accuracy rate.

A global sensitivity analysis was been performed to identify the impact of changes in the parameters on the estimated probabilities through the BN. We used a very descriptive tool for this purpose: a tornado diagram. This graph shows the most sensitive parameters for a selected state of the target node. The color of the bar shows the direction of the change in the presence of lung consolidation, red expresses negative and green positive change. The range shows the minimum and maximum posterior probability values for the presence of lung consolidation.

BNs provide the conditional probability distribution that can be used to obtain rapid results for a scenario with any combination of node states, i.e., by evidence propagation. Evidence propagation is one of the most powerful characteristics of Bayesian networks. With this technique the probabilities of each node can be updated via bidirectional propagation of new information through the whole structure. The most interesting risk scenarios are analyzed in terms of probabilities by considering evidence propagation. In each scenario, a percentage of 100% is set for one category in one node to show how the vaccine influences the presence or absence of lung

consolidation. The probability estimates for the different scenarios are reported in terms of percentages with their 95% confidence interval.

Results

A BN was built with GeNie/SMILE software and considered the following variables: density, vaccination, microorganisms, histopathology and pulmonary consolidation. Pulmonary consolidation was considered as the output response. The Bayesian network considers a direct relationship between vaccination and isolated microorganisms and histology, and direct relationships between microorganism and histology with pulmonary consolidation. The formulation of the BN is:

$$P(Consolidation, HPG, Microorganism, Vaccination, Density)$$
$$= P(Microorganism|Density, Vaccination)$$
$$\cdot P(PHPG|Microorganism, Vaccination)$$
$$\cdot P(Consolidation|HPG, Microorganism) \cdot P(Density) * P(Vaccination)$$

The BN structure and the estimated conditional probabilities are represented in Figure 2. Moreover, the strength of the relationship between two nodes connected by an arc is represented. The thickness of arcs represents the average strength between the two nodes involved. In this case, the strength has been normalized. The thickest arc is given to the arc that has the highest strength of influence, and the rest of the arcs are calculated proportionally to the thickest arc. Red-graded colored nodes contain parameters that are important for the calculation of the posterior probability distributions for consolidation. The more red the node is, the more important the parameters are to determine the presence/absence of consolidation. It can be

observed that the strongest relationship is the one between HPG and Consolidation. The strength average measure is 0.57 (varying from 0 to 1). The second strongest relation is Microorganism – HPG, similar to the strongest one with an average strength of 0.54. On the contrary, Density is the least related variable, only connected to Microorganism and with a strength of 0.09.

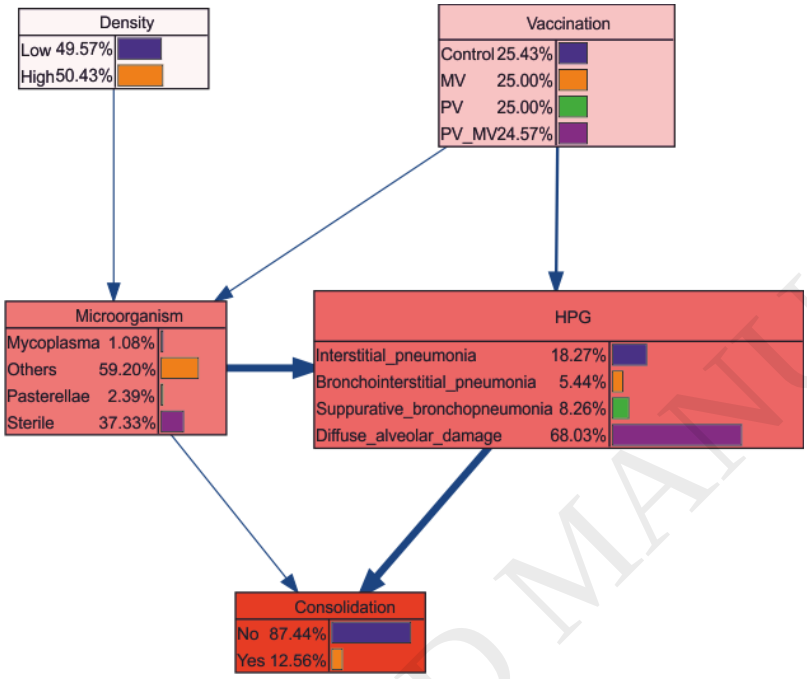

Figure 2. Bayesian network structure and estimated conditional probabilities.

A cross-validation procedure is presented to assess the model performance of the network focusing on the consolidation node. A 10-fold cross-validation leads to an accuracy of 96.3%, meaning that the model predicts very well the presence of consolidation in 96.3% of the cases. More specifically, the BN predicts well in 84.5% (sensitivity) of the animals with lung consolidation and in 98% of the animal without lung consolidation. Figure 3 represents the ROC curve for the presence of lung

consolidation, which provides an AUC of 0.9629 (very close to 1). As a result, the performance measures support the goodness-of-fit of the considered BN.

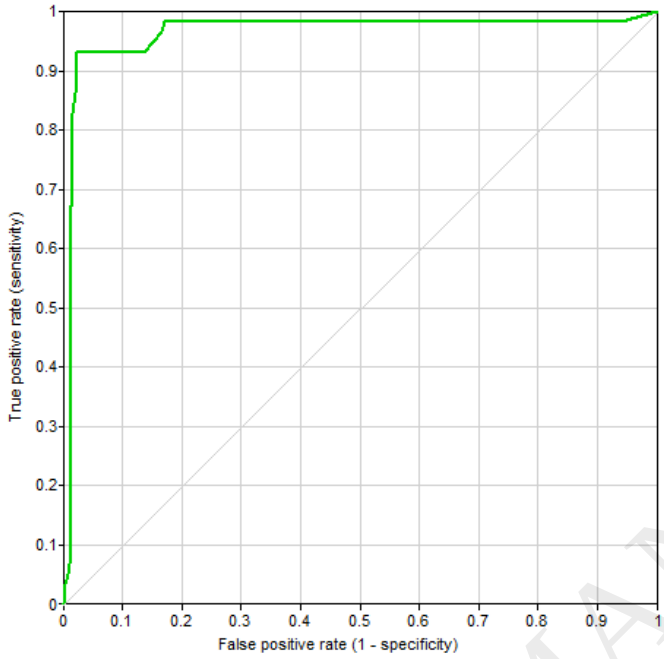

Figure 3. ROC curve for the presence of lung consolidation.

A global sensitivity analysis was also performed to determine the robustness of the calculated probabilities. Figure 4 represents the tornado diagram.

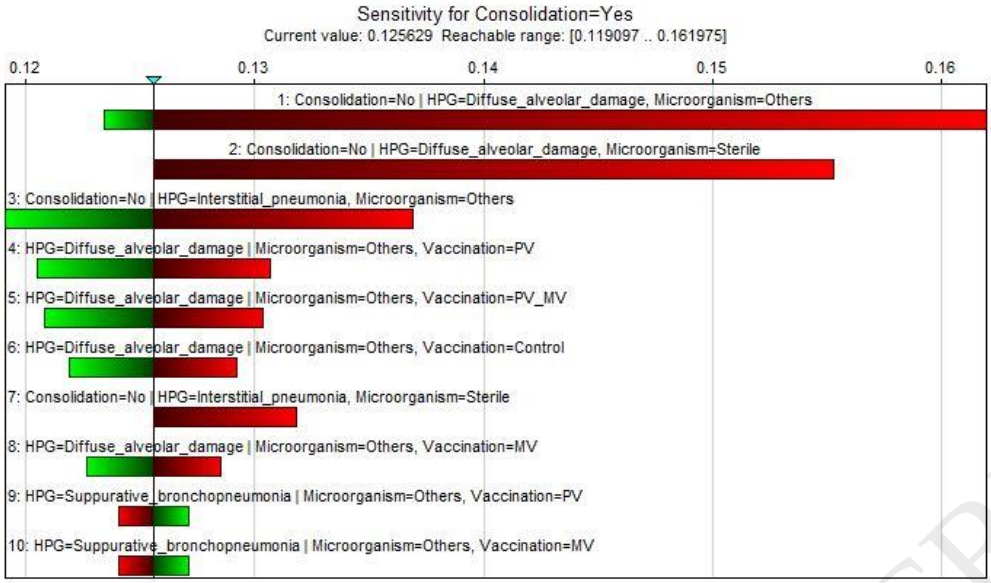

Figure 4. Tornado diagram for sensitivity analysis.

The horizontal axis shows the absolute change in the posterior probability of presence of consolidation when each of the parameters changes. The parameters associated with a state affecting the result are sorted from the most sensitive to the least. It can be observed that the maximum change is only 0.03 down and less than 0.01 up. Even more importantly, there are only 3 situations (extreme cases) out of the 117 analyzed in the sensitivity study, where the difference is greater than 1%. With these results, the model can be considered very robust.

The evidence propagation concept is used to show how one state of one variable influences the presence or absence of pulmonary consolidation. Table 1 presents the evidence propagation for some scenarios. These scenarios were considered to show the effects of the type of vaccine on the pulmonary consolidation response. Both the punctual and interval estimation (specifically, 95% confidence interval) are shown.

Scenarios	1	2	3	4	5	6
Density						
Low	100		49.57 (45.00-54.14)	49.57 (45.00-54.14)	49.57 (45.00-54.14)	49.57 (45.00-54.14)
High		100	50.43 (45.86-55.00)	50.43 (45.86-55.00)	50.43 (45.86-55.00)	50.43 (45.86-55.00)
Vaccination						
Control	25.43 (20.88-29.98)	25.43 (20.88-29.98)	100			
Pasteurellaceae	25 (20.48-29.52)	25 (20.48-29.52)		100		
M. ovipneumoniae and arginini	25 (20.48-29.52)	25 (20.48-29.52)			100	
Mixed vaccine	24.57 (20.07-29.07)	24.57 (20.07-29.07)				100
Microorganisms						
Sterile	34.99 (30.01-39.97)	39.63 (34.52-44.74)	39.75 (34.64-44.86)	36.52 (31.49-41.55)	39.92 (34.81-45.03)	36.12 (31.10-41.14)
Mycoplasma spp.	1.3 (0.12-2.48)	0.86 (0.00-1.82)	0.85 (0.00-1.81)	0.87 (0.00-1.84)	1.68 (0.34-3.02)	0.92 (0.00-1.92)
Pasteurellaceae	2.63 (0.96-4.30)	2.16 (0.64-3.68)	2.56 (0.91-4.21)	3.48 (1.57-5.39)	1.74 (0.37-3.11)	1.77 (0.39-3.15)
Other microorganisms	61.07 (55.98-66.16)	57.35 (52.18-62.52)	59.83 (54.71-64.95)	59.13 (54-64.26)	56.66 (51.48-61.84)	61.19 (56.1-66.28)
Histology						
Diffuse alveolar damage	67.37 (62.47-72.27)	68.69 (63.85-73.53)	61.54 (56.46-66.62)	72.17 (67.49-76.85)	60.88 (55.78-65.98)	77.82 (73.48-82.16)
Interstitial pneumonia	18.16 (14.13-22.19)	18.37 (14.33-22.41)	20.51 (16.29-24.73)	13,91 (10.30-17.52)	26.1 (21.51-30.69)	12.39 (8.95-15.83)
Bronchointerstitial pneumonia	6.00 (3.52-8.48)	4.89 (2.64-7.14)	11.12 (7.84-14.4)	4.36 (2.23-6.49)	4.33 (2.20-6.46)	1.78 (0.40-3.16)
Purulent bronchopneumonia	8.47 (5.56-11.38)	8.06 (5.22-10.90)	6.83 (4.2-9.46)	9.55 (6.48-12.62)	8.69 (5.75-11.63)	8.00 (5.17-10.83)
Pulmonary consolidation						
Absence	87.00 (83.93-90.07)	87.86 (84.88-90.84)	84.25 (80.92-87.58)	86.89 (83.81-89.97)	87.96 (84.99-90.93)	90.76 (88.11-93.41)
Presence	13.00 (9.93-16.07)	12.14 (9.16-15.12)	15.75 (12.42-19.08)	13.11 (10.03-16.19)	12.04 (9.07-15.01)	9.24 (6.59-11.89)

Table 1. Evidence propagation for density and vaccination scenarios. Each scenario provides a percentage of 100% for one category in one variable. Punctual estimations and 95% confidence intervals are presented.

In relation to density, two scenarios were defined (Scenario 1 and Scenario 2) with a low and high density, respectively (Table 1). The estimated probabilities of sterile lungs are 34.99% and 39.63%, respectively. In both scenarios, the estimated probability of the presence of consolidation was similar, 13.00% and 12.14%, respectively.

Regarding autogenous vaccines, when the control group (non-vaccinated) was considered (Scenario 3), the estimated probability of the presence of consolidation was the highest (15.75%). Subsequent scenarios related to autogenous vaccines will be compared to this as a reference. When animals were vaccinated with only Pasteurellaceae family (Scenario 4), the estimated probability of the presence of consolidation decreased to 13.11%, the mildest histological type (diffuse alveolar damage) increased to 72.17% and bronchointerstitial pneumonia decreased to 4.36%. If animals were only vaccinated with *M. arginini* and *M. ovipneumoniae* (Scenario 5), the estimated probability of the presence of consolidation was lower (12.04%), the estimated probability of diffuse alveolar damage was 60.88% and bronchointerstitial pneumonia was like the previous scenario (4.33%). The last scenario regarding autogenous vaccines was Scenario 6, where animals were vaccinated with both vaccines (Pasteurellaceae family and *M. arginini* and *M. ovipneumoniae*). The estimated probability of the presence of consolidation was the lowest, 9.24%, the

mildest histological type increased to 77.82% and bronchointerstitial pneumonia obtained the lowest value in all scenarios (1.78%). To determine the best results among the different vaccines, we observed that the mixed autogenous vaccine presented the highest decrease in the probability of the presence of consolidation with respect to the rest of the vaccines. Another important result was that with this vaccine, the estimated probability of the mildest histological type was the highest, and interstitial pneumonia and bronchointerstitial pneumonia in the lungs, with more pathogenic changes, were found to be less frequent.

Discussion

The study of the relationships among variables to determine health status is necessary in epidemiological studies of disease in animal groups. Bayesian networks are powerful and intuitive tools for the investigation of animal health data, providing both formal statistical inference and graphical exploratory visualization of complex data (Uusitalo 2007; Van der Gaag et al. 2009).

Some authors have used Bayesian networks to determine risk factors using different parameters as markers of animal health (Ettema et al., 2009; Jensen et al., 2009). Galapero et al. (2016) used evidence propagation to build scenarios that provided information about risk factors for lung consolidation, including environmental conditions. Takeuchi (2014) evaluated the effectiveness of vaccines for monovalent and a pentavalent rotavirus in humans using BNs. The information obtained from BNs is important for decision-making processes and can be used to improve animal health.

In this study, it is important to consider the relationship between pulmonary consolidation and vaccines (Chandrasekaran et al., 1991; Akan et al., 2006). To the best of our knowledge, Bayesian networks have not been used to evaluate the effect of vaccines on absence/presence of lung consolidation.

Previous reports showed an increase in respiratory pathologies associated with the presence of *Mycoplasma* spp. (Fernández et al., 2016; Niang et al., 1998; Sheehan et al., 2007), principally with *M. ovipneumoniae* (Sheehan et al., 2007). According to other studies, *M. Arginine* was also important, producing a coughing syndrome caused by a combination of *M. ovipneumoniae* and *M. arginine* (McAuliffe et al., 2003; Niang et al., 1998). On the other hand, other authors identified *Mannheimia haemolytica* as one of the main microorganisms in sheep respiratory processes, and this was the main agent isolated in the pulmonary consolidation processes that they studied (Lacasta et al., 2008; ORUÇ, 2006). Previous studies by Fernández et al. (2016) and Galapero et al. (2016) showed that the Pasterellaceae family played a less important role for lung consolidation than that proposed by other authors.

In New Zealand, the use of a commercial vaccine against Pasteurella showed no differences between vaccinated and control groups and between lesional groups and microbiological findings (Goodwin-Ray et al., 2008). Additionally, the outbreaks of pneumonia observed in pasteurella-vaccinated flocks in the UK suggest that a mixed selection of *M. ovipneumoniae* strains incorporated into these vaccines should provide greater protection against respiratory disease (McAuliffe et al., 2003). Our results suggest that lung consolidation is reduced with the application of the mixed vaccine compared to the other simpler vaccines. The application of commercial vaccines

without the application of strains of Mycoplasma spp. would explain the possible lack of efficacy of these vaccines as proposed by Goodwin-Ray et al. (2008). The presence of pulmonary consolidation decreased in the animals that received the mixed vaccines compared to animals that did not receive any vaccine. Mycoplasma reduces the phagocytic capacity of neutrophils in hosts; in animals with mixed vaccination, a reduction in isolated *Mycoplasma* spp. was observed, which could improve the response to *Pasteurella spp.*, with a subsequent significant reduction in the lesions. With these measures, the use of antibiotics would also be reduced in the production of fattening lambs, as shown by Gil Molino et al. (2018) in wild boar.

The influence of environmental components has been studied by Galapero et al. (2016) and Di Provvido et al. (2017). Di Provvido et al. (2017) focused on the importance of farm management as a possible cause of disease. In our case, differences were not observed in pens with low density and pens with high density, possibly due to good environmental conditions during the experiment. Based on our knowledge about the months with the highest risk, the use of vaccines is a fundamental tool for the control of this disease (Fernández et al., 2016). The feedlot factors were considered as observed by Wawegama et al. (2016), but in this case, the effect of the classification centers did not reveal differences among feedlots, so we considered the possible beneficial effects of vaccination.

Conflict of interest statement

None of the authors of this paper has a financial or personal relationship with other people or organizations that could inappropriately influence or bias the content of the paper.

Conclusions

To the best of the authors' knowledge, this is the first study that uses Bayesian networks to determine the effect of applying different autogenous vaccines for lung consolidation. The results show the advantages of the use of vaccines with strains from the studied location to reduce the amount of damage associated with the ovine respiratory syndrome. This avoids greater effects of the adverse environmental conditions in the feedlots.

Although the results are promising and may help in decision-making, it would be useful to conduct more experiments of this kind focusing on immunological and clinical studies to support the benefits of the use of these autogenous vaccines in fattening lambs.

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