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Differences in the association of cough and other clinical signs with ultrasonographic lung consolidation in dairy, veal, and beef calves

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ABSTRACT

Bovine respiratory disease (BRD) continues to be a leading cause of economic loss, hampered animal welfare, and intensive antimicrobial use in cattle operations worldwide. Reduction of antimicrobial use is hindered because it is still unclear which clinical signs are best monitored to reliably detect pneumonia. Also, these clinical signs may vary according to age and between breeds. The objective of this cross-sectional study was to identify clinical signs associated with ultrasound-confirmed pneumonia (lung consolidation ≥1 cm depth) pre- and postweaning in different production types (dairy, beef, and veal) and breeds. A total of 956 calves (70% Holstein-Friesian dairy and 30% Belgian Blue beef) from 84 herds were clinically examined using 24 parameters, scored using the Wisconsin and California BRD clinical scoring systems and subjected to thoracic ultrasonography. Of the calves, 42.8% and 19.5% had a lung consolidation ≥1 cm and ≥3 cm, respectively. Cough, both spontaneous and induced, was the only and best-performing clinical sign statistically associated with lung consolidation in all production types. Fever (rectal temperature ≥39.4°C) was the second most promising factor, being significant in beef and veal calves but not in dairy calves. Postweaning, none of the clinical signs studied were statistically associated with pneumonia, with the exception of cough in dairy calves. Spontaneous or induced cough as a single clinical sign outperformed any combination of clinical signs, including the Wisconsin and California respiratory disease scoring systems, but sensitivity remained low. This information can be useful to select appropriate clinical signs for continuous monitoring in precision livestock applications, targeted to a given breed and age. As a cross-sectional measurement, diagnostic accuracy of spontaneous cough (accuracy = 65.1%, sensitivity = 37.4%, specificity = 85.7%) is too low to be used as a criterion to select animals with pneumonia for antimicrobial treatment. At the group level, cough monitoring holds potential as an early warning sign, after which lung ultrasonography should follow.
Key words: bovine respiratory disease, pneumonia, scorecards, predictive monitoring, thoracic ultrasound

INTRODUCTION

Bovine respiratory disease (**BRD**) is a major economic issue and one of the leading causes of hampered animal welfare in the dairy and other cattle sectors (Pardon et al., 2012; Wang et al., 2018; Dubrovsky et al., 2020). The complex interactions of multiple viral and bacterial pathogens, as well as environmental and host-related risk factors, result in BRD, ranging from subclinical airway inflammation to life-threatening pneumonia (Buczinski and Pardon, 2020). To control the disease, especially in purchase-dependent production systems, antimicrobial use is crucial (Bokma et al., 2019). Public concern about the role of antimicrobial use among food-producing animals in the development of antimicrobial resistance in humans has made the reduction of antimicrobial use in these animals a top priority (Catry et al., 2016; Murphy et al., 2017). To reduce antimicrobial use without risking economic losses or compromising animal welfare, it appears rational to limit antimicrobial treatment to calves with pneumonia, withholding this treatment from animals with just an upper respiratory tract infection at first instance (Buczinski and Pardon, 2020).

A wide variety of definitions, based on clinical signs, to identify cattle with respiratory disease requiring antimicrobial treatment have been used in science and practice. More recently, development of clinical scoring systems, in particular the Wisconsin or California respiratory scores, has better standardized the case definition (Love et al., 2014; McGuirk and Peek, 2014). However, diagnostic accuracy of these scoring systems is only moderate, and between-observer agreement of clinical scoring for BRD remains rather low (Buczinski et al., 2016). A true game changer in the last years is

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the use of thoracic ultrasonography (**TUS**) on farm, which has been evidenced on multiple occasions to be the most accurate diagnostic test for pneumonia in calves (Buczinski et al., 2013; Ollivett and Buczinski, 2016). Despite the fact that rapid scanning techniques with short learning curves have been developed to better meet practitioners' demands, continuously scanning all animals is practically and economically impossible (Pardon, 2019; Jourquin et al., 2022). Therefore, the need for development of monitoring systems for timely detection of animals with pneumonia, either based on a measurement at a given time or continuously, is ever growing. To date, systems have been developed and commercialized to automatically detect temperature, movement, drinking behavior, and cough in calves (Ferrari et al., 2010; Timsit et al., 2011; Schaefer et al., 2012; White et al., 2015; Carpentier et al., 2018). In contrast to this rapid technological evolution, the reality is that very few studies have actually determined which clinical signs are suitable to differentiate animals with pneumonia from animals with only an upper respiratory tract infection. Also, current scoring systems can be quite time consuming, and it is not known whether it is necessary to score all signs. Because existing scoring systems were developed and tested almost exclusively in preweaning dairy calves, the question arises whether the same clinical signs can be used postweaning or in other breeds or production systems. Therefore, the objective of this study was to determine which clinical signs are associated with ultrasonographic lung consolidation in different breeds and production types (dairy, beef, and veal), pre- and postweaning. The second aim was to compare the diagnostic performance of single clinical signs with the diagnostic performance of California and Wisconsin BRD scorecards in correctly detecting ultrasound-confirmed pneumonia.

MATERIALS AND METHODS

Study Design, Sample Size Calculation, and Population

A cross-sectional study was conducted. The target population were all calves present on cattle farms (dairy, beef, and veal farms) in Belgium. The study population was conveniently selected based on farmers' willingness to cooperate. Only animals that were not treated with antimicrobials in the last 14 d were included in the data set. The data set used in this study consisted of 3 parts. The first part was a data set of 273 dairy, 215 beef, and 61 veal calves originating from 42 dairy, 28 beef, and 2 veal farms in Flanders, Belgium, examined between January and April 2017 (van Leenen et al., 2020a,b). The second part consisted of 291 veal calves (preweaning male Holstein-Friesian) from a single veal farm, examined between October 2020 and June 2021. The third part consisted of 21 dairy, 54 beef, and 41 veal calves originating from 3 dairy, 5 beef, and 3 veal farms, examined between October 2020 and June 2021. In total the data set consisted of 956 calves from 84 different farms, most of which were sampled during the winter period. This sample size allowed determination of a 10% difference (50% versus 60%) in pneumonia risk between calves with and without the given clinical sign, with 95% confidence and 80% power (386 observations needed per category). The sample size was determined before completion of this study. Study protocols were approved by the local ethical committee under license numbers EC2016-89, EC2020-068, and EC2020-092.

Clinical Scoring and Thoracic Ultrasonography

The following 28 observations regarding herd information and clinical signs were evaluated and scored for each individual calf (Table 1). The data set was collected by 6 different veterinarians. First, from outside the pen, visible clinical signs (e.g., mental state and respiratory rate) were evaluated. Next, clinical signs requiring animal contact were determined.

Following clinical examination, each calf was subjected to TUS. This was performed by the same 6 veterinarians, having completed a training course beforehand. This training consisted of a theoretical and a practical part. Theory was composed of recognizing ultrasound landmarks, normal lung, and lung lesions, as described in (Jourquin et al., 2022); afterward this was converted to practice. Three different portable ultrasound machines with a linear 7.5-MHz probe, set on similar settings (8-cm depth) were used (Tringa Linear Vet, Esaote; KX5200 VET, Kaixin; and Sonosite M-Turbo, Fujifilm). As transducing agent, to minimalize air, consequently improving contact between skin and probe, 75% isopropyl alcohol was used. The protocol of quick thoracic ultrasonography was followed, but, to increase diagnostic accuracy, scanning was performed at lower speed (Pardon, 2019; Jourquin et al., 2022). The whole lung surface was scanned, starting from the tips of the diaphragmatic lobes, and ending with the cranial lobes left and right. Details on the technique are available elsewhere (Pardon, 2019; Jourquin et al., 2022). Lung lesions were documented according to body site (left vs. right and cranial vs. caudal) and type of lesion. The following lesions were recorded: reverberations (A-lines), comet tails (B-lines, including recording of the maximum number in a single image: few comet tails: ≤3, multiple comet tails: 3–7, diffuse comet tails: ≥8),

Table 1. Overview of evaluated clinical signs at calf level

Subject	Description
Herd info	Production type (dairy, dairy-mixed, beef, and veal); breed (Holstein-Friesian, Belgian Blue)
BW	Estimated BW (<100 kg, 100–200 kg, >200 kg)[1]; age (wk)
Clinical signs	Rectal temperature (°C); eye mucosae (pink, hyperemic, pale, cyanotic, icteric); skin pinch test (<2 s, 2–3 s, >3 s); respiratory rate (breaths/min); breathing type (abdominal, costal, costo-abdominal); stridor [yes (y)/no (n)]; mentation (normal, depressed = decreased activity and reduced awareness of the environment, severely depressed = no activity and no awareness of the environment); body posture [standing (normal), sternal recumbency, lateral recumbency]; umbilical infection (y/n); diarrhea (y/n); (poly)arthritis (y/n); head tilt (y/n); ear position (normal, unilateral ear droop, bilateral ear droop); nasal discharge (y/n); nasal discharge (uni- or bilateral); type of nasal discharge (serous, seromucous, mucopurulent, purulent); eye discharge (y/n), eye discharge (uni- or bilateral); type of eye discharge (serous, seromucous, mucopurulent, purulent), spontaneous cough (y/n); induced cough at larynx level (positive/negative); induced cough at trachea level (positive/negative); auscultation trachea (normal, stridor, tracheal wheeze); auscultation thorax left/right/cranial/caudal (vesicular, increased vesicular sounds, rales, rhonchi, wheezes, and absent sound)
Scorecards[2]	Wisconsin respiratory score card,[3] California respiratory score card[4]

[1]Weight assessed via educated guess by the eye.

[2]Wisconsin score and California score: if the assigned total score of the individual scored clinical signs is ≥5, calf is considered positive for bovine respiratory disease.

[3]McGuirk and Peek, 2014.

[4]Love et al., 2014.

consolidation (including maximum consolidation depth measured perpendicular from the pleural line, by using the grid on the ultrasound screen: consolidation 0–0.9 cm, consolidation ≥1 cm, consolidation ≥3 cm), and pleurisy (pleural effusion).

Statistical Analysis

Data were collected in Excel (Windows 10, 2019, Microsoft Corp.), descriptive statistics were calculated in SPSS version 27 (IBM Corp.), and software and statistic modeling was performed in SAS version 9.4 (SAS Institute Inc.). The elementary unit was the individual calf. The outcome of interest was pneumonia, defined as a lobular consolidation ≥1 cm or lobar consolidation ≥3 cm depth. A total of 8 models were built, comprising the whole data set; dairy, beef, or veal only; and dairy and beef pre- and postweaning. Categorical predictors were regrouped if the number of observations within a group was lower than 10. Continuous variables (temperature and respiratory rate) were tested continuously and categorically as binary factors based on an optimal estimated cut-off value, using receiver operating characteristics curve analysis and the Youden index. Associations of the variables with the binary outcome were determined using a generalized linear mixed model (PROC GLIMMIX) with binomial distribution and logit link function with Wald's statistics for type 3 contrast. Herd was added as random factor to take clustering of calves within a herd into account. All variables with $P < 0.20$ in the univariable analysis were maintained for construction of the multivariable model. Multicollinearity was checked before construction of the multivariable model, and the relationship between the different clinical signs was explored using logistic regression, a causal diagram, chi-squared test, and Pearson's correlation. The multivariable model was constructed stepwise backward, gradually excluding non-statistically significant factors. Model fit was evaluated using the Hosmer-Lemeshow goodness-of-fit test. Further, diagnostic performance was determined in terms of the area under the curve (**AUC**), accuracy, sensitivity, specificity, and positive and negative predictive values. This entire procedure was repeated according to production type and breed, classified as preweaning or postweaning. An age of 8 wk was used as cut-off for weaned calves, as almost all farms weaned in that period. In a second round of analysis, all statistics (8 models) were re-run with (lobar) consolidation ≥3 cm as outcome of interest. Statistical significance was set at $P < 0.05$ in all models.

RESULTS

Herd Characteristics

A total of 956 calves were clinically examined, scored using the Wisconsin and California BRD clinical scoring systems, and subjected to TUS. The final study population consisted of 956 calves originating from 45 dairy, 33 beef, and 6 veal farms. The dairy and beef farms belonged to the most frequent production type throughout Europe, being medium-sized (average number of 28 beef and 85 dairy adults) family-owned operations. Details on housing and feeding of the calves are available in the article by van Leenen et al. (2021). Briefly, calves were housed individually (igloos or pens) or in groups on straw-bedded concrete floors and were supplied with milk or milk replacer, roughage, and concentrates. The 6 veal herds were of the white veal type, with feeding and housing according to the mainstream production type of the European Union and North America (Pardon et al., 2014). Calves were housed individually for the first 6 wk in baby boxes, after which group housing in pens of 6 to 8 animals on wooden slatted floors is standard, which is in accordance with local legislation. Individually housed calves were fed from individual drinking buckets, and group-housed calves were fed from a common feeding trough. All veal calves received milk replacer at least twice a day, roughage, and concentrates. The majority (70%; n = 671) of the data set were Holstein-Friesian calves, of which 71.4% (n = 464) were preweaning and 28.6% (n = 186) weaned. The remaining part (29.8%; n = 285) were Belgian Blue beef calves, of which 50% (n = 141) were preweaning. Distribution of production types was as follows: 31.1% dairy (n = 297), 27.2% beef (n = 260), and 41.7% veal (n = 399). The veal category consisted predominantly of preweaning male Holstein-Friesian calves. One veal farm housed dairy-mixed calves (n = 16); this herd was categorized as Belgian Blue, given their crossbreeding with Belgian Blue. Of all calves, depending on the scoring system used, 12 to 16% were clinically ill, and 42.8% (409/956) and 19.5% (186/956) had lung consolidation ≥1 cm and ≥3 cm, respectively (Table 2).

The age distribution of calves with an ultrasound-confirmed pneumonia (lung lesion ≥1cm) was as follows: 35.6% (122/342) <4 wk old; 58.6% (154/263) between 4 and 8 wk old; 39.8% (130/327) >8 wk old. Of 24 calves the age was unknown. Stratified by breed, the following distribution was obtained: Holstein-Friesian, 35.8% (115/321) <4 wk, 71.3% (102/143) 4 to 8 wk, and 45.7% (85/186) > 8 wk; Belgian Blue, 33.3% (7/21) <4 wk, 43.3% (52/120) 4 to 8 wk, and 31.9% (45/141) >8 wk.

Clinical Signs Associated with Ultrasonographic Lung Consolidation

For continuous variables, the following descriptive statistics were obtained. Mean rectal temperature was 38.9°C [minimum (**min.**): 36.6°C; maximum (**max.**): 41.2°C; standard deviation (SD) = 0.49] in dairy calves, 39°C (min.: 37.4°C; max.: 40.8°C; SD = 0.52) in beef calves, and 38.9°C (min.: 37°C; max.: 41.1°C; SD = 0.62) in veal calves. Mean respiratory rate in dairy calves was 37 breaths/min (min.: 16; max.: 116; SD = 13.7), 35 breaths/min in beef calves (min.: 14; max.: 84; SD = 12.34), and 37 breaths/min in veal calves (min.: 16; max.: 116; SD = 16.79). An optimal estimated cut-off value using receiver operating characteristics curve analysis and the Youden index was determined for the continuous variables. The obtained optimal cut-off value for rectal temperature was ≥39.4°C and ≥43 breaths/min for respiratory rate. Accordingly, these variables were used as categorical variables.

Descriptive statistics of the categorical clinical signs in different production types and their association with lung consolidation ≥1 cm are shown in Table 3.

The corresponding odds ratios (**OR**) and 95% confidence intervals (CI) of the statistically significant variables associated with ultrasound-confirmed pneumonia (lung consolidation ≥1 cm) for dairy calves were as follows: induced cough reflex (trachea; OR = 2.58; 95% CI = 1.26–5.3); induced cough reflex (larynx; OR = 4.5; 95% CI = 1.1–17.8). The OR and CI of the statistically significant variables associated with ultrasound-confirmed pneumonia (lung consolidation ≥1cm) for beef calves were as follows: rectal temperature (≥39.4°C; OR = 2.58; 95% CI = 1.26–5.3), spontaneous cough (OR = 2.1; 95% CI = 1.08–4.2). Finally, the OR and CI of the statistically significant variables associated ultrasound-confirmed pneumonia (consolidation >1 cm) in veal calves were as follows: rectal temperature (≥39.4°C;

Table 2. Prevalence of pneumonia according to production type based on clinical scoring and thoracic ultrasonography (2017–2021, Belgium)

Production type (breed)	Percentage (number/total) of animals[1]			
	Wisconsin score positive	California score positive	Consolidation ≥1 cm	Consolidation ≥3 cm
Dairy (Holstein-Friesian; n = 297)	14.1 (42/297)	17.5 (52/297)	46.1 (137/297)	34.0 (101/297)
Beef (Belgian Blue; n = 260)	20.0 (52/260)	26.5 (69/260)	33.5 (87/260)	17.7 (46/260)
Veal (Holstein-Friesian; n = 399)	20.8 (83/399)	18.7 (75/399)	46.4 (185/399)	9.8 (39/399)
Total	18.5 (177/956)	23.9 (229/956)	42.8 (409/956)	19.5 (186/956)

[1]Wisconsin and California scores positive: if the assigned total score of the individual scored clinical signs is ≥5, calf is considered positive for bovine respiratory disease.

Table 3. Association of clinical signs with pneumonia as determined by thoracic ultrasonography in calves, stratified by production type

		Percentage (number/total) of animals with pneumonia (lung consolidation ≥1 cm)							
		Dairy (n = 297)		Beef (n = 260)		Veal (n = 399/n = 107)[1]		Total (n = 956)	
Clinical sign	Category	Characteristic present	*P*-value	Characteristic present	*P*-value	Characteristic present	*P*-value	Characteristic present	*P*-value
Rectal temperature (≥39.4°C)[2]	Yes	53.2 (25/47)	0.53	49.0 (24/49)	<0.01	69.8 (60/86)	<0.001	59.9 (109/182)	<0.001
	No	44.8 (112/250)		29.9 (63/211)		39.9 (125/313)		38.8 (300/774)	
Respiratory rate (≥43 breaths/min)[2]	Yes	53.0 (44/83)	0.43	35.4 (23/65)	0.51	73.5 (83/113)	0.03	57.5 (150/261)	<0.01
	No	43.5 (93/214)		32.8 (64/195)		35.7 (102/286)		37.3 (259/695)	
Induced cough reflex (trachea)	Yes	67.9 (38/56)	<0.01	42.0 (21/50)	0.2	69.8 (44/63)	0.03	60.9 (103/169)	<0.001
	No	41.1 (99/241)		31.4 (66/210)		42.0 (141/336)		38.9 (306/787)	
Induced cough reflex (larynx)	Yes	76.5 (13/17)	0.03	28.6 (2/7)	0.81	95.7 (22/23)	0.49	78.7 (37/47)	<0.03
	No	44.3 (124/280)		33.6 (85/253)		70.2 (59/84)		43.4 (268/617)	
Spontaneous cough	Yes	59.1 (39/66)	0.11	47.1 (24/51)	0.03	78.9 (90/114)	<0.001	66.2 (153/231)	<0.001
	No	42.4 (98/231)		30.1 (63/209)		33.3 (95/285)		35.3 (256/725)	
Eye discharge	Present	40 (8/20)	0.41	16.7 (1/6)	0.44	80.9 (34/42)	<0.001	59.5 (25/42)	<0.01
	Absent	46.6 (129/277)		33.9 (86/254)		42.3 (150/355)		45 (280/622)	
Type of eye discharge	Serous	37.5 (3/8)	1.0	0 (0/2)	—	93.8 (15/16)	0.67	69.2 (18/26)	1.0
	Seromucous–purulent	50.0 (5/10)	1.0	33.3 (1/3)	1.0	100 (1/1)	1.0	50.0 (7/14)	1.0
	None (ref.)	46.2 (129/279)		33.7 (86/255)		71.4 (65/91)		44.8 (280/625)	
Nasal discharge	Present	50 (30/60)	0.39	34.1 (29/85)	0.62	82.4 (28/34)	0.02	48 (84/175)	0.06
	Absent	45.1 (107/237)		33.1 (58/175)		43.1 (157/364)		45.2 (221/489)	
Type of nasal discharge	None (ref.)	45.4 (109/240)		32.1 (59/184)		72.0 (54/75)		44.5 (222/499)	
	Serous	27.3 (3/11)	1.0	45.5 (5/11)	1.0	88.9 (16/18)	1.0	60.0 (24/40)	1.0
	Seromucous	50.0 (6/12)	1.0	31.0 (9/29)	1.0	76.9 (1/13)	0.41	46.3 (25/54)	1.0
	Muco-purulent	50.0 (5/10)	1.0	33.3 (4/12)	1.0	50.0 (1/2)	1.0	41.7 (10/24)	1.0
	Purulent	58.3 (14/24)	1.0	41.7 (10/24)	1.0	0	—	50.0 (24/48)	1.0
Ear position	Unilateral ear droop	50.0 (3/6)	1.0	33.3 (3/9)	1.0	54.5 (6/11)	1.0	46.2 (12/26)	1.0
	Bilateral ear droop	40.0 (2/5)	0.97	26.7 (4/15)	1.0	81.5 (22/27)	1.0	59.6 (28/47)	1.0
	Normal	46.2 (132/286)		34.2 (80/234)		77.9 (53/68)		45.1 (265/588)	
Head tilt	Yes	55.6 (5/9)	0.53	20.0 (2/10)	0.57	66.7 (6/9)	0.53	46.4 (13/28)	0.94
	No	45.8 (131/286)		33.7 (84/249)		76.5 (75/98)		45.8 (290/633)	
Arthritis	Yes	0	—	0 (0/3)	0.99	0 (0/1)	0.96	0 (0/4)	0.79
	No	45.9 (136/296)		33.9 (87/257)		76.4 (81/106)		46.1 (304/659)	
Diarrhea	Semiformed-pasty	66.7 (8/12)	0.43	41.2 (7/17)	1.0	75 (6/8)	0.79	56.8 (21/37)	0.78
	Watery	17.7 (1/6)	0.82	28.6 (2/7)	1.0	40.0 (2/5)	0.98	27.8 (5/18)	0.95
	Normal	45.9 (128/279)		33.1 (78/236)		78.5 (73/93)		45.9 (279/608)	
Umbilical infection	Yes	100 (4/4)	0.99	28.6 (2/7)	0.92	37.5 (3/8)	0.56	47.4 (9/19)	0.14
	No	45.4 (133/293)		33.6 (85/283)		78.8 (78/99)		45.9 (296/645)	
Body posture	Abnormal	81.8 (9/11)	0.05	37.5 (9/24)	0.92	92.9 (39/42)	0.3	74.0 (57/77)	0.07
	Normal	43.0 (119/277)		3.1 (78/236)		64.6 (42/65)		41.3 (239/578)	
Mental status	Abnormal	85.7 (6/7)	0.11	57.1 (8/14)	0.06	0	—	66.7 (14/21)	0.01
	Normal	44.0 (114/259)		34.7 (67/193)		95.5 (64/67)		47.2 (245/519)	
Stridor	Yes	33.3 (1/3)	0.91	66.7 (2/3)	0.26	62.5 (5/8)	0.42	57.1 (8/14)	0.69
	No	46.2 (133/288)		33.1 (85/257)		76.8 (76/99)		45.7 (294/644)	
Eye mucosae	Abnormal	44.4 (4/9)	0.82	16.7 (1/6)	0.44	85.7 (6/7)	0.53	50.0 (11/22)	0.83
	Normal	47.3 (131/277)		33.9 (86/254)		75.0 (75/100)		46.3 (292/631)	
Skin tension	Abnormal	66.7 (2/3)	0.52	0 (0/3)	0.99	66.7 (2/3)	0.52	44.4 (4/9)	0.81
	Normal	46.9 (130/277)		33.9 (87/257)		40.5 (15/37)		40.6 (232/571)	
Abnormal lung auscultation	Yes	61.7 (79/128)	<0.01	51.8 (43/83)	<0.01	74.8 (77/103)	0.54	39.9 (179/449)	<0.01
	No	34.3 (58/169)		24.9 (44/177)		80.0 (4/5)		58.3 (126/216)	

[1]107 veal calves had a full clinical exam; the remaining 292 calves were scored only for the signs included in the Wisconsin and California score cards. Consequently, the data of these 292 calves could be used only for the following variables: rectal temperature, cough, induced cough, breathing rate, and eye and nasal discharge.

[2]Cut-off values are determined using the Youden index.

OR = 2.93; 95% CI = 1.62–5.3), respiratory rate (≥43 breaths/min; OR = 2.2; 95% CI = 1.1–4.4), induced cough reflex (trachea; OR = 2.1; 95% CI = 1.1–4.1), spontaneous cough (OR = 3.6; 95% CI = 1.97–6.56), eye discharge (present; OR = 5.2; 95% CI = 2.2–12.3), and nasal discharge (present; OR = 7.9; 95% CI = 1.47–43.6). Across the complete data set, the following variables were statistically associated with ultrasound-confirmed pneumonia (consolidation >1 cm): rectal temperature (≥39.4°C; OR = 2.37; 95% CI = 1.6–3.5), respiratory rate (≥43 breaths/min; OR = 1.68; 95% CI = 1.15–2.47), induced cough reflex (trachea; OR = 2.2; 95% CI = 1.44–3.36), induced cough reflex (larynx; OR = 2.81; 95% CI = 1.12–7.1), spontaneous cough (OR = 2.61; 95% CI = 1.8–3.8), eye discharge (present; OR = 2.22; 95% CI = 1.2–4.0), and mental status (OR = 4.13; 95% CI = 1.33–12.8).

In a second analysis with lung consolidation ≥1 cm, the entire data set (956 calves) was stratified based on breed, and afterward the breed was classified according to weaning status (Table 4). Induced cough (trachea and larynx), rectal temperature (≥39.4°C), and respiratory rate (≥43 breaths/min) were significantly correlated with spontaneous cough. Results of the multivariable analysis are shown in Table 4. Respiratory rate (≥43 breaths/min) and spontaneous cough were significant in dairy and veal industry calves [dairy (P = 0.01; AUC = 0.555); veal (P < 0.01; AUC = 0.526)]. For beef industry calves, rectal temperature (≥39.4°C) and respiratory rate (≥43 breaths/min) were the only statistically significant multivariable models (P = 0.03; AUC = 0.572).

Table 5 shows the results for lung consolidation ≥3 cm (lobar pneumonia) but limited to the significant clinical signs only. In dairy calves, both induced cough reflexes (trachea and larynx) were statistically associated with lobar pneumonia. In beef calves only, spontaneous cough was significant. Finally, in veal calves, both induced cough reflexes, spontaneous cough, and rectal temperature were statistically associated with lobar pneumonia. The corresponding OR and 95% CI are shown in Table 5.

Table 6 presents the diagnostic performance of the California and Wisconsin BRD scorecards on the study data set. In general, the California and Wisconsin BRD scorecards performed poorly in both dairy (Holstein-Friesian) and beef (Belgian Blue) cattle, pre- and postweaning.

DISCUSSION

To our knowledge, this is the first study examining the association of clinical signs with ultrasonographic lung consolidation in calves of different production types and breeds both pre- and postweaning. The incentive for this study was two-fold. On the one hand, the goal was to provide information on what clinical signs are most suitable for scoring systems and automatic monitoring purposes to detect pneumonia. On the other hand, we wanted to verify any difference in diagnostic performance of single clinical signs and existing scoring systems when applied to different production systems, breeds, and stages of weaning.

The main finding of this study is that of all clinical signs studied, cough (both spontaneous and induced) is most statistically associated with lung consolidation in calves in all production types. Similarly, spontaneous cough is the best-performing clinical sign [accuracy (**Acc.**): 65.1%, sensitivity (**Se**): 37.4%, specificity (**Sp**): 85.7%], followed by tracheal reflex (Acc.: 61.1%, Se: 25.2%, Sp: 87.9%). The laryngeal reflex performed the most poorly (Acc.: 58.1%, Se: 12.13%, Sp: 97.2%) of the cough parameters. Poor performance of the laryngeal reflex may be due to more difficult manual stimulation. Cough is a natural defense mechanism that protects the respiratory tract from inhaling foreign bodies (e.g., dust), caustic substances (e.g., ammonia), and pathogens, as these components could impair mucociliary and respiratory defense mechanisms and subsequently increase the risk of an aggravated respiratory tract infection (Callan and Garry, 2002). In addition, respiratory tract infections can trigger the cough reflex themselves (Polverino et al., 2012; Andrani et al., 2019; Htun et al., 2019). Likewise, in human medicine, acute bronchitis of a nonallergic nature (e.g., influenza) and infectious pneumonia are characterized by the development of cough (Nowicki and Murray, 2020). Next to cough, rectal temperature and breathing rate were statistically associated with lung consolidation, which was in line with previous studies on pneumonia in cattle (Grissett et al., 2015; Eberhart et al., 2017). Both performed almost as well as cough in terms of diagnostic accuracy (temperature, Acc.: 61.0%, Se: 26.7%, Sp: 86.7%; breathing rate, Acc.: 61.3%, Se: 36.7%, Sp: 79.7%, respectively). In contrast to cough, which is rather specific for the respiratory tract, various drawbacks must be taken into account when considering rectal temperature and respiratory rate as predictors of pneumonia. Increased rectal temperature could be triggered by many different active inflammatory processes occurring elsewhere in the body. Further, in a BRD episode, temperature is commonly increased during early onset and only for a short time (Timsit et al., 2011; Grissett et al., 2015; Maier et al., 2019). Therefore, increased temperature may be missed and subsequently lead to false negatives in a cross-sectional measurement. Additionally, heat stress, excitement, humidity, activity, and daily fluctuations in body and ambient temperature are

Table 4. Diagnostic performance of clinical signs and combination of clinical signs for detection of lung consolidation ≥1 cm in calves, expressed as area under the curve (AUC), stratified by breed and weaning status[1]

	Holstein-Friesian														
	Preweaning (n = 464)					Postweaning (n = 186)					Total (n = 671)				
Item	Acc. (%)	Se (%)	Sp (%)	*P*-value	AUC	Acc. (%)	Se (%)	Sp (%)	*P*-value	AUC	Acc. (%)	Se (%)	Sp	*P*-value	AUC
Rectal temperature (≥39.4°C)	60.3	24.4	91.9	<0.001	0.590	58.1	29.4	82.2	0.4	0.558	60.1	25.7	88.6	<0.001	0.555
Respiratory rate (≥43 breaths/min)	64.7	35.9	89.9	<0.001	0.666	57.0	40.0	71.3	0.6	0.556	62.0	37.5	82.3	<0.02	0.597
Spontaneous cough	64.7	38.3	87.9	<0.001	0.664	61.8	40.0	80.2	0.12	0.601	64.7	38.8	86.1	<0.001	0.641
Cough reflex (trachea)	59.5	25.8	89.1	<0.001	0.569	62.9	23.5	96.0	<0.001	0.598	61.1	25.0	91.0	<0.001	0.597
Cough reflex (larynx)	65.3	27.9	96.8	0.07	0.572	60.2	15.3	98.0	0.04	0.567	55.2	17.5	97.2	0.01	0.574
Eye discharge (present)	58.1	16.2	94.7	<0.001	0.555	53.2	5.9	93.1	0.25	0.495	57.6	13.2	94.3	<0.001	0.537
Rectal temperature (≥39.4°C) and respiratory rate (≥43 breaths/min)	57.5	11.5	98.0	0.02	0.547	58.1	17.7	92.1	0.39	0.549	58.4	13.2	95.9	0.04	0.545
Respiratory rate (≥43 breaths/min) and spontaneous cough	62.1	21.7	97.6	0.01	0.596	62.9	27.1	93.1	0.02	0.601	63.2	23.4	96.2	<0.01	0.598
Rectal temperature (≥39.4°C) and spontaneous cough	57.1	10.6	98.0	0.08	0.543	58.6	16.5	94.1	0.37	0.553	58.4	12.2	96.7	0.09	0.545
Rectal temperature (≥39.4°C), respiratory rate (≥43 breaths/min), and spontaneous cough	56.5	7.8	99.2	0.2	0.535	59.7	14.1	98.0	0.06	0.561	58.3	9.5	98.6	0.05	0.541
Spontaneous cough and eye discharge	56.5	7.83	99.2	0.02	0.535	54.9	3.5	98.0	0.72	0.508	57.1	6.6	98.9	0.03	0.527
	Belgian Blue														
	Preweaning (n = 141)					Postweaning (n = 141)					Total (n = 285)				
	Acc. (%)	Se (%)	Sp (%)	*P*-value	AUC	Acc. (%)	Se (%)	Sp (%)	*P*-value	AUC	Acc. (%)	Se (%)	Sp (%)	*P*-value	AUC
Rectal temperature (≥39.4°C	61.0	30.5	82.9	0.34	0.567	65.3	28.9	82.3	0.15	0.556	63.2	29.5	82.8	0.03	0.562
Respiratory rate (≥43 breaths/min)	61.0	35.6	79.3	0.47	0.574	58.2	31.1	70.8	0.8	0.510	59.7	34.3	59.7	0.18	0.544
Spontaneous cough	68.1	39.0	89.0	<0.001	0.640	63.8	26.7	81.3	0.3	0.540	66.0	33.3	85.0	<0.01	0.592
Cough reflex (trachea)	61.0	30.5	82.9	0.44	0.567	60.9	17.8	81.3	0.89	0.495	61.1	25.7	81.7	0.25	0.537
Cough reflex (larynx)	58.0	1.7	97.6	0.68	0.496	66.7	2.2	96.9	0.77	0.495	62.1	1.9	97.2	0.65	0.496
Rectal temperature (≥39.4°C) and respiratory rate (≥43 breaths/min)	58.9	10.2	93.9	0.6	0.520	68.8	15.6	93.8	0.1	0.547	63.9	12.4	93.9	0.08	0.531
Respiratory rate (≥43 breaths/min) and spontaneous cough	64.5	20.3	96.3	0.04	0.583	70.2	8.9	98.9	0.05	0.539	67.7	15.2	97.8	<0.01	0.565
Rectal temperature (≥39.4°C) and spontaneous cough	62.4	16.9	95.1	0.13	0.560	69.5	11.1	96.9	0.08	0.540	66.0	14.3	96.1	<0.01	0.552
Rectal temperature (≥39.4°C) respiratory rate (≥43 breaths/min), and spontaneous cough	61.0	8.5	98.8	0.35	0.536	68.8	2.2	100	0.99	0.511	64.9	5.7	99.4	0.08	0.526

[1]Acc. = accuracy; Se = sensitivity; Sp = specificity.

Table 5. Clinical signs significantly associated with pneumonia (lobar consolidation ≥3 cm) as determined by thoracic ultrasonography in 186 calves, stratified by production type[1]

Dairy		Beef		Veal		Total	
Clinical signs	*P*-value (OR; 95% CI)	Clinical signs	*P*-value (OR; 95% CI)	Clinical signs	*P*-value (OR; 95% CI)	Clinical signs	*P*-value (OR; 95% CI)
Induced cough reflex (trachea)	$P < 0.001$ (3.9; 171–8.96)	Spontaneous cough	$P < 0.001$ (3.96; 1.61–9.69)	Rectal temperature (≥39.4°C)	$P < 0.001$ (5.96; 2.83–12.54)	Rectal temperature (≥39.4°C)	$P < 0.001$ (2.96; 1.82–4.83]
Induced cough reflex (larynx)	$P = 0.01$ (5.4; 1.42–20.64)			Respiratory rate (≥43 breaths/min)	$P = 0.02$ (2.78; 1.14–6.77)	Induced cough reflex (trachea)	$P < 0.001$ (2.25; 1.52–4.19)
				Induced cough reflex (trachea)	$P < 0.01$ (3.17; 1.38–7.3)	Induced cough reflex (larynx)	$P = 0.04$ (3.1; 1.05–9.2)
				Spontaneous cough	$P < 0.001$ (3.87; 1.82–8.23)	Spontaneous cough	$P < 0.001$ (2.32; 1.47–3.7)

[1]OR = odds ratio. Only significant clinical signs are reported.

major limiting factors to properly interpreting (rectal) temperature as a predictor of respiratory tract infection (Hill et al., 2016). Similar shortcomings are related to increased respiratory rate. The study of Eberhart et al. (2017) showed that increased respiratory rate might be caused by an episode of BRD but may also be the result of heat stress, humidity, excitement, pain, or acidosis (Nienaber and Hahn, 2007; Smith et al., 2015). Taking all these limitations into account, cough is likely the most specific and promising clinical sign to be used as early warning for respiratory disease and identification of individual animals in need of antimicrobial treatment.

Notably, in our study, multiple clinical signs commonly used in scoring systems performed moderately to poorly in detecting pneumonia. In particular, findings on nasal discharge (Acc.: 56.7%, Se: 21.3%, Sp: 83%), ocular discharge (Acc.: 59.1%, Se: 10.5%, Sp:95.4%), head tilt (Acc.: 53.9%, Se: 4.3%, Sp: 95.8%), and ear drop (Acc.: 58.0%; Se: 11.0%, Sp: 93.2%) are not in line with current literature (Love et al., 2014; McGuirk and Peek, 2014). Previous work has shown that nasal discharge is associated with various respiratory tract diseases, but many other noninfectious etiologies exist (Divers, 2008). Also, nasal discharge (as well as type of nasal discharge) is a highly subjective clinical sign to judge, and between-observer variation could also have contributed to the observations made in this study (Berman et al., 2021). Calves self-clean their noses as long as they feel reasonably well, hiding clinical signs at the moment of clinical examination. Similar shortcomings could affect observation of eye discharge. Eye discharge may be due to local infection, environmental irritants, or a systemic disease. These observations are in line with the study of Buczinski et al., 2018. In that study, the California BRD scorecard was re-evaluated and re-weighted, whereby eye discharge was weighted lower compared with the original California scorecard. Finally, ear drop and head tilt secondary to otitis media performed poorly in the detection of pneumonia in our study. *Mycoplasma bovis* is the most frequent cause of group outbreaks of otitis media, and is present in about 100% of veal and 25% of dairy farms in the study region, respectively (Pardon et al., 2011; Gille et al., 2018). Possibly, relative differences in *M. bovis* prevalence between Belgian dairy farms and larger North American dairies explain why head tilt is statistically associated with pneumonia in one study and not in another (Francoz et al., 2004; Radaelli et al., 2008; Pardon et al., 2011, 2020).

A second important finding is that clinical signs associated with lung consolidation differed according to production types, breeds, and weaning status. However, the differences in performance were minor (Table 4).

Table 6. Diagnostic performance of Wisconsin and California scorecards for the detection of ultrasound-confirmed lung consolidation in calves, stratified by production type, breed, and weaning status[1]

Performance overview of scorecards to identify pneumonia (lung consolidation ≥1 cm) in calves

Stratification	Prev. [% (n)]	Wisconsin BRD scorecard (Positive n = 115/409)					California BRD scorecard (Positive n = 229/409)				
		Acc. (%)	Se (%)	Sp (%)	PPV (%)	NPV (%)	Acc. (%)	Se (%)	Sp (%)	PPV (%)	NPV (%)
By production type											
Dairy	46.1 (137/297)	57.3	19.0	90.0	61.9	56.6	57.3	25.6	84.4	58.3	57.3
Beef	33.5 (87/260)	65.0	27.6	83.8	46.2	69.7	58.5	36.8	70.5	40.7	67.0
Veal	46.4 (185/399)	65.4	35.1	91.6	78.3	62.0	66.2	36.8	91.6	79.1	62.2
By breed and weaning status											
Holstein-Friesian	45.3 (304/671)	61.7	26.0	91.3	71.2	59.8	61.9	29.0	89.1	68.8	60.2
Preweaning	46.8 (217/464)	62.1	26.3	93.5	78.1	59.1	62.3	26.7	93.5	78.4	59.2
Weaned	45.7 (85/186)	59.7	24.7	89.1	65.6	58.4	60.2	32.9	83.2	62.2	59.6
Belgian Blue	36.8 (105/285)	65.3	34.3	83.3	54.5	68.5	60.7	44.8	70.0	46.5	68.5
Preweaning	41.8 (59/141)	62.4	37.3	80.5	57.9	64.1	63.1	49.2	73.2	56.8	66.7
Weaned	31.9 (45/141)	68.8	31.1	86.5	51.8	72.8	58.2	37.8	67.7	35.4	69.9
Total	42.8 (409/956)	62.8	28.1	88.7	65.0	62.2	61.5	33.0	82.8	60.0	82.8

Performance overview of scorecards to identify pneumonia (lung consolidation ≥3 cm) in calves

Stratification	Prev. [% (n)]	Wisconsin BRD scorecard (Positive n = 45/186)					California BRD scorecard (Positive n = 50/186)				
		Acc. (%)	Se (%)	Sp (%)	PPV (%)	NPV (%)	Acc. (%)	Se (%)	Sp (%)	PPV (%)	NPV (%)
By production type											
Dairy	34.0 (101/297)	64.7	18.8	88.3	45.2	67.9	60.6	21.8	80.6	36.7	66.7
Beef	17.7 (46/260)	71.5	26.1	81.3	23.1	83.7	61.9	32.6	68.2	18.1	82.5
Veal	9.8 (39/399)	76.4	35.9	80.8	16.9	92.1	75.0	33.3	79.5	15.1	91.7
By breed and weaning status											
Holstein-Friesian	20.3 (136/671)	71.5	20.6	84.5	25.3	80.7	70.2	22.8	82.3	24.7	80.7
Preweaning	18.5 (86/464)	70.8	22.1	85.7	32.1	78.3	74.2	23.3	85.7	27.0	83.1
Weaned	26.3 (49/186)	66.2	18.4	83.2	28.1	74.1	60.2	20.4	74.5	22.2	72.4
Belgian Blue	17.5 (50/285)	71.3	34.0	79.2	25.7	85.0	60.4	38.0	65.1	18.7	83.2
Preweaning	23.4 (33/141)	68.1	39.4	76.9	34.2	80.6	60.3	42.4	65.7	27.5	78.9
Weaned	12.1 (14/141)	74.4	23.5	81.5	14.9	88.6	61.0	29.4	65.3	10.5	87.1
Total	19.5 (186/956)	71.4	24.2	82.9	25.5	81.9	67.0	26.9	76.8	21.9	81.3

[1]BRD = bovine respiratory disease; Prev. = prevalence, ultrasound-confirmed pneumonia (≥1 cm consolidation); Acc. = accuracy; Se = sensitivity; Sp = specificity; PPV = positive predictive value; NPV = negative predictive value.

Looking at the various production types, one or more cough parameter was always statistically associated with ultrasound-confirmed pneumonia, likely because cough is a more specific sign of a respiratory tract infection. Also, in both breeds, pre- and postweaning, the cough parameters were the best-performing clinical sign in the detection of ultrasound-confirmed pneumonia. Differences between production types in the association of clinical signs with lung consolidation and in their performance for detecting pneumonia can potentially be explained by differences in breed, housing, prevalence of infectious agents, vaccination, or general health status of the calves. In contrast to dairy calves, in Belgian Blue calves the induced cough reflex at the level of both the larynx and the trachea was not positively associated with lung consolidation, despite the fact that a similar number of calves were positive for induced cough. Although the overall accuracies of both cough reflexes were similar to that of Holstein-Friesians, the sensitivity and specificity were considerably lower (Table 4). Possibly, differences in anatomy (muscularity and a relatively smaller respiratory tract) or response to pathogens (genetics) explain this (Gustin et al., 1987; Grobet et al., 1998). Whether this is also the case for other common beef breeds, such as Angus or Limousin, remains to be determined. Housing conditions differ between production systems. Dairy and beef calf housing systems are fairly similar in the study region (outdoor igloos and indoor pens), but highly different from high-density housing on slatted floors in the veal industry. As regards indoor-housed animals, part of the data set used was previously collected to study barn climate, and higher concentrations of particulate matter (fine dust) were measured in beef than in dairy farms (van Leenen et al., 2021). This may have played a role in prevalence and expression of clinical signs in a given production type. Infectious disease prevalence differs between dairy, beef, and veal calves, with, for example, a much higher prevalence of *M. bovis* in the veal industry (Pardon et al., 2011, 2020). Although not extensively documented, expression of common clinical signs may differ according to the type of respiratory tract infection and whether bacterial superinfection is present or not (Peek et al., 2018). In contrast to dairy and beef calves, veal calves are not vaccinated in the studied region, which may cause more severe clinical signs in this production type (Kolb et al., 2020). Similarly, host resilience may be different between production types, with, for example, veal calves facing many more stressors, failure of passive transfer of immunity, and poorer body condition (Renaud et al., 2018; Masmeijer et al., 2019, 2021). Unexpectedly, we observed that the association of clinical signs and pneumonia differed pre- and postweaning. Clinical signs performed slightly better in preweaning calves compared with postweaning claves. Again, only induced cough remained of statistical significance in postweaning dairy calves, whereas no signs remained associated with pneumonia in beef calves. Possible explanations for this observed age effect in the association between clinical signs and pneumonia may be differences in vaccination status, incompletely developed immunity, pathogens that may more severely affect young animals, and weaned calves that may be able to hide their clinical signs better than preweaning calves. This observation is important, because in dairy calves BRD scoring systems are also used postweaning (Maier et al., 2019) but, based on our study, likely underperform at that age. Most of the lesions in this study occurred in preweaning veal calves. Variation in age could therefore affect the presence of clinical signs. However, to the authors' knowledge, differences in expression of clinical signs in different age groups have not been explored.

The secondary objective of this study was to evaluate the performance of the widely used Wisconsin and California respiratory scorecards (Love et al., 2014; McGuirk and Peek, 2014). Remarkably, both scorecards performed particularly low on the present study population (Tables 2 and 6), especially as regards sensitivity. In contrast to previous findings, the California scorecard performed slightly worse than Wisconsin. Nonetheless, the low performance of both scorecards contradicts previous studies, summarized in a recent review (Buczinski and Pardon, 2020). These studies made use of Bayesian latent class modeling to assess score card performance, which is recommended when no gold standard exists. Despite the fact that TUS is not a gold standard, it systematically had the highest diagnostic accuracy in Bayesian evaluations (Buczinski et al., 2015). Despite the limitations of using a non-gold-standard test as reference test, the low performance of the scorecards on this study population already suggest that these scorecards will also perform weakly in Bayesian latent class models using the present population. Further, evaluations of these scoring systems in populations similar to the ones they were developed on, namely calves housed in North American dairies, already showed only moderate accuracy (Buczinski et al., 2015). Our study showed that in calves in other settings, including different breeds and postweaning calves, performance of these scoring systems is unsatisfactory and therefore should not be recommended to guide antimicrobial therapy. We found important interobserver discrepancies in the assessment of clinical signs, and this may have played a role in our study as well (Buczinski et al., 2016). However, the conclusion remains the same, as other scorecard users will also face this limitation. Our study showed that cough (spontaneous or induced) as a clinical sign of illness actually outperformed the evaluated scoring systems. The positive aspect of this is that this greatly simplifies monitoring requirements, and a recent paper showed that, of all clinical signs, interrater agreement between technicians, producers, and veterinarians active in the veal industry was highest for cough (Berman et al., 2021). The negative side is that the diagnostic accuracy of cough as a single clinical sign remained too low to be of any significant use to detect animals with pneumonia for antimicrobial treatment. However, cough could give farmers and veterinarians an indication that something is affecting the respiratory tract, either pathogens or environmental factors. To differentiate and initiate an appropriate treatment, thoracic ultrasound is recommended. The fact that calves are prey animals and instinctually hide clinical signs makes detection of pneumonia by a point observation very challenging (Weary et al., 2009). Therefore, hope lies in more continuous measurements of clinical parameters to improve detection of pneumonic animals. Cough appears a promising candidate for this, and possibly temperature is a good addition. Cough detectors for continuous measurements are already commercially available for swine, and preliminary work has been done in calves (Vandermeulen et al., 2016). Also, lung auscultation was significantly associated with ultrasonographic lung consolidation in dairy and beef calves, whereas this was not the case in veal calves. The most likely explanation is that a large proportion of the veal calves were auscultated by a single observer. Previous studies showed that inter-rater agreement between observers is very poor, and large differences in diagnostic accuracy occur (Buczinski et al., 2014; Pardon et al., 2019). This is also one of the reasons why implementing lung auscultation in a scoring system would likely not be successful.

A strength of the study is the size and variety of the data set, which is a mixture of medium-sized family-owned farms, representing the dominating dairy and beef farming system in the European Union, and veal calves housed almost identically as in North America. We need to be careful not to generalize the information on Holstein-Friesian dairy and Belgian Blue beef for all dairy and beef breeds. Belgian Blue beef cattle more easily develop severe clinical signs and are more susceptible to bronchopneumonia because of their small lung volume relative to body mass and a higher small-airway resistance. Potentially other breed differences exist (Gustin et al., 1987; Grobet et al., 1998). Therefore, the authors encourage that clinical scoring systems should be tested specifically on the target breed, age, and housing system, rather than extrapolating scoring systems. The present data set included a wide range of clinical presentations, whereby spectrum bias was limited. However, based on ultrasonography, to our knowledge, it is not possible to distinguish between an acute or chronic pneumonia in the absence of an abscess. Expression of clinical signs may be different in chronic infections, but to our knowledge this has not been explored in calves. Further, misclassification bias and observer bias cannot be excluded, as they are inherent to the subjective recording of some clinical signs, such as mental status or nasal and ocular discharge. The same is true for lung ultrasonography. The collection of the study data by multiple observers (6) represents a serious limitation of this study. By using multiple operators, the interobserver effect plays an even more important role. However, we believe this better reflects real-word practices, in which a great number of different people may use clinical scorecards. All observers involved received appropriate training. The poor performance of the clinical BRD scorecards suggests that the systematic use of TUS is inevitable, for now. Thoracic ultrasound, which is much less ambiguous than assessing clinical signs, is seen as a near-gold standard. It can be performed even by novice operators (Buczinski et al., 2013). To minimize bias between observers, regarding TUS, an adequate training was given beforehand. Additionally, farm visits were always conducted with at least 2 veterinarians. Whenever doubt existed, a joint decision was made, to minimize ambiguities. An important limitation is that appetite and movement of animals were not included in this study, due to the fact that this was a cross-sectional study design that tested independently of the time of day. The fact that animals were examined independently of the time of the day and season may have influenced the expression of certain clinical signs. However, little is known about the expression of clinical signs as functions of time of day and season. Nevertheless, it is well known that body temperature has a diurnal pattern and can vary on the same day due to environmental factors (Hill et al., 2016). Finally, lung ultrasonography was used for detection of pneumonia. Despite lung ultrasound being considered a near-gold standard, it is still not a gold standard. Therefore, a follow-up evaluation of the scoring systems and cough as a single sign in a Bayesian latent class model would be interesting.

CONCLUSIONS

The concept of this study was to further reduce the number of required parameters and different categories within a clinical sign in scorecards to the absolute minimum, because this would enhance and facilitate their use on farms. Cough as a clinical sign outperformed existing scoring systems based on multiple parameters, but its accuracy was still too low to be useful for decision making regarding antimicrobial therapy. Of the evaluated clinical signs, cough, rectal temperature, and breathing rate appeared the most promising for further exploration of continuous monitoring ("precision livestock farming") systems for pneumonia detection in calves. Given that the association of clinical signs with ultrasonographic pneumonia differed between production systems, breeds, and pre- and postweaning status, validation of a scoring system in each breed, age category, and housing system is recommended.

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REFERENCES

Andrani, F., M. Aiello, G. Bertorelli, E. Crisafulli, and A. Chetta. 2019. Cough, a vital reflex. Mechanisms, determinants and measurements. Acta Biomed. 89:477–480. https://doi.org/10.23750/abm.v89i4.6182.

Berman, J., D. Francoz, A. Abdallah, S. Dufour, and S. Buczinski. 2021. Evaluation of inter-rater agreement of the clinical signs used to diagnose bovine respiratory disease in individually housed veal calves. J. Dairy Sci. 104:12053–12065. https://doi.org/10.3168/jds.2021-20503.

Bokma, J., R. Boone, P. Deprez, and B. Pardon. 2019. Risk factors for antimicrobial use in veal calves and the association with mortality. J. Dairy Sci. 102:607–618. https://doi.org/10.3168/jds.2018-15211.

Buczinski, S., C. Faure, S. Jolivet, and A. Abdallah. 2016. Evaluation of inter-observer agreement when using a clinical respiratory scoring system in pre-weaned dairy calves. N. Z. Vet. J. 64:243–247. https://doi.org/10.1080/00480169.2016.1153439.

Buczinski, S., G. Fecteau, J. Dubuc, and D. Francoz. 2018. Validation of a clinical scoring system for bovine respiratory disease complex diagnosis in preweaned dairy calves using a Bayesian framework. Prev. Vet. Med. 156:102–112. https://doi.org/10.1016/j.prevetmed.2018.05.004.

Buczinski, S., G. Forté, and A. M. Bélanger. 2013. Short communication: Ultrasonographic assessment of the thorax as a fast technique to assess pulmonary lesions in dairy calves with bovine respiratory disease. J. Dairy Sci. 96:4523–4528. https://doi.org/10.3168/jds.2013-6577.

Buczinski, S., G. Forté, D. Francoz, and A. M. Bélanger. 2014. Comparison of thoracic auscultation, clinical score, and ultrasonography as indicators of bovine respiratory disease in preweaned dairy calves. J. Vet. Intern. Med. 28:234–242. https://doi.org/10.1111/jvim.12251.

Buczinski, S., T. L. Ollivett, and N. Dendukuri. 2015. Bayesian estimation of the accuracy of the calf respiratory scoring chart and ultrasonography for the diagnosis of bovine respiratory disease in pre-weaned dairy calves. Prev. Vet. Med. 119:227–231. https://doi.org/10.1016/j.prevetmed.2015.02.018.

Buczinski, S., and B. Pardon. 2020. Bovine respiratory disease diagnosis: What progress has been made in clinical diagnosis? Vet. Clin. North Am. Food Anim. Pract. 36:399–423. https://doi.org/10.1016/j.cvfa.2020.03.004.

Callan, R. J., and F. B. Garry. 2002. Biosecurity and bovine respiratory disease. Vet. Clin. North Am. Food Anim. Pract. 18:57–77. https://doi.org/10.1016/S0749-0720(02)00004-X.

Carpentier, L., D. Berckmans, A. Youssef, D. Berckmans, T. van Waterschoot, D. Johnston, N. Ferguson, B. Earley, I. Fontana, E. Tullo, M. Guarino, E. Vranken, and T. Norton. 2018. Automatic cough detection for bovine respiratory disease in a calf house. Biosyst. Eng. 173:45–56. https://doi.org/10.1016/j.biosystemseng.2018.06.018.

Catry, B., J. Dewulf, D. Maes, B. Pardon, B. Callens, M. Vanrobaeys, G. Opsomer, A. De Kruif, and F. Haesebrouck. 2016. Effect of antimicrobial consumption and production type on antibacterial resistance in the bovine respiratory and digestive tract. PLoS One 11:e0146488. https://doi.org/10.1371/journal.pone.0146488.

Divers, T.J. 2008. Respiratory diseases. Pages 79–129 in Rebhun's Diseases of Dairy Cattle. 2nd ed. T. J. Divers and S. F. Peek, ed. https://doi.org/10.1016/B978-141603137-6.50007-7.

Dubrovsky, S. A., A. L. Van Eenennaam, S. S. Aly, B. M. Karle, P. V. Rossitto, M. W. Overton, T. W. Lehenbauer, and J. G. Fadel. 2020. Preweaning cost of bovine respiratory disease (BRD) and cost-benefit of implementation of preventative measures in calves on California dairies: The BRD 10K study. J. Dairy Sci. 103:1583–1597. https://doi.org/10.3168/jds.2018-15501.

Eberhart, N. L., J. M. Storer, M. Caldwell, A. M. Saxton, and P. D. Krawczel. 2017. Behavioral and physiologic changes in Holstein steers experimentally infected with Mannheimia haemolytica. Am. J. Vet. Res. 78:1056–1064. https://doi.org/10.2460/ajvr.78.9.1056.

Ferrari, S., R. Piccinini, M. Silva, V. Exadaktylos, D. Berckmans, and M. Guarino. 2010. Cough sound description in relation to respiratory diseases in dairy calves. Prev. Vet. Med. 96:276–280. https://doi.org/10.1016/j.prevetmed.2010.06.013.

Francoz, D., G. Fecteau, A. Desrochers, and M. Fortin. 2004. Otitis media in dairy calves: A retrospective study of 15 cases (1987 to 2002). Can. Vet. J. 45:661–666.

Gille, L., J. Callens, K. Supré, F. Boyen, F. Haesebrouck, L. Van Driessche, K. van Leenen, P. Deprez, and B. Pardon. 2018. Use of a breeding bull and absence of a calving pen as risk factors for the presence of *Mycoplasma bovis* in dairy herds. J. Dairy Sci. 101:8284–8290. https://doi.org/10.3168/jds.2018-14940.

Grissett, G. P., B. J. White, and R. L. Larson. 2015. Structured literature review of responses of cattle to viral and bacterial pathogens causing bovine respiratory disease complex. J. Vet. Intern. Med. 29:770–780. https://doi.org/10.1111/jvim.12597.

Grobet, L., D. Poncelet, L. J. Royo, B. Brouwers, D. Pirottin, C. Michaux, F. Ménissier, M. Zanotti, S. Dunner, and M. Georges. 1998. Molecular definition of an allelic series of mutations disrupting the myostatin function and causing double-muscling in cattle. Mamm. Genome 9:210–213. https://doi.org/10.1007/s003359900727.

Gustin, P., F. Lomba, J. Bakima, P. Lekeux, and K. P. Van de Woestijne. 1987. Partitioning of pulmonary resistance in calves. J. Appl. Physiol. 62:1826–1831. https://doi.org/10.1152/jappl.1987.62.5.1826.

Hill, T. M., H. G. Bateman II, F. X. Suarez-Mena, T. S. Dennis, and R. L. Schlotterbeck. 2016. Short communication: Changes in body temperature of calves up to 2 months of age as affected by time of day, age, and ambient temperature. J. Dairy Sci. 99:8867–8870. https://doi.org/10.3168/jds.2016-10994.

Htun, T. P., Y. Sun, H. L. Chua, and J. Pang. 2019. Clinical features for diagnosis of pneumonia among adults in primary care setting: A systematic and meta-review. Sci. Rep. 9:7600. https://doi.org/10.1038/s41598-019-44145-y.

Jourquin, S., J. Bokma, L. De Cremer, K. van Leenen, N. Vereecke, and B. Pardon. 2022. Randomized field trial comparing efficacy of florfenicol and oxytetracycline in a natural outbreak of calf pneumonia using lung reaeration as a cure criterion. J. Vet. Intern. Med. 36:820–828. https://doi.org/10.1111/jvim.16348.

Kolb, E. A., R. E. Buterbaugh, C. L. Rinehart, D. Ensley, G. A. Perry, K. W. Abdelsalam, and C. C. L. Chase. 2020. Protection against bovine respiratory syncytial virus in calves vaccinated with adjuvanted modified live vaccine administered in the face of maternal antibody. Vaccine 38:298–308. https://doi.org/10.1016/j.vaccine.2019.10.015.

Love, W. J., T. W. Lehenbauer, P. H. Kass, A. L. Van Eenennaam, and S. S. Aly. 2014. Development of a novel clinical scoring system for on-farm diagnosis of bovine respiratory disease in pre-weaned dairy calves. PeerJ 2:e238. https://doi.org/10.7717/peerj.238.

Maier, G. U., J. D. Rowe, T. W. Lehenbauer, B. M. Karle, D. R. Williams, J. D. Champagne, and S. S. Aly. 2019. Development of a clinical scoring system for bovine respiratory disease in weaned dairy calves. J. Dairy Sci. 102:7329–7344. https://doi.org/10.3168/jds.2018-15474.

Masmeijer, C., P. Deprez, K. van Leenen, L. De Cremer, E. Cox, B. Devriendt, and B. Pardon. 2021. Arrival cortisol measurement in veal calves and its association with body weight, protein fractions, animal health and performance. Prev. Vet. Med. 187:105251. https://doi.org/10.1016/j.prevetmed.2020.105251.

Masmeijer, C., B. Devriendt, T. Rogge, K. van Leenen, L. De Cremer, B. Van Ranst, P. Deprez, E. Cox, and B. Pardon. 2019. Randomized field trial on the effects of body weight and short transport on stress and immune variables in 2- to 4-week-old dairy calves. J. Vet. Intern. Med. 33:1514–1529. https://doi.org/10.1111/jvim.15482.

McGuirk, S. M., and S. F. Peek. 2014. Timely diagnosis of dairy calf respiratory disease using a standardized scoring system. Anim. Health Res. Rev. 15:145–147. https://doi.org/10.1017/S1466252314000267.

Murphy, D., A. Ricci, Z. Auce, J. G. Beechinor, H. Bergendahl, R. Breathnach, J. Bureš, J. P. Duarte Da Silva, J. Hederová, P. Hekman, C. Ibrahim, E. Kozhuharov, G. Kulcsár, E. Lander Persson, J. M. Lenhardsson, P. Mačiulskis, I. Malemis, L. Markus-Cizelj, A. Michaelidou-Patsia, M. Nevalainen, P. Pasquali, J. Rouby, J. Schefferlie, W. Schlumbohm, M. Schmit, S. Spiteri, S. Srčič, L. Taban, T. Tiirats, B. Urbain, E. Vestergaard, A. Wachnik-Święcicka, J. Weeks, B. Zemann, A. Allende, D. Bolton, M. Chemaly, P. S. Fernandez Escamez, R. Girones, L. Herman, K. Koutsoumanis, R. Lindqvist, B. Nørrung, L. Robertson, G. Ru, M. Sanaa, M. Simmons, P. Skandamis, E. Snary, N. Speybroeck, B. Ter Kuile, H. Wahlström, K. Baptiste, B. Catry, P. S. Cocconcelli, R. Davies, C. Ducrot, C. Friis, G. Jungersen, S. More, C. Muñoz Madero, P. Sanders, M. Bos, Z. Kunsagi, J. Torren Edo, R. Brozzi, D. Candiani, B. Guerra, E. Liebana, P. Stella, J. Threlfall, and H. Jukes. 2017. EMA and EFSA Joint Scientific Opinion on measures to reduce the need to use antimicrobial agents in animal husbandry in the European Union, and the resulting impacts on food safety (RONAFA). EFSA J. 15. https://doi.org/10.2903/j.efsa.2017.4666.

Nienaber, J. A., and G. L. Hahn. 2007. Livestock production system management responses to thermal challenges. Int. J. Biometeorol. 52:149–157. https://doi.org/10.1007/s00484-007-0103-x.

Nowicki, J., and M.T. Murray. 2020. Bronchitis and pneumonia. Pages 1196–1201 in Textbook of Natural Medicine. 5th ed. J. E. Pizzorno and M. T. Murray, ed. https://doi.org/10.1016/B978-0-323-43044-9.00155-2.

Ollivett, T. L., and S. Buczinski. 2016. On-farm use of ultrasonography for bovine respiratory disease. Vet. Clin. North Am. Food Anim. Pract. 32:19–35. https://doi.org/10.1016/j.cvfa.2015.09.001.

Pardon, B. 2019. A quick scan lung ultrasound method and flow chart as a decision aid for bronchopneumonia diagnosis. Pages 258–260 in XXIV Congreso Internacional ANEMBE de Medicina Bovina, 2019, Sevilla, Spain. Asociación Nacional de Especialistas en Medicina Bovina de España (ANEMBE).

Pardon, B., S. Buczinski, and P. R. Deprez. 2019. Accuracy and interrater reliability of lung auscultation by bovine practitioners when compared with ultrasonographic findings. Vet. Rec. 185:109. https://doi.org/10.1136/vr.105238.

Pardon, B., J. Callens, J. Maris, L. Allais, W. Van Praet, P. Deprez, and S. Ribbens. 2020. Pathogen-specific risk factors in acute outbreaks of respiratory disease in calves. J. Dairy Sci. 103:2556–2566. https://doi.org/10.3168/jds.2019-17486.

Pardon, B., B. Catry, R. Boone, H. Theys, K. De Bleecker, J. Dewulf, and P. Deprez. 2014. Characteristics and challenges of the modern Belgian veal industry. Vlaams Diergeneeskd. Tijdschr. 83:155–163. https://doi.org/10.21825/vdt.v83i4.16641.

Pardon, B., B. Catry, J. Dewulf, D. Persoons, M. Hostens, K. De Bleecker, and P. Deprez. 2012. Prospective study on quantitative and qualitative antimicrobial and anti-inflammatory drug use in white veal calves. J. Antimicrob. Chemother. 67:1027–1038. https://doi.org/10.1093/jac/dkr570.

Pardon, B., K. De Bleecker, J. Dewulf, J. Callens, F. Boyen, B. Catry, and P. Deprez. 2011. Prevalence of respiratory pathogens in diseased, non-vaccinated, routinely medicated veal calves. Vet. Rec. 169:278. https://doi.org/10.1136/vr.d4406.

Peek, S.F., T.L. Ollivett, and T.J. Divers. 2018. Respiratory diseases. Pages 94–167 in Rebhun's Diseases of Dairy Cattle. 3rd ed. S. F. Peek and T. J. Divers, ed. https://doi.org/10.1016/B978-0-323-39055-2.00004-8.

Polverino, M., F. Polverino, M. Fasolino, F. Andò, A. Alfieri, and F. De Blasio. 2012. Anatomy and neuro-pathophysiology of the cough reflex arc. Multidiscip. Respir. Med. 7:5. https://doi.org/10.1186/2049-6958-7-5.

Radaelli, E., M. Luini, G. R. Loria, R. A. J. Nicholas, and E. Scanziani. 2008. Bacteriological, serological, pathological and immunohistochemical studies of *Mycoplasma bovis* respiratory infection in veal calves and adult cattle at slaughter. Res. Vet. Sci. 85:282–290. https://doi.org/10.1016/j.rvsc.2007.11.012.

Renaud, D. L., T. F. Duffield, S. J. LeBlanc, S. Ferguson, D. B. Haley, and D. F. Kelton. 2018. Risk factors associated with mortality at a milk-fed veal calf facility: A prospective cohort study. J. Dairy Sci. 101:2659–2668. https://doi.org/10.3168/jds.2017-13581.

Schaefer, A. L., N. Cook, C. Bench, C. Chabot, J. Colyn, T. Liu, E. Okine, M. Stewart, and J. Webster. 2012. The non-invasive and automated detection of bovine respiratory disease onset in receiver calves using infrared thermography. Res. Vet. Sci. 93:928–935. https://doi.org/10.1016/j.rvsc.2011.09.021.

Smith, B. P., A. A. Gunn, S. M. McGuirk, and M. Izzo. 2015. Manifestations and management of disease in neonatal ruminants. Pages 303–306 in Large Animal Internal Medicine. 5th ed. B. P. Smith, ed. Elsevier.

Timsit, E., S. Assié, R. Quiniou, H. Seegers, and N. Bareille. 2011. Early detection of bovine respiratory disease in young bulls using reticulo-rumen temperature boluses. Vet. J. 190:136–142. https://doi.org/10.1016/j.tvjl.2010.09.012.

van Leenen, K., J. Jouret, P. Demeyer, L. Van Driessche, L. De Cremer, C. Masmeijer, F. Boyen, P. Deprez, and B. Pardon. 2020b. Associations of barn air quality parameters with ultrasonographic lung lesions, airway inflammation and infection in group-housed calves. Prev. Vet. Med. 181:105056. https://doi.org/10.1016/j.prevetmed.2020.105056.

van Leenen, K., J. Jouret, P. Demeyer, P. Vermeir, D. Leenknecht, L. Van Driessche, L. De Cremer, C. Masmeijer, F. Boyen, P. Deprez, E. Cox, B. Devriendt, and B. Pardon. 2021. Particulate matter and airborne endotoxin concentration in calf barns and their association with lung consolidation, inflammation, and infection. J. Dairy Sci. 104:5932–5947. https://doi.org/10.3168/jds.2020-18981.

van Leenen, K., L. Van Driessche, L. De Cremer, C. Masmeijer, F. Boyen, P. Deprez, and B. Pardon. 2020a. Comparison of bronchoalveolar lavage fluid bacteriology and cytology in calves classified based on combined clinical scoring and lung ultrasonography. Prev. Vet. Med. 176:104901. https://doi.org/10.1016/j.prevetmed.2020.104901.

Vandermeulen, J., C. Bahr, D. Johnston, B. Earley, E. Tullo, I. Fontana, M. Guarino, V. Exadaktylos, and D. Berckmans. 2016. Early recognition of bovine respiratory disease in calves using automated continuous monitoring of cough sounds. Comput. Electron. Agric. 129:15–26. https://doi.org/10.1016/j.compag.2016.07.014.

Wang, M., L. G. Schneider, K. J. Hubbard, and D. R. Smith. 2018. Cost of bovine respiratory disease in preweaned calves on US beef cow-calf operations (2011–2015). J. Am. Vet. Med. Assoc. 253:624–631. https://doi.org/10.2460/javma.253.5.624.

Weary, D. M., J. M. Huzzey, and M. A. G. von Keyserlingk. 2009. Board-Invited Review: Using behavior to predict and identify ill health in animals. J. Anim. Sci. 87:770–777. https://doi.org/10.2527/jas.2008-1297.

White, B., D. R. Goehl, and D. Amrine. 2015. Comparison of a remote early disease identification (REDI) system to visual observations to identify cattle with bovine respiratory diseases. Int. J. Appl. Res. Vet. Med. 13:23–30.

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